Sex Differences in Praxic and Linguistic Lateralisation

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A thesis submitted for the degree of

Doctor of Philosophy

Trinity Term 2008

Acknowledgments

This thesis is finally over and I feel grateful for the faith many people have shown in me throughout all the years I have been studying. This manuscript is the result of a few years of training under the guidance of my supervisors, Professor Maryanne Martin and Dr. Marcus R. Munafò. I would like to express my deepest gratitude to both of them for their support, guidance, challenges they posed, and for helping me when I needed help most. I truly enjoyed our collaboration.

I am thankful to the Greek State Scholarship Foundation for supporting my graduate studies, as well as to the A.G. Leventis Foundation for a special grant that was awarded to me to help fund my last study. A great many colleagues and staff at the Department of Experimental Psychology, the scene of the crime, as well as at St. Edmund Hall have also sustained me over the years.

I would also like to extend my thanks to Dr. Christine Mohr for her useful insights and for providing me with the visual half-field test stimuli, as well as to Professor Kenneth Hugdahl for sending his dichotic listening stimuli for me to use. Moreover, I would like to thank Professor Francis Marriot and Dr. Vanja Kovic for their helpful comments on the statistical analysis, and Professor Greg V. Jones for his truly useful input in the interpretation of findings of the meta-analysis. I am also grateful to my transfer viva examiners, Professor Dorothy

Bishop and Dr. Ann Dowker, for their valuable comments and suggestions on my work.

Special thanks to Professor Dorothy Bishop and the OSCCI lab (Helen Flanagan, Noel Orpen, Dr. Mervyn Hardiman) for collaborating with me on my last study and for letting me use their Doppler equipment. The friendly and fun atmosphere in their lab was one of the happiest moments of my DPhil work.

A big thanks to all the participants who offered their heads, hands and... saliva to contribute to this research.

I am blessed to be surrounded by dear friends and family. My parents, Maria and Yiannis, and my brother Dionysis were always there for me throughout all these years and for that I am deeply thankful. The friendship of my best friends and housemates Alexandra, Vassilis, Fanis, Christina, and especially Myrtani, is the most valuable gift I received in this country. Patapia, Maria, Marina, and Alexia were always a phone call away to hear my problems. Last but not least, my partner, Yiannis, is the one who kept me going.

Some parts of this work have been presented at various conferences or submitted for publication. The meta-analysis has been published in the *Psychological Bulletin* (Papadatou-Pastou et al., 2008). In the end, I confirm that any errors of fact or interpretation are entirely my own.

Abstract

Praxic and linguistic lateralisation share a close relationship, whereby laterality for praxis is an indirect index for hemispheric language dominance. Both functional asymmetries have been claimed to be sexually dimorphic. The present thesis investigates the putative sex differences using both meta-analytical and experimental methods, the latter ranging from questionnaire administration to behavioural and neuropsychological testing, all the way to brain imaging. A large-scale meta-analysis showed that males have greater odds of being left-handed than females and that the sex difference in praxic lateralisation is likely to be due to innate biological differences between the two sexes, such as genetic, hormonal, and somatic maturation differences, even though evidence that environmental factors exert moderating influences also emerged. Experimental findings further suggested that sex differences are best captured when assessing skill differences between the right and left hands and further pointed to the fact that left- and right-handers have different reactions to the wording of hand preference questionnaires. Moreover, hormonal influences were investigated and findings suggested that testosterone has independent effects on praxic and linguistic lateralisation in such a way that higher testosterone concentrations are associated with left-handedness and at the same time with greater asymmetry of linguistic lateralisation. It is argued that the sex differences in laterality are determined by multiple environmental and biological factors, some of which have a role in both praxis and language.

Extended Abstract

The present thesis focuses on the sex differences in praxic and linguistic lateralisation, two functional asymmetries known to share an intimate relationship, whereby laterality for praxis is an indirect index for hemispheric language dominance. It aims at quantifying the sex differences in praxic lateralisation, exploring the adequacy of competing explanatory theories on the laterality of both praxis and language, and at further investigating possible mechanisms underlying these differences.

Chapter 1 provides an overview of the theories and studies concerning praxic and linguistic laterality. The definitions, origin, and anatomical substrate of these functional lateralities are presented and the factors proposed to explain the sex differences in praxic and linguistic laterality are described. These include biological factors, namely differences in the genetic make-up (as described by the differential right-shift model, the modifier-gene theory, and the recessive-gene model), in the physical maturation rate, and in the pre-natal hormonal environment of the two sexes (as described by the Geschwind and Galaburda hypothesis, the callosal hypothesis, and the sexual differentiation hypothesis). Other potential sources of sex differences specific to praxic lateralisation described in this chapter include conditions that men are more susceptible to than women and which are associated with an increased incidence of left-handedness, the putative ability of females to be more successful than males in switching writing hand from left to right, and statistical artefacts. A number of

other factors, which had not been studied in relation to sex differences in praxic lateralisation before, are also discussed, namely birth stress, pathological conditions, ancestry, age, intelligence, sporting ability as well as the way in which handedness is measured (assessment method, instrument used, questionnaire length, nature of questionnaire items, response format, handedness classification scheme, report). Lastly, the importance of an investigation on the sex differences in praxic and linguistic lateralisation is also put forth.

Chapter 2 presents a meta-analysis investigating whether sex differences in handedness are reliable and, if so, what the overall magnitude of the differences are, and what the systematic influences upon it are. A total of 144 studies were included in the analysis, comprising 208 separate data sets and totaling 1,787,629 individuals (831,537 male, 956,092 female). The hypothesis that the sex difference is a Type 1 error was rejected, by assessing the presence of ascertainment bias in the field. The most inclusive comparison provided an estimate of 1.23 for the ratio of male-to-female left-to-right handedness odds (95% confidence interval 1.19-1.27) and a significant sex difference was further detected in each of four other meta-analyses carried out on smaller sets of data. There was also a trend towards the direction of the odds ratio increasing as the criterion for left-handedness becomes more lax. Three factors were found to moderate significantly the size of the sex difference odds ratio, namely the way in which handedness had been assessed, the year of publication of the study, and the ancestry of the participants, whereas the educational status of the participants, the number of questionnaire items used, the type of response categories used, whether the main purpose of the study had been to measure handedness, and whether the data were collected by self-report were not found to exert any moderating effects. It was concluded that the sex differences in

praxic lateralisation should be attributed to biological differences between the sexes, even though environmental factors also exert moderating effects.

Chapter 3 presents the experimental investigation of the claim that the sex difference in praxic laterality is artificially produced by the fact that the two sexes have different reactions to the wording of the response formats of hand preference questionnaires. It was also investigated whether an “either” response is translated differently into a binary left-right response according to the handedness and/or the sex of the individual as well as whether the Edinburgh Handedness Inventory (EHI) in its 5-point graded response format differs significantly in producing “either” responses from the EHI in its graphic graded response format. Two hundred healthy student volunteers (50 male right-handers, 50 female right-handers, 50 male left-handers, and 50 female left-handers) participated in the study. Two versions of the same inventory were administered, which included the items from the 12-item version of Annett’s Hand Preference Questionnaire (AHPQ), the 10-item EHI, the 68-item Waterloo Handedness Questionnaire (WHQ), and the 55-item Healy, Liederman and Geschwind Inventory (HLGI). The graphic graded response version of the EHI was also included. The first version of the inventory had a binary response format, whereas the second version used a 5-point graded response format. It was demonstrated that both the translation of an “either” response into a binary response questionnaire and the reluctance to give extreme responses are subject to one’s handedness and not to one’s sex. It was moreover shown that right-handers tend to give a “right” response in the place of an “either” response more often than left-handers give a “left”response in the place of an “either” response. Furthermore, the rank order of participants was found not to be significantly dependent upon which questionnaire was used or upon the response format used.

Chapter 4 presents a study on the moderating effects of the different laterality tests on the magnitude of the sex difference in praxic lateralisation. This investigation was deemed necessary because the meta-analysis was an indirect test and it further did not include studies that used behavioural tests of praxic lateralisation, such as the Peg-Moving, the Dot-Filling, the Tapping Speed or the Quantification of Hand Preference Tests (QHPT), or studies that measured other behavioural asymmetries such as footedness or eyedness, which were here included. The aim of this study was mainly to inform the subsequent studies with regards to which instruments to employ for the experimental study of the sex differences in praxic lateralisation. Two hundred healthy student volunteers (50 male right-handers, 50 female right-handers, 50 male left-handers, and 50 female left-handers) participated in the study; 120 participants were administered all laterality tests whereas 80 participants were administered only the questionnaire-based tests. Hand, foot, and eye preference questionnaires were not found to significantly differentiate amongst them with regards to their sensitivity in capturing the sex difference in handedness. The QHPT, the Peg-Moving and the Tapping Speed tests, however, did prove to be sensitive in capturing sex differences, at least for right-handed participants; right-handed females were found to present a greater difference in skill between their right and left hands (or to prefer the right rather than the left hand for reaching actions) relative to right-handed males. It was concluded that these three behavioural tests are more sensitive tools than hand preference inventories when it comes to the study of sex differences in praxic lateralisation and its correlates.

Chapter 5's study investigates hormonal theories of the sex differences in praxic and linguistic lateralisation. Sixty participants (15 male right-handers, 15 female right-handers, 15 male left-handers, and 15 female left-handers) participated in the study. The three behavioural tests identified in chapter 4

together with the EHI were used to measure praxic lateralisation. Linguistic lateralisation was measured using the consonant-vowel dichotic listening (CV-DL) test as well as the visual half-field lexical decision (VHLD) test. Salivary testosterone (T) and cortisol (C) concentrations were measured using luminescence immunoassay. A linear relationship was detected between the Peg-Moving test score and T concentrations for males and a trend towards a negative linear relationship was demonstrated between the Tapping Speed test and T concentrations, again for males. In both cases, higher T concentrations were associated with the right hand being less skillful than the left hand. No relationships were detected between T concentrations and hand preference, as defined by either the EHI or the QHPT. Moreover, a quadratic relationship between the VHLD test accuracy scores and T concentrations was shown. No relationships were detected for C concentrations, thus hormonal relationships were found to be specific to T. Findings suggest that higher levels of T are associated with a praxic intrahemispheric organisation located at the right hemisphere and with a higher degree of interhemispheric share of linguistic information.

Chapter 6 sets out looking for convergent evidence to chapter 5's findings with regards to the relationship of linguistic lateralisation and hormonal concentrations, using a more reliable technique than neuropsychological testing, namely brain imaging by means of functional transcranial Doppler ultrasound (fTCD). Thirty-six (13 right-handers and 23 left-handers) of the male participants that had taken part in chapter 5's study participated in this study. Further to the fTCD, a number of behavioural tests were administered which represent well-established differences between left- and right-handers, namely the Line Bisection, Drawing "H", Drawing a Head in Profile, Verbal Recall of Coin Head Orientation, and the Ambiguous Figures tests, and in addition three postural lateral preferences were recorded, namely Arm-Folding, Leg-Crossing, and

Finger-Clasping. Their relationship with T levels was also investigated. Adult salivary T and C concentrations were measured directly using luminescence immunoassay and prenatal T concentrations were measured indirectly using the second to fourth digit length ratio (2D:4D). The finding that higher T concentrations are associated with a higher degree of linguistic lateralisation was replicated. The results on the relationship of T with praxic lateralisation were similarly replicated, as participants showing behaviour typical for left-handers (remembering the Queen's head as facing right) had higher T levels. No associations were found between any laterality indices and C or 2D:4D length ratios.

The final chapter gives an overview of the studies comprising this thesis and describes a number of patterns arising from their findings. It moreover discusses the implications of the findings and the limitations of the research work, and it further presents ways in which this work can be carried forward. It is concluded that the sex differences in praxic and linguistic lateralisation are determined by biological factors, with the sex difference in praxic lateralisation being further influenced by a number of environmental factors.

Word count: 68,300 approximately

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Abbreviations

AHPQ	Annett's Hand Preference Questionnaire
AI	Androgen Insensitivity
ANOVA	Analysis of Variance
C	Chance
CAH	Congenital Adrenal Hyperplasia
CBFV	Cerebral Blood Flow Velocity
CC	Corpus Callosum
CI	Confidence Interval
CUREC	Central University Research Ethics Committee
CV-DL	Consonant–Vowel Dichotic Listening
D	Dextral
DES	Diethylstilbestrol
DL	Dichotic Listening
EHI	Edinburgh Handedness Inventory
ELPI	Eyedness from the Lateral Preference Inventory
F	Females
FMRI	Functional Magnetic Resonance Imaging
FTCD	Functional Transcranial Doppler Sonography
HLGI	Healy, Liederman, and Geschwind Inventory
LEA	Left Ear Advantage

LI	Laterality Index
LIA	Luminescence Immunoassay
LRRTM1	Leucine-Rich Repeat Transmembrane Neuronal 1
LSD	Least Significant Difference
LVFA	Left Visual Field Advantage
M	Males
MCA	Middle Cerebral Artery
MRI	Magnetic Resonance Imaging
MR	Magnetic Resonance
OR	Odds Ratio
PET	Positron Emission Tomography
PT	Planum Temporal
QHPT	Quantification of Hand Preference Test
REA	Right-Ear Advantage
R-L	Right- or Left-Handed
R-M-L	Right-, Mixed-, or Left-Handed
R-nonR	Right- or Non-Right-Handed
RPS	Research Participation Scheme
RS	Right Shift
SD	Standard Deviation
SPSS	Statistical Package for the Social Sciences
T	Testosterone
TMS	Transcranial Magnetic Stimulation
VHF	Visual Half-Field
VHLD	Visual Half-Field Lexical Decision
WFQ	Waterloo Footedness Questionnaire
WHQ	Waterloo Handedness Questionnaire
2D:4D	Second to Fourth Digit Length Ratio

Chapter 1

Introduction

Morphological left-right asymmetry appears to be the rule, rather than the exception in nature, all the way from chiral molecules (Quack, 1989) to the Baryon asymmetry in the universe (Sakharov, 1991). Asymmetry is the rule for biological systems as well (Geschwind and Galaburda, 1987; Kimura, 1973), whereby even single-celled organisms are commonly asymmetric (Nelson, 2003). Greater morphological complexity is reflected in greater functional specialisation, and thus in more elaborate asymmetry of function and structure (Good et al., 2001).

Human beings are certainly structurally and functionally asymmetric from the size of their feet, sex organs, and hands to the placement of visceral organs and facial features (Kimura, 1973; Levy and Levy, 1978; Purves et al., 1994), and they exhibit lateralised behaviour as early as 10 weeks postconception (Hepper et al., 1998). In fact, the two aspects of behaviour best known to characterise hominid evolution, one relating to the use of language (Lieberman, 1975, 1984) and the other to the population bias towards right-hand preference for manual praxis (Annett, 1996; McManus, 1991c), are both asymmetric, lateralised traits.

Manual praxic lateralisation and the neurobiological substrate for language are, moreover, intimately linked, with the former being an index for linguistic lateralisation in the brain. Both praxic and linguistic lateralisation have further been claimed to be sexually dimorphic (e.g., Oldfield, 1971; Hiscock, 1993; Voyer, 1996; Knecht, 2000) even though not all evidence points in this direction (e.g., Frost et al., 1999; Salmaso and Longoni, 1985).

The focus of this thesis is to examine and quantify the putative sex difference in praxic lateralisation, to explore the adequacy of competing explanatory theories on the sex difference in laterality of both praxis and language, and to further investigate possible mechanisms underlying such a difference.

1.1 Praxic lateralisation

Praxis is the ability to perform learned skilled movements (Heilman and Rothi, 1993) and it commonly refers to manual praxis (even though the feet can also perform such movements). Manual praxis is typically lateralised, a phenomenon described by the term "handedness".[1] Handedness is the best-known and most studied human asymmetry, and it can be defined as "the individual's preference to use one hand predominately for unimanual tasks and/or the ability to perform these tasks more efficiently with one hand" (Corey et al., 2001b). Left-handedness incidence is a point of dispute among different studies; percentages range from 1.6% (Hoosain, 1990) to 32.2% (Gladue and Bailey, 1995) and are usually reported as "around 10%" (Cavill and Bryden, 2003; Hardyck and Petrinovich, 1977; Holtzen, 1994). An unpublished, large-scale systematic review including 1.8 million participants showed that the incidence of left-handedness lies between 7.52% (using the most stringent

[1] For the purposes of the present thesis, the terms praxic lateralisation and handedness are used interchangeably.

criterion of extreme left-handedness) to 17.42% (using the most lenient criterion of non-right handedness; Papadatou-Pastou et al., 2008).

Handedness is a uniquely human characteristic; humans appear to be almost alone in exhibiting a strong population-level preference for the use of one limb – the right hand – rather than its mirror limb (Corballis, 1991; Martin and Jones, 1999b). While individual members of other species may exhibit preferences for the use of a right or a left limb, there is little or no evidence for a species-wide preference (Annett, 1985). Considering studies in which hand or paw preference has been measured directly there is no evidence for population-level handedness in mice (Collins, 1985), rats (Kirk, 1935; Uguru-Okorie and Arbuthnott, 1981), cats (Burgess and Villablanca, 1986), and probably apes (Annett and Annett, 1991; Byrne and Byrne, 1991), although the latter case is controversial (MacNeilage et al., 1987; Marchant and McGrew, 1991; McGrew and Marchant, 1992). In non-mammalian species, the parrot may be an unusual exception to the above rule (Harris, 1989).

A wealth of evidence is available supporting the notion that handedness is an early developmental characteristic, both phylogenetically (i.e., in the evolution of the human species) and ontogenetically (i.e., in the development of the individual). As far as phylogenesis is concerned, comparative observations suggest that the event that shaped the evolution of human handedness must have taken place after the split between humans and chimpanzees (Corballis, 1991). The oldest published evidence of human handedness is from the Pleistocene (Toth, 1985; Lewin, 1986; deCastro et al., 1988; Bahn, 1989; Lalueza and Frayer, 1997), where incisive marking indicates the existence of right- and left-handed *Homo neanderthalensis* for sharp tool manipulation. In the *Homo sapiens* taxa, the oldest evidence is from the upper Palaeolithic, when right and left tube holders for paint blowing were both present, with a predominance of right tube holders, as indicated by the record of negative hand

painting in caves (Groenen, 1988, 1997). Other artefacts such as bone and antler implements from the Neolithic period, about 7000 years ago, also show evidence of a predominance of right-handedness (Spenneman, 1984). The assessment of manual preference from 12,000 works of art from European, Asian, African, and American sources (Coren and Porac, 1977), and rich evidence from anthropological research (Mason, 1896; Black et al., 1933; Dart, 1949; Magoun, 1966; Brinton, 1986), have further shown that the approximated magnitude of this preference does not seem to have undergone any systematic change over the past 50 centuries.

Ontogenetically, handedness also appears quite early in development. In most human embryos, the right hand is more developed than the left at seven weeks post-conception (O'Rahilly and Muller, 1987). Hepper et al. (1991) observed, using ultrasound, that 92% of the foetuses who sucked their thumbs tended to choose the right thumb. Hepper et al. (1998) also reported that 10-week-old foetuses moved their right arm more often that their left, with 75% of foetuses showing a right arm bias. Goodwin and Michel (1981) studied hand preference among neonates at 19 weeks of age: 64% preferred the right hand in a reaching task. Gesell and Ames (1947) found that the tonic neck reflex observed in newborns strongly predicted handedness at ages 1, 5, and 10 years. Other researchers have observed sidedness in hand use (or other motor behaviours associated with handedness) among neonates and infants (see Liederman and Kinsbourne, 1980; Cioni and Pellegrinetti, 1982; Bates et al., 1986) and have noted significant stability over time (Archer et al., 1988).

Handedness has been shown to be associated with anatomical asymmetries in the cerebral cortex. Kertesz et al. (1986) suggested a larger leftward asymmetry of the planum temporal (PT), a triangular structure on the supratemporal plane in the depth of the sylvian fissure, in right-handers, while Steinmetz et al. (1991) reported decreased leftward asymmetry of the PT in left-

handers (see also Geschwind and Galaburda, 1985a, 1985b, 1985c). Habib et al. (1995) reported that both the PT and parietal operculum showed larger leftward asymmetries in consistently right-handed individuals than in inconsistently right-handed individuals. Foundas et al. (1995) investigated handedness differences in both the anterior speech zone (pars triangularis) and the PT and found that right-handers showed significant leftward asymmetries in both regions while left-handed individuals displayed no significant anatomical asymmetry.

In the primary somatosensory cortex, studies using magnetic source imaging have shown that the cortical representation of the right hand is larger than the representation of the left hand in right-handers and vice versa in left-handers (Sörös et al., 1999). Moreover, the left central sulcus, a large inward fold marking the division between the frontal and parietal lobes, is deeper than the right central sulcus in right-handers (Amunts et al., 1996). Inter-hemispheric comparison has further revealed a significant increase of the hand and finger movement representation in the primary motor cortex opposite to the preferred hand (Volkmann et al., 1998). In contrast to these findings, other reports have shown no obvious correlation of handedness and brain asymmetries. For example, using voxel-based morphometry, Good et al. (2001) did not detect effects of hand use on asymmetrical morphology in sensorimotor regions. Although the different methodologies used in these studies could, in principle, lead to opposite conclusions, the analyses of anatomical asymmetries associated with handedness in the primary sensory and motor cortices are compelling (Sun and Walsh, 2006). The same pattern of asymmetries observed at the neocortical level is also present in the metencephalon, with dextrals showing more asymmetry than nondextrals (Snyder et al., 1995).

An individual's preference for manual praxis could be explained by the fact that specialising one hand for unimanual actions can result to advanced

performance through practice (Bishop, 1990). Moreover, lateralisation of manual praxis may further convey increased neural capacity, because specialising one hemisphere for a particular function leaves the other hemisphere free to perform other, additional, functions (Levy, 1977). This would enable brain evolution to avoid useless duplication of functions in the two hemispheres, saving in neural circuitry. This rationale, however, fails to explain the presence of handedness at the population level. The latter is better explained by genetic models, which typically assume that the genetic variation that underlies variation in handedness is preserved through heterozygote advantage, either cognitive (Annett, 1985; Corballis, 1991; McManus and Bryden, 1992) or through an advantage in aggressive interactions through frequency dependence (Raymond et al., 1996).

Nonetheless, this does not explain right preference, as opposed to a possible left preference. Evolutionary theories claim that right hand preference may have evolved from warriors who were carrying their shields with their left hand, leaving the right hand free for fighting, and who consequently had better survival rates since their hearts were protected (Van Biervleit, 1899). Alternatively, they put forward the tendency of human (and presumably pre-human) mothers to hold infants on the left side (Huheey, 1975). This latter practice is ascribed to imprinting and the soothing sound of the mother's heartbeat on the infant. Given the practice of holding the child in this manner, dextral mothers are more skillful at manipulation of objects and thus selectively favoured. Previc (1991) claims some asymmetries derive from the maternal anatomy, in that the intrauterine environment is laterally asymmetric in many different respects (for a review see Previc, 1991). These asymmetries lead to a leftward bias in foetal positioning (Calkins, 1939), which has been shown to predict later handedness (Churchill et al., 1962). Yet, the most compelling theory to date is the one explaining right-handedness population level preference by brain hemisphere division of labour: since both speaking and handiwork require

fine motor skills, having one hemisphere of the brain (that would be the left hemisphere for reasons described in detail later) do both would be more efficient than having it divided up.

1.2 Linguistic lateralisation

A brain is considered to be asymmetrical or lateralised if one hemisphere or other brain region is structurally different from the other and/or performs a different set of functions (Bisazza et al., 1998). The human brain is typically lateralised with the left hemisphere being the locus of language skills and of analytical processing of stimuli, whereas the right hemisphere is dominant for spatial-constructional skills, for a more global way of processing information, and it is moreover the locus of emotions (McManus and Bryden, 1993). Traditionally, hemispheric asymmetries were considered dichotomous. Today, the generally accepted view is that the two hemispheres show complementary specialisation (Bradshaw and Nettleton, 1983).[2]

This critical insight concerning functional lateralisation, with linguistic functions being generally located in the left hemisphere was first clearly enunciated by Paul Broca in 1863: “Nous parlons avec l’hemisphère gauche” (“We speak with the left hemisphere”; Broca, 1965) (although he had undoubtedly been anticipated by Wigan and Dax – for more detailed historical accounts see Hécaen, 1977, and Harrington, 1987). Broca reached this conclusion when he examined over 25 patients, all of whom suffered from a type of aphasia causing an impairment in language production, and all of whom had suffered lesions to the left side of the brain, in the most anterior part of the frontal

[2] Although Bryden (1986; 1990) has pointed out that a more accurate description is statistical complementarity, with localisation of the two types of function being independent, but appearing to be associated because each is highly biased in its distribution, one principally to the left hemisphere and the other to the right hemisphere.

lobe (Berker et al., 1986), in an area now known as Broca's area. In 1874, Carl Wernicke further discovered that damage to a region of the left hemisphere posterior to Broca's area, now known as Wernicke's area, could cause another type of aphasia that resulted in a language comprehension impairment (Wernicke, 1984).

Linguistic lateralisation patterns are often described as typical (left-hemispheric) or atypical (symmetrical and right-hemispheric), but categorisation schemes of this kind are probably an oversimplification (Szaflarski et al., 2002). Although language-related activation in normal right-handed individuals is predominantly left-hemispheric, almost all individuals activate right hemisphere areas to some extent in functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) language studies (Buckner et al., 1995; Tzourio et al., 1998; Pujol et al., 1999; Springer et al., 1999). Quantitative studies with large subject samples indeed support the existence of a continuum of linguistic lateralisation patterns ranging from strongly left-dominant to strongly right-dominant (Buckner et al., 1995; Tzourio et al., 1998; Pujol et al., 1999; Springer et al., 1999; Frost et al., 1999; Knecht et al., 2000). In other words, language is better described as being "actuated by a distributed cerebral network with differences in regional involvement related to specific language subfunctions, with essential regions within this network lateralised to one hemisphere, typically the left" (Frith et al., 1991).

Left sylvian fissure asymmetry is the best known anatomical asymmetry with regards to linguistic lateralisation (for a review see Jancke and Steinmetz, 1993). Studies mainly focus on the PT, although findings remain inconclusive. A number of studies have shown that individuals with left-hemispheric language representation show a strong leftward asymmetry in the PT, while individuals with right-hemispheric language representation do not exhibit a consistent PT asymmetry (Ratcliff et al., 1980; Moffat et al., 1998). Foundas et al. (1994)

reported that asymmetry of the PT correlated to cerebral dominance as assessed with the Wada test in 11 individuals. Tzourio et al. (1998), however, found no correlation between the same measurements in 14 individuals. In a much larger sample, Jäncke and Steinmetz (1993) replicated the finding of no significant relationship between dichotic listening (DL) scores and PT asymmetry. Similarly, Hellige et al. (1998) were not successful in demonstrating this link. Güntürkün and Hausmann (2003) suggested that it might be not the asymmetry of the PT as such, but the absolute size of the left PT what determines linguistic lateralisation, as a number of studies, which could not reveal meaningful relationships between linguistic lateralisation measures from imaging data and PT-asymmetry, showed stronger relations to absolute left PT-size (for a review see Habib and Robichon, 2003).

The differences in neuronal cell type or cell organisation that may underlie these gross anatomical differences remain unclear. Studies have demonstrated that language-related areas of the left cortex may contain more and larger layer-3 pyramidal cells than corresponding areas in the right hemisphere (Hutsler, 2003). Rosen (1996) and Galaburda et al. (1990) conducted histological studies and suggested that the asymmetrical regions in the cortex might be the result of differences in neuron numbers but not in packing density. However, the tremendous size of the human cortex and its extensive and variable folding pattern make corresponding areas difficult to compare with certainty (Sun and Walsh, 2006).

Patterns of linguistic lateralisation can vary in two, at least, seemingly independent axes referred to as the degree and the direction of hemispheric specialisation (Habib et al., 1995). The degree of lateralisation is discussed in terms of interhemispheric connectivity and communication (e.g., how much information is shared between the two hemispheres during normal processing), while the direction of lateralisation is thought of in terms of intrahemispheric

organisation (e.g., within which hemisphere is the information processed most efficiently, fastest, or most accurately; Zaidel, 1995). Even though it is possible, it is not necessary, that both attributes (direction and degree) are coupled to the same underlying mechanism (Eling, 1981).

While language, like handedness, is a striking human characteristic, the basic aspects of brain lateralisation are common to both birds and mammals (Nottebohm, 1970; Denenberg, 1978, 1981; Bradshaw and Nettleton, 1983; Vallortigara et al., 1999). From a phylogenetic point of view this indicates that lateralisation emerged early in vertebrate evolution (Vallortigara et al., 1999). Language-related functional asymmetry also seems to emerge early in individual development. For example, asymmetry in auditory perception exists at or shortly after birth (see Hahn, 1987). Moreover, the left sylvian fissure asymmetry probably originates during the first trimester of pregnancy (LeMay, 1976).

Similarly to praxic lateralisation, linguistic lateralisation may have come about because the segregation of functions of the separate halves of the brain allows for simultaneous parallel processing (Vallortigara and Rogers, 2005). Thus, it represents a solution to the competition for space within the brain and to the problem of functional incompatibility (Vallortigara et al., 1999). Processing and storing of information about invariance and variance among experiences are mutually incompatible problems, which might best be handled by functionally separate systems (ibid.) Moreover, functional neuronal clustering in one hemisphere during language development allows faster linguistic processing because transition times are shorter than in interhemispheric operations (Lieberman, 1984). Linguistic lateralisation may thus have an adaptive value and it has even been claimed to present a prerequisite for the full realisation of the linguistic potential (Luria, 1973; Geschwind and Galaburda, 1985b; Hiscock, 1998).

An important question is why the left hemisphere is the locus of linguistic function. Timing differences between the hemispheres have been proposed to explain left-hemispheric dominance for language (Belin et al., 1998). More specifically, a pre-linguistic advantage of the left-hemisphere for processing information with a high temporal precision has been described (Efron, 1963; Lackner and Teuber, 1973; Hammond, 1982). The presence of this advantage is supported by psychoacoustic and neuropsychological studies, which have outlined the very rapid acoustic changes of speech and their critical importance for speech perception (Tallal and Piercy, 1973; Schwartz and Tallal, 1980; Merzenich et al., 1996; Tallal et al., 1996; Belin et al., 1998). Another explanation focuses on action coding. In the left hemisphere, actions are coded through auditory, visual, and motor components, whereas in the right hemisphere action coding seems to occur only via the visual and motor channels (Aziz-Zadeh et al., 2004). Therefore, the coding in the left hemisphere encompasses all the contents of an action. This greater number of modalities available selectively to the left hemisphere may have allowed more abstract representation of actions in this hemisphere that make it well suited for facilitating the emergence of language (Hauser et al., 2002). In addition to the above theories, it has been suggested that the right hemisphere matures before the left (Geschwind and Galaburda, 1987), which means that it is less subject to disrupting influences during development. Thus, the right hemisphere is the locus of the processes essential to survival, such as attention and analysis of external space and emotion (ibid.)

1.3 Relationship between praxic and linguistic lateralisation

A strong relationship has been described between cognitive and motor systems: cognitive functions can be expressed by the motor system, and motor activities can influence the cognitive system, via complex feedback circuits within

the brain (Tan, 1988). The best-known example of such a relationship is the relationship between praxic and linguistic lateralisation, with handedness being an indirect index of individual differences in the neurological organisation of language.

Due to all of Broca's patients being right-handed and having their language areas lateralised to the left hemisphere, it was initially speculated that the reverse, that is right-hemisphere language dominance, should be true for left-handers. This claim has been widely accepted as the "Broca rule", although Broca never explicitly postulated such a rule (Harris, 1983). Such explanations would have restored a higher order symmetry of the brain, in which left-handers simply showed the reverse pattern of language dominance to right-handers (McManus and Bryden, 1993). Luria (1976) was amongst the first to point out that such an association could not be universally true because even in left-handers aphasia usually occurs after a lesion in the left hemisphere.

The relationship between praxic and linguistic lateralisation is now known to be much more complex. Knecht et al. (2000) measured lateralisation directly by functional transcranial Doppler ultrasonography (fTCD) in 326 healthy individuals using the Word Generation task and showed that language dominance depends not only on the direction, but also on the degree of handedness. More specifically, they showed that the incidence of right-hemispheric dominance increases linearly with the degree of left-handedness as measured by the Edinburgh Handedness Inventory (EHI; Oldfield, 1971), from 4% in strong right-handers, to 15% in ambidextrous individuals, to 27% in strong left-handers. This relationship can be approximated by the formula:

likelihood of right-hemispheric language dominance (%) = 15% - handedness (%)/10

As far as brain anatomy is concerned, Moffat et al. (1998) used the fused

dichotic words test and showed that left-handed participants with left-hemispheric language function had a larger corpus callosum and a stronger leftward PT asymmetry, than either left-handed participants with right-hemispheric language representation or right-handed participants. Foundas et al. (1994) investigated PT asymmetry in a sample of individuals who had undergone amytal testing for the determination of linguistic lateralisation. All 10 of the right-handed individuals with known left-hemisphere language functions had a leftward asymmetry of the PT, while the one left-handed participant who had exclusive right-hemisphere language dominance, had a rightward PT asymmetry.

The predominance of right-handedness and left-hemispheric linguistic lateralisation has led to the suggestion that a gestural system of communication with dominance of the right hand provided the neural architecture for vocal articulation in human evolution (Hewes, 1973; Kimura, 1984). This communication system may be based on “mirror” neurons, that is premotor neurons that fire when monkeys perform goal-directed actions but also when monkeys observe another monkey making the same actions (Gallese et al., 1996; Rizzolatti and Arbibi, 1998; Arbib, 2001). A mirror system for manual actions may have been important in establishing a means of nonverbal communication and, from this system, neural properties supporting language might have evolved (Hari et al., 1998; Fadiga et al., 2002; Meister et al., 2003). The critical role of Broca’s area in manual imitation (Krams et al., 1998; Iacoboni et al., 1999; Grezes et al., 2003; Heiser et al., 2003; Koski et al., 2003) supports this hypothesis. In fact, Rizzolatti and Arbib (1998) showed that the mirror system in monkeys is the homologue of Broca’s area and argued that this observation provides the missing link for the suggestion that primitive forms of communication based on manual gesture preceded speech in the evolution of language. Furthermore, the recent discovery of auditory mirror neurons that fire

when monkeys make an action, watch the same action, or hear the sound of the action (e.g., breaking a peanut) in the dark, has tied this system to the auditory modality, which is of crucial importance to human language (Kohler et al., 2002; Keysers et al., 2003). Using transcranial magnetic stimulation (TMS) for measuring motor corticospinal excitability of hand muscles in humans while listening to sounds, Aziz-Zadeh et al. (2004) recently showed that sounds associated with manual actions produced greater corticospinal excitability than sounds associated with leg movements or control sounds. More importantly, they demonstrated that this facilitation was exclusively lateralised to the left hemisphere.

McManus (1991), on the other hand, claimed that handedness and language dominance are perhaps a result of a genetic mutation whereby a gene that once influenced the asymmetry of the viscera instead caused the asymmetric development of the brain. Thus, the hypothesis was put forward (Corballis, 1997) that right-handedness, along with the capacity to make and use tools, use language, and show functional and anatomical cerebral specialisation, are characteristics which together are intimately tied together in the divergence of man from the apes, an evolutionary event placed at around two and a half million years ago (Frost, 1980; Varney and Vilensky, 1980; Calvin, 1982).

1.4 Sex[3] differences in praxic and linguistic lateralisation

A relatively consistent finding in the corpus of handedness research is that males are more prone to left-handedness than females (Oldfield, 1971; Bryden, 1977; Annett, 1985; Chapman and Chapman, 1987; Gilbert and

[3] Throughout the present thesis, the term “sex” rather than “gender” is used. Whereas sex represents biological characteristics of males and females, gender represents a much more complex set of social and psychological constructs (Lott and Maluso, 1993), which are beyond the scope of this thesis.

Wysocki, 1992; Perelle and Ehrman, 1994; Reiss and Reiss, 1997). However, not only does the size of this sex difference vary considerably from one study to another, but also a number of studies have failed to replicate this finding (e.g., Salmaso and Longoni, 1985). Moreover, females are known to outperform males in fine motor tasks (for a review see Kimura, 1999). Interestingly, there is some indication that left-handedness can be linked with masculinisation and defeminisation in females, with regards, for example, to sex-typed personality characteristics (Baron-Cohen et al., 2004).

A few studies have investigated the effects of both sex and handedness on the underlying brain anatomy. Witelson and Nowakowski (1991) showed that handedness was associated with callosal size in males, but not in females. Right-handed males had thinner isthmus (an area in the posterior corpus callosum [CC]) than non-right-handed males. This sex by handedness interaction has subsequently been replicated by other researchers (Habib et al., 1991; Clarke and Zaidel, 1994). Denenberg et al. (1991) found opposite handedness effects in males and females in the anterior CC area. However, a study in which magnetic resonance imaging (MRI) was used to examine the CC of 104 children failed to find a convincing sex difference or a significant difference between handedness groups (Kertesz et al., 1987). Amunts et al. (2000) used in vivo Magnetic Resonance (MR) morphometry to analyse interhemispheric asymmetric activation in the depth of the central sulcus in the region of cortical hand representation and found that anatomical asymmetry was associated with handedness for males, but not for females.

Sex differences in cognitive processes have also been reported by numerous of studies (Baron-Cohen et al., 2004). The general picture is that, as a group, men are typically stronger at non-verbal mathematical reasoning and spatial tasks and that, as a group, women are stronger at verbal and social tasks (for a review see Kimura, 1999). With regards to verbal abilities, women tend to

have better verbal memory, spelling ability, and verbal fluency, although their vocabularies are not larger than those of men. Developmentally, however, a number of studies have reported faster rates of language acquisition in girls (Hyde and Linn, 1988; Huttenlocher et al., 1991; Fenson et al., 1994).

The above sex differences in cognition are claimed to stem from sex differences in laterality (Voyer, 1996; Sommer et al., 2004), in the sense that if language is represented in both hemispheres in women, this may account for female superiority in some verbal tasks (Levy, 1976). Levy first suggested that males exhibit a greater degree of neural asymmetry when she noted that language functioning is carried out primarily in the left hemisphere in males, while in females these abilities are more evenly distributed throughout both hemispheres (Levy, 1971; 1973). A more recent view is that sex differences exist for both degree and direction of asymmetry: males tend to exhibit more accentuated asymmetries and stronger right hemisphere dominance compared to females, while females typically exhibit more diffuse lateralisation patterns and greater left hemisphere bias compared to males (Wisniewski, 1998). Nonetheless, experimental evidence on the sex differences in linguistic lateralisation is conflicting and confusing.

A sex difference in cerebral dominance of language has been shown in some studies using DL techniques (Lake and Bryden, 1976; van Duyne and Sass, 1979; Hiscock and Hiscock, 1988; Coney, 2002), but not in all (Witelson, 1976; Carter-Salzman, 1979; Demarest and Demarest, 1981; Hiscock and MacKay, 1985; Hugdahl, 2003). Overall, on the basis of a review of a small number of DL studies, Mc Glove (1980) concluded that females are more symmetric than males.

Hiscock et al. (1994; 1995; 1999; 2001), after screening the entire content of six neuropsychological journals, presented a series of reviews on the sex differences on laterality. With regards to auditory laterality, Hisckock et al.

(1994) found that out of 11 outcomes that met stringent criteria for sex differences in laterality, nine supported the hypothesis of greater hemispheric specialisation in males than in females. The results of the review of visual half-field (VHF) experiments closely resembled results for auditory laterality studies (Hiscock et al., 1995). Out of 20 criteria-satisfying outcomes, 17 supported the hypothesis of greater hemispheric specialisation in males than in females. Hiscock et al. (1995) conclude that the overall pattern of results is compatible with a weak population-level sex difference in hemispheric specialisation that accounts for 1% to 2% of the variance in laterality. A meta-analysis by Voyer (1996) including 396 significance levels from 266 studies using auditory, visual or tactile stimuli suggests that sex differences in laterality are significant in the visual and auditory modalities, but not the tactile modality, with males generally obtaining larger laterality effects than females. However, both the reviews by Hiscock et al. (1994; 1995) and the meta-analysis from Voyer included both verbal and non-verbal stimuli, not focusing solely on linguistic lateralisation (even though the meta-analyses concluded that neither the modality (visual vs. auditory) nor the nature of the stimuli (verbal vs. non-verbal) affected the probability of finding a sex difference in hemispheric asymmetry). Moreover, the included studies used solely neuropsychological testing for assessing brain laterality.

Shaywitz et al. (1995) used brain imaging by means of fMRI in order to assess brain laterality in 19 males and 19 females. He found that activation related to a rhythmic task was more bilateral in females than in males, which supports the idea that females are less lateralised for language than males. However, these researchers did not find sex differences in other language tasks. Vikinstad et al. (2000) also used fMRI to demonstrate that for males, activation during language was primarily lateralised to the left, whereas for females, approximately half of the sample had left-hemispheric activation and the other

half had bilateral activation. Rossell et al. (2002) used an fMRI paradigm similar to a lexical decision task and they also found that females show a more symmetrical pattern in language-related areas. On the other hand, Frost et al. (1999), again using fMRI, found no difference between the sexes during a language comprehension task when group averages were compared. Knecht et al. (2000), using fTCD provided further evidence that linguistic lateralisation during Word Generation in males and females is equivalent in variability. Knecht et al. (ibid.), nevertheless, added that equivalence of hemispheric lateralisation between sexes during word generation does not exclude sex differences in subfunctions of language like rhyming, as found by Shaywitz (1995).

Sommer et al. (2001) performed a meta-analysis of functional imaging techniques (PET, fMRI, and fTCD) and concluded that the difference in linguistic lateralisation between men and women was not significant. They argue that this negative finding – if not true of the absence of sex differences in functional lateralisation of language – may be due to three reasons: (a) that the sex difference at the population level is relatively small so that it is only sporadically observed, (b) that the sex difference is task-dependent, or that (c) language activation during brain imaging may also be detected at sites that are not critical for that language function, but may be activated for non-specific supporting functions (Binder et al., 1997).

In addition to experimental studies on typical adults, the greater male than female proportion of aphasics after left hemisphere damage (McGlone, 1977; Kimura, 1980) has been claimed to support the notion that it is increased bilaterality of language in women that leads to this decreased susceptibility to unilateral lesions (McGlone, 1980). Kimura and Harshman (1984), on the other hand, proposed that a crucial factor underlying the sex difference is not increased symmetry in females, but a differential organisation of language functions within the left hemisphere. According to Kimura (1983), in females,

language appears to be critically dependent on the left anterior cerebral region, with left posterior damage rarely producing aphasia; in contrast, aphasia in males is produced equally often from anterior or posterior damage. Kertesz and Sheppard (1981), however, showed that aphasias are as frequent in males as in females, as long as sex differences in the incidence of infarcts are taken into account. Similar results were obtained in a more recent epidemiological study (Pedersen et al., 1995).

Further to the evidence regarding functional laterality, there is wealth of findings on anatomical asymmetries in language-related brain areas between males and females, such as the PT and the CC. Studies that measure the anatomical size of the PT are inconsistent with regards to a sex difference in asymmetry. Several studies reported that asymmetry of the PT was larger in males (Wada et al., 1975; Kulynych et al., 1994; Foundas et al., 2002), which probably results from a larger left PT in males compared to females (Kulynych et al., 1994; Foundas et al., 2002). A large voxel-based analysis on MRI scans of 465 healthy adults reported increased asymmetry of the PT in males compared to females, which was caused by a smaller left plain in females (Good et al., 2001). Knaus (2004) reports contrary findings, also by means of MRI, with females exhibiting leftward asymmetry of the PT and with males not exhibiting PT asymmetry. On the other hand, a number of studies have failed to observe a sex difference in the asymmetry of the PT (Kertesz et al., 1986; Duara et al., 1991; DeLisi et al., 1994; Jancke, 1994). Interestingly, two recent studies have reported that rather than being more symmetrical in females, the PT may be proportionately larger (Harasty et al., 1997) and more densely packed with neurons (Witelson et al., 1995) in females, than in males, suggesting that the PT may be a sexually differentiated cortical region in humans.

Differences in the width and shape of the CC have also been proposed to underlie cognitive sex differences. Possibly, the two hemispheres of the female

brain are better connected than those of the male brain, which may give a higher speed of information transfer between the hemispheres, and could explain the female advantages in some language tasks (Witelson, 1989). DeLacoste-Utamsing and Holloway (1982) first reported that the posterior part of the CC was larger and more bulbous in women, in a post-mortem study of nine males and five females. This was confirmed by Holloway et al. (1993). In addition, other commissures of the brain have also been reported to be wider in females than in males, for example the cross-sectional area of the anterior commissure (Allen and Gorski, 1992). Furthermore, the massa intermedia, which connects the two halves of the thalamus, has been found to be more frequently absent in males than in females (ibid). In a review, Driesen and Raz (1995) concluded that the absolute CC area and the area of the splenium is somewhat greater in males than in females. By contrast, when examining only those studies that controlled for overall brain size, the direction of the sex difference was reversed; total CC area adjusted for brain size was greater in females.

Another candidate cerebral substrate for the sex differences in cognition has been described by Witelson (1995), who studied cytoarchitecture in post-mortem brains. In a small sample she observed that the density of neurons in layers II and IV of the posterior temporal cortex was greater by 11% in females, with no overlap of scores between the sexes.

1.5 Potential sources of sex differences in praxic and linguistic lateralisation

1.5.1 Genetic theories

A number of factors have been proposed that may be responsible for the sex differences in praxic and linguistic lateralisation. Genetic theories are particularly interesting. Annett's right shift (RS) theory (Annett, 1972) postulates a gene for left cerebral dominance that increases the probability of right-

handedness (handedness here defined as hand skill rather than hand preference). The RS gene is a systematic influence on human asymmetry that works by impairing the growth of the right hemisphere in early life and incidentally weakening the left hand and channeling language functions to the left side. A sex difference in handedness is not integral to the theory, but can be attributed to the displacement of the chance distribution of asymmetry farther to the right in females than in males by about 20% (Annett, 1999). This might be because the RS gene is more penetrant in females than in males (Annett, 1973, 1985), or because females are slightly more mature at birth than males; as the expression of the RS gene is considered to be a function of growth *in utero*, this difference in maturation accounts for the fact that females are slightly more often right-handed than males (Annett, 1996; Annett, 1998).

McManus (1984) has proposed a similar model consisting of two alleles for handedness: D (for Dextral) and C (for Chance) at a single locus. Homozygotes for the D allele (DD genotype) are all right-handed, whereas homozygotes for the C allele (CC genotype) show chance levels of left-handedness. The heterozygous phenotype (DC) exhibits handedness incidences that are midway between the two homozygotes. This theory did not originally account for a sex difference, so it was extended by McManus and Bryden (1992), who proposed that a second relevant gene, a sex-linked recessive modifier gene on the X chromosome, can suppress the dextrality gene. As males only have one copy of the X chromosome, they are more likely to express the suppressor gene and show an increased rate of phenotypic left-handedness.

Alternatively, Jones and Martin (2000), following Corballis (1997), proposed a single-gene recessive model and showed that a lower level of left-handedness in females than in males could reflect a lower phenotypic penetrance of the CC genotype. Their proposal is supported by striking maternal and grandparent effects (Jones and Martin, 2001; 2003). The maternal effect

refers to the finding of McKeever (2000) that the probability of a son being left-handed is influenced by the handedness of his mother but not by that of his father. The grandparent effect refers to the finding of Klar (1996), where the grandchild of a right-handed parent who is the child of two left-handed grandparents is as likely to be left-handed as is the child of a left-handed parent.

In terms of physical chromosomal mapping, Laval et al. (1998) have argued for an X-linked recessive influence on handedness. ProtocadherinXY, a gene located in the Xq21.3/Yp region of homology between the X and the Y chromosomes, is another candidate gene for asymmetry (Crow, 2002). Sequence differences between the X and Y copies of ProtocadherinXY could account for the gender differences in lateralisation. More conclusive support for a genetic role in handedness is provided by the recent discovery (Francks et al., 2007) that the Leucine-rich repeat transmembrane neuronal 1 (LRRTM1) gene chromosome 2p12, which is a maternally suppressed gene, is associated paternally with handedness in a set of dyslexic siblings.

A number of other genetic theories of praxic and linguistic lateralisation have also been formulated, but they have not accounted for the sex difference in lateralisation, thus they are mentioned here only in brief. For example, Levy and Nagylaki (1972) proposed that the different asymmetry patterns depend on at least two genetic loci, whereby one locus determines which cerebral hemisphere is dominant, whereas the other specifies whether hemispheric control of the hands is contralateral or ipsilateral. Yeo and Gangestad (1993; Gangestaad and Yeo, 1995), on the other hand, argued that it is polygenic homozygosity that leads to a deviation from the species-typical pattern of moderate right-handedness in either direction. Laland et al. (1995) proposed a gene-culture model, which maintains that natural selection, favouring either right-handedness or the genetic variation that originally underlay it, has distorted the probability of individuals becoming right-handed from chance levels to a probability estimated

to be approximately .78. In other words, left- and right-handers do not have different genotypes but, rather, the same genotype, which increases the probability that individuals will become right-handed to above-chance levels. Even though Laland et al. did give an explanation of the sex differences in handedness, they did so only by using a mechanism of cultural transmission whereby (a) mothers spend more time with their children than fathers and (b) females are subjected to greater pressures to change their handedness from left to right.

1.5.2 Physical maturation theories

Differences in the physical maturation rate between the two sexes is another potential source of sex differences in praxic and linguistic lateralisation. A delayed rate of maturation has been found to be associated with an increased incidence of left-handedness regardless of sex (Coren et al., 1986; Coren, 1989; Pollard, 1995; Mulligan et al., 2001; Van Strien et al., 2005, but also see Eaton et al., 1996, who failed to find such an association). Moreover, there is evidence that males develop hand preference, or at least right hand preference, later than females (Buffery and Gray, 1972; Annett, 1974; Carlson and Harris, 1985; Archer et al., 1988; Humphrey and Humphrey, 1987).

Waber (1977) further found that, regardless of sex, individuals who mature somatically faster than average (according to Tanner's staging criteria for secondary sexual development; Marshall and Tanner, 1969, 1970) perform better on tests of verbal ability than on tests of spatial ability, whereas the performance of those individuals who mature more slowly than average shows the opposite pattern. Moreover, Kaufman et al. (1978) reported that individuals demonstrating an early right-hand preference show advanced development of language and cognitive abilities. Other studies have observed developmental differences favouring females over males for tasks known to be mediated by the

left hemisphere. For example, girls outperform boys in early vocabulary growth (Fenson et al., 1994; Morisset et al., 1995). Boys have been reported to follow the same sequence in language production as girls but at a later age (Huttenlocher et al., 1991).

As males mature later than females (Frisch, 1974), the sexual component of praxic and linguistic lateralisation could thus be influenced by physical maturation rate (Maehara et al., 1988), or it could perhaps be a specific result of the later functional maturation of the left hemisphere (Shucard et al., 1981). Variation in maturational rate probably reflects endocrinological differences (Waber, 1977). For example, a longitudinal study by Haslsler (1991) reported that early maturing boys had significantly higher salivary testosterone (T) concentrations than late maturing boys. Such differences are explored in the following section.

1.5.3 Hormonal theories

The sex differences in both praxic and linguistic lateralisation have been further hypothesised to be controlled, at least in part, by gonadal hormones or sex steroids, which are essential for the sexual differentiation of the foetus (Baron-Cohen et al., 2004). Gonadal hormones include androgens (e.g., T, dihydrotestosterone), estrogens (e.g., estradiol, estrone, estriol), and progestins (e.g., progesterone), but most theories focus on the effects of prenatal T.

Hormones may affect behaviour directly through changes to brain regions directly involved in behaviour. Gonadal hormones have been found to affect neuronal size, survival, and outgrowth, synapse number and organisation, dendritic branching patterns, gross volume, cortical thickness, and neurotransmitter systems (Berenbaum, 1998). A pathway through which this might occur is the aromatisation of T to estradiol. From animal studies, it is known that this process has a critical role in the masculinisation and

defeminisation of specific brain structures as it enables T to bind to estrogen as well as to T receptors. This process has a smaller effect in females since they are protected from the masculinising effects of estrogen via a protein called alpha-fetoprotein, which binds to freely circulating estrogen and prevents it from crossing the blood-brain-barrier and consequently from entering the neuron (for a review see Fitch and Deneberg, 1998).

The most influential theories on hormonal effects in lateralisation are Gechwind and Galaburda's, the callosal hypothesis, and the sexual differentiation theories. According to the theory of Geschwind and Galaburda (Galaburda et al., 1987; Geschwind and Galaburda, 1987), T has differential effects in the development of the cerebral hemispheres, acting during a critical period of brain development so as to increase the probability of atypical dominance by slowing down left hemisphere development, especially the temporal language region, and thus acting as a source of left-handedness and atypical language dominance (but see also Bryden et al., 1994, for a critique of this theory). Geschwind acknowledged that other prenatal and postnatal factors (e.g., length of gestation or timing of puberty) could have a role in cerebral lateralisation, but Geschwind's emphasis was on the intra-uterine environment. Males are necessarily exposed to more prenatal T than females because this hormone is produced by their own developing testes. Serum measurements of T from week 12 to week 18 show that male foetuses have an average of 249 ng/100 ml (±93) and female foetuses an average 29 ng/100 ml (±19; Abramovich and Rowe, 1973). Therefore, increased left-handedness and atypical language lateralisation in men is to be expected. Critical to the hypothesis is the fact that females are also exposed to small amounts of T, as the mother provides small quantities of masculinising hormones via her adrenals and ovaries. If not, the hypothesis could not account for the variability of asymmetry between females.

Geschwind pointed out that the effects of T depend on the availability of free unbound hormone and on the sensitivity of target tissues.

The callosal hypothesis, as laid out by Witelson and Nowakowski (1991), states that cerebral lateralisation results from the pruning of callosal cells during foetal and neonatal development, and that this process is mediated, at least in part, by T. Manipulation of early levels of sex hormones has indeed been found to affect naturally occurring cell death (Arnold and Breedlove, 1985). This means that increased foetal T activity will result in a smaller corpus callosum, decreased connectivity between the hemispheres (especially in the temporo-parietal region) and greater lateralisation of cognitive functions (Witelson, 1991). According to this hypothesis, it is therefore lower levels of prenatal T that are associated with increased left-handedness and atypical dominance. This effect has not been observed in females (Witelson, 1985; 1991). Only in males is callosal size, and particularly the isthmal area, related to hand preference. Similarly, only in males does posterior Sylvian fissure morphology vary with hand preference. Such sex differences suggest that some sex-related factor may influence the regressive mechanisms hypothesised to play a role in determining brain structure related to lateralisation. In this context, prenatal or perinatal levels of T in males may regulate callosal axon elimination and development of associated structures related to functional asymmetry. In Witelson's (1991) words, "in men, lower levels of T lead to less axon elimination, a larger callosal isthmus and associated temporo-parietal structures, greater left-handedness (less consistent-right-hand preference), and greater bihemispheric representation of cognitive skills (less functional asymmetry), and […] these same factors are not similarly operative in the development of the female brain."

Finally, the sexual differentiation hypothesis (Hines, 1984) is based on data showing neural and behavioural masculinisation when exposing animals prenatally to androgens (Goy and McEwen, 1980). The higher rates of left-

handedness in males and some evidence that females are less lateralised for cognitive function than males, have led to the suggestion that higher levels of prenatal T are related to left-handedness and greater cerebral language dominance, following conversion to estradiol.

The only study to date that has directly measured prenatal T concentrations (Grimshaw, 1995) found that girls who had higher amniotic fluid T levels tended, at age 10, to be more strongly lateralised for language and to be more strongly right-handed. Among boys, it was found that higher prenatal T levels were associated with greater left-ear/right-hemisphere processing. The mere lack of experimental studies using prenatal T levels as well as the fact that sampling amniotic fluid may not reflect hormone exposure during early critical periods of development, as it may simply reflect maternal levels (Reinisch, 1984), has led to the collection of evidence for hormonal influences by several other lines of research: (1) nonhuman animal studies, (2) studies of normal human adult populations, (3) twin studies, (4) studies in clinical samples or individuals exposed to abnormal concentrations of sex steroid hormones prenatally, (5) experimental populations receiving exogenous hormone treatment, and (6) studies of spontaneously menstruating women. A brief summary of the research corpus will be described below, as an exhaustive review is beyond the scope of this thesis.

Regarding nonhuman animal research, studies in a variety of nonhuman mammalian species, including rodents and primates, have demonstrated that gonadal hormones play a major role in the development of sex differences in behaviour and in brain functions (for reviews see Goy and McEwen, 1980; MacLusky and Naftolin, 1981; Arnold and Gorski, 1984; Beatty, 1992; Becker et al., 1992; Breedlove, 1994). In studies exclusively using rats, a sexual dimorphism has been observed with the male rat having a thicker cortex on the right hemisphere, and the female rat showing the opposite pattern. However, if

the female rat is ovariectomised at birth and the testes of the male rat are removed, the typical cerebral patterns in each sex can be altered (Goy and McEwen, 1980; Geschwind and Galaburda, 1987; Diamond, 1991). With respect to the corpus callosum it is the male rat that has a larger one (Fitch et al., 1991). Neonatal T injections have been found to masculinise the corpus callosum of the female rat, while neonatal castration does not appear to affect the size of the corpus callosum of the male rat (Nunez and Juraska, 1998), with prenatal T levels appearing to be the critical factor in the male (Mack et al., 1996). The size of the spenium is increased in females from litters with a high male-to-female ratio (Nunez and Juraska, 1998), suggesting that exposure to higher levels of T actively feminise the corpus callosum in the female rat, and that masculinisation and feminisation of the corpus callosum are two distinct processes, with different sensitive periods (Fitch et al., 1991).

Research investigating relationships between T levels and behavioural and brain lateralisation in healthy human volunteers has provided interesting, yet inconclusive, findings. The rationale of this approach is that individual differences in early life hormone concentrations are preserved over relatively long time periods, thus T differences obtained in adulthood are at least moderately representative of individual differences in early life T secretion (Jamison, 1993). Meikle (1988), for example, reported a high concordance in the production rate of T in adult monozygotic twins and suggested that there is a significant genetic component to individual differences in T secretion. They estimated that genetic factors account for over 80% of the variance in the production rate of T. Indeed, at least some of the same inherited physiological constrains may operate during early development, given that T concentration in foetal testes approach adult per-unit values (George, 1987). Although this approach allows only for limited inferences to be drawn regarding the prenatal hormonal environment, it is advantageous in that it allows for the direct

measurement of T levels, the selection of considerably larger sample sizes, and for the specific recruitment of individuals whose asymmetry patterns are atypical.

Regarding praxic lateralisation, Tan (1990c) has reported that serum T concentrations correlate with right hand skill, as measured using a modified version of the Annett Peg-Moving test: right-handed males showed a positive correlation between serum T concentrations and right hand skill, while right-handed females showed a negative correlation. In another study, Tan (1990b) found that right hand superiority on the Dot-Filling test increased with increasing serum T concentrations in males, but was unaffected by T in females. Next, Tan (1991b) showed that high T concentrations in right-handed females were associated with poorer Peg-Moving performance, generally replicating his 1990a study. Subsequently, Tan (1991c) found the opposite pattern in males, for whom high T levels were associated with better Peg-Moving performance. These findings generally show that increased serum T is associated with increased right hand performance in males, but not in females. However, Tan (1991a) also reported that T concentrations are significantly higher in females with atypical dominance than those with standard dominance, with the atypical dominance group including left-handers, weak right-handers and right-handers with a history of familial sinistrality.

On the contrary, Moffat and Hampson (1996) found significantly higher mean T concentrations for right-handers of both sexes, compared to left-handers, although this was not replicated in the Moffat and Hampson (2000) study, in which no difference between groups emerged. McKeever (1987) did not find significant handedness-related differences in serum T; although left-handers of both sexes did show lower mean T concentrations than right-handers, the effects were not statistically significant. Left-handed women showed significantly lower mean salivary T than right-handed women (Gadea, 2003). With regards to the degree of hand preference, Tan (1991a) found, in right-handed females, a

positive correlation with T in moderately right-handers and a negative correlation with T in strongly right-handers, whereas Gadea (2003) reported that right-handers who were strongly lateralised and left-handers who were weakly lateralised had similar T levels (Gadea, 2003).

As far as linguistic laterality is concerned, Moffat and Hampson (1996, 2000) studied the relationship between direction of hand preference, direction of ear advantage on DL and T concentrations. The data showed that left-handed individuals with a left ear advantage had higher T concentrations than left-handed individuals with a right ear advantage. A tendency for the opposite pattern in right-handed individuals was also observed. This led the authors to propose an association between higher T concentrations and lateralisation of praxic and linguistic functions in the same hemisphere. Higher T concentrations were also associated with a lesser degree of linguistic lateralisation, independent of the subject's hand performance in a study by Gadea (2003). With regards to brain anatomy one study of 68 young adult right-handed males found a positive correlation between salivary T concentrations and the cross-sectional area of the posterior body of the corpus callosum (Moffat et al., 1997).

Research on twins also provides an opportunity to investigate the possible prenatal effects of T on brain and behaviour. In animal research, it has been shown that exposure to T or its metabolites is influenced by the ultrauterine position of the foetus. Thus, female foetuses located between two male foetuses are exposed to higher levels of T than foetuses situated between two female or one female and one male foetus (Vom Sall, 1989; Gandelma, 1992). Elkadi (1999) tested whether there would be an altered incidence of sinistrality in twins sharing the womb with a male foetus, by comparing the hand preference of opposite and same-sex twins. No sex difference in hand preference was observed. Cohen-Bendahan et al. (2004) studied 55 same-sex and 67 opposite-sex twin girls, all right-handed, under the rationale that foetuses located between

opposite-sex twin girls would be exposed to higher levels of prenatal T. They moreover measured circulating T concentrations using saliva samples. Opposite-sex girls were found to have a more lateralised pattern of cerebral lateralisation as assessed by the DL test but no correlation between circulating T concentrations and functional cerebral laterality scores was found. It was, therefore, argued that the difference in laterality could be due to differential prenatal exposure to T.

Another means of studying the effects of hormones is by studying individuals with disorders of sexual differentiation, which are characterised by an abnormal prenatal hormonal environment, such as congenital adrenal hyperplasia (CAH), whereby a genetic defect results in the production of high levels of androgens beginning in the third month of gestation. A number of studies have found, among other findings pointing to the direction of a more masculine pattern of lateralisation (e.g., Dittman, 1990), that females with CAH have an increased incidence of left-handedness (Nass, 1987), increased levels of language disabilities (Plante, 1996) as well as an increased rate of atypical brain asymmetry, as measured by MRI (ibid.). Other studies, however, have failed to support the finding that females with CAH differ from controls on hand preference or DL asymmetry (Helleday, 1994). Another disorder of sexual differentiation is androgen insensitivity (AI), which occurs when there is a partial or complete deficit of androgen receptors. An increased level of left-handedness has been found in children with AI in support of the idea that prenatal T exerts some effects in these individuals by first being converted to estradiol, for which receptors are believed to be intact in AI (Hampson, 1994). Similarly, Kleinfelter syndrome males, who have a postnatal and perhaps prenatal deficiency of androgen, show a high incidence of left-handedness (Netley and Rovet, 1982).

The hormonal condition of the foetus can be further disrupted by external factors, such as ingestion of synthetic hormones, like diethylstilbestrol (DES), by

the mother. In a study of Hines and Shipley (1984) on 13 sibling pairs (females who had been exposed to DES in utero and their unaffected sisters) a more masculine pattern of results on a DL test was found in DES children than in the controls (i.e., the left-ear and right-ear performances of the DES children were negatively correlated and their right-ear scores exceeded their left-ear scores), but no difference between the two groups was found in the degree of cerebral lateralisation. In another study, involving 10 DES exposed males and their unaffected brothers, DES exposure was found to be associated with a feminine pattern of reduced hemispheric laterality (Reinisch, 1992).

However, the findings from clinical samples should be treated with caution when generalising to the non-clinical population. First of all, these studies are necessarily carried out with small samples. Moreover, it is impossible to differentiate between the effects of the hormonal environment and those of any gene abnormalities associated with the disorder. Also, because the hormone levels involved are abnormal, they might lead to abnormal patterns of development, which do not relate well to normal development. For example, it is known that a large proportion of CAH patients suffers from salt-wasting which may lead to episodes of hypotension or hypoanemia, conditions which can permanently affect the functioning of the brain (Nass and Baker, 1991). Finally, the above studies are not truly experimental, in that children could obviously not be randomly assigned to the treatment groups (Hines, 1984).

Hormonal effects on behaviour are not confined to early development, but may continue to affect behaviour through changes in the brain at later periods (Arnold and Breedlove, 1985). Therefore, hormones can have both organisational and activational effects in the brain. Organisational effects are those that influence the neural development that underlies behaviour, are permanent and happen early in development, usually during a sensitive period. Such organisational effects include an increase in the size of androgen-sensitive

brain regions (e.g., Diamond, 1991), or an inhibition on brain development (Stewart and Kolb, 1988). Activational effects are those that influence pre-existing neural circuits non-permanently, happen later in development and are superimposed on the early organisational effects (Phoenix et al., 1959; Goy and McEwen, 1980; Arnold and Breedlove, 1985).[4] Such effects are thought to involve temporary fluctuations in neurotransmitter level of synthesis (McEwen, 1981; Arnold and Breedlove, 1985), ultrasound changes in neurons (Gould et al., 1990), temporary changes in receptor numbers (MacLusky and McEwen, 1978) or direct effects of steroids on the cell membrane which alter neurotransmissions (McEwen, 1991). Studies in a variety of species have revealed the behavioural importance of these activational effects for nonsexual behaviour (for reviews see Becker, 1992; Kimura and Hampson, 1994). Interestingly though, the theories presented here (i.e., Geschwind and Galaburda's, the corpus callosum, and the sexual differentiation theories), do not make any mention of activational effects of hormones.

Activational hormonal effects can be studied in experimental populations receiving exogenous hormone treatment. For example, in a study by Janowsky et al. (1994) older men were supplemented with T for a 3-month period. Fine motor dexterity and speed as assessed by the grooved Pegboard test did not change after T enhancement.

The main corpus of studies on activational effects of hormones focuses on the female menstrual-cycle-dependent hormonal fluctuations. A number of authors have reported a differential modulation of processing of the two hemispheres during the menstrual cycle (Altemus, 1989; Bibawi, 1995;

[4] According to Janowsky (1998), "activation" may not be the best description for the neuromodulatory roles of sex hormones on neural activity, as it implies the initiation of a previously absent behaviour, and he proposed that the term "modulation" may be better to describe the moment-to-moment, or day-to-day, effects of hormones on the brain and behaviour.

Hampson, 1990; Chiarello, 1989; Heister, 1989; Mead, 1996; Bibawi, 1995) as a function of gonadal hormone levels. Yet, different studies paint a remarkably controversial picture as to when in the menstrual cycle asymmetry is greater: some studies claim it is greater at menses (e.g., Rode et al., 1995; Hausmann and Güntürkün, 2000), whereas others report greater asymmetry in the mid-luteal phase (e.g., Hampson, 1990; for a review see Sanders, 1998).

One possible explanation for these inconsistencies could be that rather than assessing the serum concentrations of steroid hormones directly, investigators in most studies have estimated the position in the cycle by counting days backwards from the predicted start date of the next menstruation. This improper validation of cycle phase inevitably increases the data pool with women tested outside the optimal time window. The few studies (Hausmann, 2000; Mead, 1996; Rode, 1995) that have included hormonal assays from blood samples of participating women had to exclude about 23-27% of the sample because these women were not in the expected cycle phases, whereas in a study by Gordon et al. (1986) half of the female participants had to be excluded when post-hoc hormone assays revealed these participants not to have been in their expected cycle phase.

A second explanation is that hormonal effects may be task-dependent and could depend on different properties such as task difficulty, modality, or degree and direction of hemispheric specialisation (Holländer, 2005). In particular, tasks associated with greater asymmetry during the mid-luteal phase have been found to be those involving processes for which the left hemisphere is superior (Bibawi, 1995; Hampson, 1990; Sanders, 1998). Sanders (1998), on the other hand, found that a right ear advantage for a verbal task was greater during the mid-luteal phase, whereas a left ear advantage for a music task was greater during menses.

Contrary to these findings, Hausmann and Güntürkün (2000) observed greater cerebral asymmetry during menses and a more symmetrical functional organisation during the mid-luteal phase, for left-hemisphere as well as for right-hemisphere dominated tasks. More specifically, they tested cerebral symmetries in visual half-field tasks, among those a left-hemisphere advantage task (lexical decision) using three participant groups: a group of normally cycling young women, a group of men, and a group of postmenopausal women. All participants were tested twice: normally cycling women were tested once during menses and once during the mid-luteal phase (day 20-22) and men and postmenopausal women in temporally corresponding sessions. Only young women showed asymmetrical performance measures during menses, but less pronounced functional asymmetries during the mid-luteal phase. Men and postmenopausal women showed stable asymmetries for all tasks.

Fernandez et al. (2003) in the only imaging study to date, used fMRI to measure the brain activity in 12 women in a search for neural correlates of hormonally mediated neural plasticity in humans using a semantic language task and a perceptual task. A repeated-measures design during menses and in the mid-luteal phase was employed. Menstrual-cycle-dependent changes were accompanied by the recruitment of symmetric brain areas involved in a semantic decision task, located in the superior temporal gyrus and the medial wall of the superior frontal gyrus. The cycle-dependent changes in linguistic lateralisation found were due to a symmetric increase of neural recruitment during the mid-luteal phase. The authors concluded that neural plasticity in the language domain is task and region-specific, a conclusion in line with the findings of Hausmann and Güntürkün (2000).

No menstrual cycle study that compares the mid-luteal phase with menses can differentiate between the possible influence of estrogen and progesterone; both hormones are low at menses and high during the mid-luteal

phase. However, there are two reasons for believing that estrogen is the critical hormone (Sanders, 2002). The first comes from Hampson (1990), who tested women during the pre-ovulatory phase when estrogen peaks, but progesterone is low, and found perceptual asymmetry for a verbal task to be greater during the preovulatory peak. The second comes from studying the effects of cross-sex hormone treatment of transsexuals, where a 3-month administration of estrogen to male-to-female transsexuals did result in an altered pattern of cognitive abilities, by improving verbal ability at the expense of visuospatial ability (Van Goozen, 1995).

Another point of interest in the line of menstrual-cycle-dependent hormonal fluctuations is that a number of studies across the human menstrual cycle suggest that estrogen may further affect overt motor behaviour, such as speed and accuracy tests of motor sequencing. Motor ability is improved at higher estrogen levels (Szekely et al., 1998; Sanders et al., 2002) that are to be found in the mid-luteal phase. This result has been replicated in various groups, including women with normal menstrual cycles, postmenopausal women receiving estrogen-replacement therapy and women taking oral contraceptives (for reviews see Hampson, 1992; Sommer, 1992).

Overall, as Hausmann and Güntürkün (1999) concluded, there appears to be a coherence between sexual dimorphism in brain asymmetry tasks and the influence of the menstrual cycle, this coherence supporting the notion that not sex per se, but rather the different underlying gonadal steroid hormone levels is the important factor in sex–specific tasks.

1.5.4 Potential sources of sex differences specific to praxic lateralisation

Apart from the above-described factors, which relate to innate characteristics of sexual differentiation, the sex difference in handedness could

further be a by-product of certain characteristics which men seem to be more susceptible to than women. These characteristics are associated with an increased incidence of left-handedness, such as homosexuality (Laumann et al., 1994), or pathological conditions such as dyslexia (Rutter et al., 2004) or autism spectrum disorders (Wing, 1981; Gualtieri and Hicks, 1985; Skuse, 2000). It has been claimed, a sex difference might not be detectable among samples without these characteristics (Lalumiere et al., 2000).

Females being more successful than males in switching writing hand from left to right is an alternative explanation (Thompson and Marsh, 1976; Porac et al., 1986; Lansky et al., 1988). It might also be that in most societies there is more pressure upon females to conform to cultural norms than upon males, which could apply to the use of the left hand in particular (Harris, 1990). Evidence, though, leans more toward the first hypothesis. Schimizu and Endo (1983), in a study of Japanese high school students, found a higher percentage of conversion to right hand use in left-handed girls than in left-handed boys but no evidence that the girls had been subjected to more social pressure. Porac et al. (1986) asked 650 undergraduates at a Canadian university whether they had experienced any pressures to change their hand preference in any way. The likelihood that an individual had experienced pressure was not related significantly to sex, but the success of the hand change varied with sex, with 61.3% of the females reporting success in making the shift compared to only 26.3% of males (S. Coren, personal communication reported in Harris, 1990). Harris (1990) has proposed two possible reasons for girls accommodating more than boys to right hand training: girls are generally more socially compliant than boys or they are inherently more capable of complying, either because of their greater motoric maturity or because of underlying sex differences in neurobiological organisation.

Finally, the sex difference in praxic lateralisation has been apportioned to a statistical artefact arising from the fact that sex is a variable that is relatively easy to record and analyse. Hence, given the fact that null results are less likely to be reported, it is possible that reports of sex differences in handedness are Type 1 errors, while numerous non-significant sex differences are not published (Williams, 1991). On the other hand, the difference may be real and the cases where no difference is detected may be due to the inherent lack of power in small sample sizes (Porac and Coren, 1977). Furthermore, the failure of some studies to find a sex difference may be due to non-random sampling (Lansky et al., 1988). (Evidently, these statistical artefacts may well be found in studies on linguistic lateralisation as well.) The sex difference may further be a measurement artefact arising from the different reactions the two sexes have to the wording of a hand preference inventory. Bryden (1977), for example, has reported that males tend to avoid giving extreme responses to hand preference questionnaires.

1.5.5 Other potential sources of laterality specific to praxic lateralisation

There is a number of other factors that influence the incidence of handedness which have not been studied in relation to sex differences, but which may, nevertheless, be important. For example, factors pertaining to the characteristics of the populations under study may account for the variability in the incidences of handedness as measured by different studies. Pathological populations, as discussed earlier, have been reported to have increased percentages of non-right handedness compared to the normal population. Such pathological populations include, apart from those presented above, people with epilepsy, Down's syndrome, schizophrenia, alcoholism, stuttering, children with emotional disturbances, and people suffering from autoimmune pathologies, especially thyroid diseases, ulcerative colitis, regional ileitis, celiac disease, and

myasthenia gravis (Merrell, 1957; Lishman, 1976; Boucher, 1977; Colby and Parkinson, 1977; Geschwind, 1982; London, 1985; Geschwind, 1987; Bishop, 1990; Lewin, 1993; Sommer, 2001). Although the concept of "pathological left-handedness" is not entirely uncontroversial (McManus, 1983; Harris and Carlson, 1988) it now seems probable that about one in twenty cases of left-handedness can be regarded as "pathological" in origin (Bishop, 1990). Moreover, a higher incidence of left-handedness has been found in twins compared to singletons (Sicotte et al., 1999).

Ancestry is one of the much-studied factors that have been proposed to moderate the incidence of handedness between populations. Porac et al. (1990), for example, surveyed studies on handedness in different cultures and concluded that the incidence of left-handedness is lower in Oriental cultures than in North America and Europe. Thompson and Marsh (1976) in their study of Blacks and Whites living in the USA similarly found that Blacks were more likely to be dextral than Whites, but he ascribed these findings to the fact that Blacks, more than Whites, are subject to cultural pressures against the use of the left hand.[5] The latter explanation seems likely to also account for the oriental samples, considering that only 3.5% and 0.7% of schoolchildren living in China (Teng et al., 1979) and Taiwan (Hung, 1985) respectively have been found to be left-handed, but at the same time 6.5% of oriental schoolchildren living in the United States use their left hand for writing (Hardyck et al., 1975). Indeed, low incidences of left-handedness have been repeatedly found in strict or conforming societies like Tanzania (Brain, 1977), Japan (Komai and Fukuoka, 1934; Scimizu and Enso, 1983), and Taiwan (Hung, 1985), where it has been shown that less than 1% of the large population samples surveyed used the left hand for writing.

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[5] *Blacks* and *Whites* are terms used by Thompson and Marsh in their 1976 paper.

Age has also been suggested to moderate research findings on the incidence of left-handedness, with evidence from cross-sectional studies in the direction of a decrease in left-handedness with age (Annett, 1973; Fleminger et al., 1977; McGee and Cozad, 1980; Smart et al., 1980; Brackenridge, 1981; Porac and Coren, 1981; Ashton, 1982; Salmaso and Longoni, 1985; Schachter et al., 1987; Maehara et al., 1988; Coren and Halpern, 1991; Dellatolas et al., 1991; Dargent-Pare et al., 1992; Gilbert and Wysocki, 1992). For example, Lee-Feldstein and Harburg (1982) found that the proportion of left-handers is nearly twice as great for people under 40 years of age than in people over 40 (14.8% vs. 8.4% for men and 13.4% vs. 7% for women). Fleminger et al. (1977) have considered the age differences in handedness to be a natural tendency towards dextrality. Lalumiere et al. (2000) argue that this trend reflects either cohort effects or biased mortality rates associated with handedness, a rather popular view (Coren, 1989a; Coren and Halpern, 1991). Porac's et al. (1981) developmental hypothesis, on the other hand, postulates that this decrease in the incidence of left-handedness reflects the pressure of living in a right-handed world. Another influential theory is that of the gradual easing of cultural pressures against sinistrality (Schachter et al., 1987). A variant of this theory is that because in the early 20th century left-handedness represented a social stigma, individuals may have concealed their true handedness in questionnaire surveys (McManus, 1984). The effect has also been attributed to the underreporting of left-handedness in parents by their offspring (Porac and Coren, 1979; Kang and Harris, 1996). All the above hypotheses have been subjected to criticism and a consensus has yet to be reached (e.g., Coren and Halpern, 1991; Annett, 1993; Harris, 1993; Porac, 1993; Coren, 1994).

A disparity has also been observed between general population samples and college students samples; while the incidence of left-handedness is usually estimated between 8% and 10%, for the general population, when using college

students as samples this incidence climbs to between 9% and 14% (Annett, 1973; Briggs and Nebes, 1975; Peterson, 1979; Spiegler and Yeni-Komshian, 1983; Saunders and Campbell, 1985). Harvey (1988) has proposed that this difference can be explained in terms of intelligence; it is the most intelligent of the high-school graduates that go on to become college students and comprise the sample of many studies on handedness. Tan (1988) has in fact claimed that handedness, familial sinistrality and intelligence are interrelated traits, whereby an attenuation in cerebral asymmetry as a result of an increase in the right hemisphere's mental abilities, reflecting itself in weak right-handedness in conjunction with familial sinistrality, could be a prerequisite for well-developed nonverbal intelligence. This is in line with Annett's claim of a heterozygote advantage at the cognitive level (Annett, 1998).

Another debate concerns whether or not left-handedness gives an advantage to sportsmen, especially those engaged in interactive sports, and consequently, whether higher percentage of left-handers is to be found among the high achievers of sporting populations (Raymond et al., 1996; Grouios et al., 2000; Holtzen, 2000). Casey (1996) claims that such advantages are neuroanatomically-based and facilitate left-handed people in performing certain neurocognitive tasks, such as visuospatial and whole body tasks. It has been similarly claimed the left hand and right hemisphere respond faster than the right hand and left hemisphere, thus the left hand is preferred in some sports, even by people otherwise right-handed. Wood and Aggleton (1989), on the other hand, support the idea that any excess of left-handers in certain sports is simply due to the nature of the game; left-handers merely have a tactical advantage, as they are having more practice against right-handed opponents than the latter have against left-handed ones.

The assessment of handedness may be another source of divergence in the handedness literature. Although it might seem trivial to the layperson, a

major difficulty in studies of handedness lies with the definition of handedness. There is no general agreement among investigators of praxic lateralisation as to what constitutes right- or left-handedness. Furthermore, some individuals are neither; they are ambidextrous.

Type of handedness assessment is among the most prominent of these factors (Bishop, 1990). Assessment methods can be largely grouped into hand preference inventories and hand skill tests; the former assess which hand is preferred over the other for a number of everyday activities (e.g., EHI; Oldfield, 1971; Annett, 1985), whereas the latter measure the relative proficiency of the two hands in performing skilled activities (e.g., Dot-Filling; Tapley and Bryden, 1985). These two types of assessment are correlated, even though imperfectly (.6 to .7; Todor and Doane, 1977). Writing hand has frequently been used as the criterion, and it has been noted by Perelle and Ehrman (1994) that self-assessment of handedness also usually devolves to writing hand. Even when restricted to hand preference inventories though – the method most widely used both in experimental and clinical settings (Rigal, 1992) – it is still the case that different instruments produce predictable differences in patterns of distribution (Holder, 1992). Provins et al. (1982), for example, have reported collecting different percentages for different inventories resulting in even reclassifying left-handers as clear right-handers.

The apparent incidence may also vary by virtue of questionnaire length (Holder, 1992; Peters, 1992), the latter varying from the use of a single item such as writing hand (e.g., Silva and Satz, 1979) to the utilisation of 75 items (e.g., Provins et al., 1982). Still, when the number of items is kept constant, the content of the questionnaire, that is the nature of the items used, could affect the distribution of the results (Gureje, 1988). Indeed, the choice of the items included seems to be a matter of idiosyncratic preference and tradition, rather than deriving from any theoretical considerations (Bishop, 1990).

Further, the nature of the response permitted to each item can alter the way participants report their hand preferences (Peters, 1992). Raymond (2004), for example, observed that a 5-point scale gives inconsistent results. Williams (1991) compared the 10-item EHI, a 5-point graded responses questionnaire, with the 12-item Annett's Hand Preference Questionnaire (AHPQ; Annett, 1970), a binary responses questionnaire, and found that participants would give more "either hand" choices in Oldfield's questionnaire, when for the same items the same participants were more likely to give "left" rather than "right" choices with Annett's questionnaire.

The incidence of handedness additionally depends upon the choice of handedness categories used: these may either be discrete, usually right and left, and usually by using writing hand as the criterion (e.g., McManus, 1984), or continuous, in which case the partition of the continuum into two or more parts depends on an arbitrarily-adopted criterion (e.g., Hardyck and Petrinovich, 1977; Maehara, 1988; Annett, 1994). These methodological variations make it more difficult to judge whether the same characteristic is being investigated when purporting to study "handedness".

An additional factor is whether the reporting of hand preference takes place by self-report or not (e.g., filial report or report by a sibling), as this can have an effect on the measured incidence of handedness. For example, right-handers take handedness for granted and are often unaware of left-handedness in relatives (Annett, 1998), which can for example be seen, in the underreporting of left-handedness in parents by their offspring, as mentioned earlier (Porac and Coren, 1979; Kang and Harris, 1996).

1.6 Importance of investigating the sex difference in praxic and linguistic lateralisation

Individual differences in neurological organisation, such as the

lateralisation of praxis and language, are of key importance to psychiatric, neurological, and neuropsychological research and practice. By studying normal variations in neuropsychological organisation, along with their functional consequences, one can begin to understand how particular biological characteristics constrain or enhance functional abilities (Kimura and Harshman, 1984). Sex is an important analytical tool in this understanding. Thus, in conditions where a sex bias exists, information regarding its origin is essential in understanding the aetiology of the condition (Baron-Cohen et al., 2004).

When it comes to praxic lateralisation, the putative sex difference together with the twin effect (i.e., that monozygotic and dizygotic twins have essentially the same concordance rates for handedness, even though the incidence of left-handedness is higher among twins than among singletons), the parental effect (i.e., that the handedness of children is related to that of their parents), and the grandparent effect (i.e., that an individual with a parent who is right-handed but who is also the offspring of two left-handed grandparents shows the same increased chance of left-handedness as an individual with one parent who is left-handed) have been repeatedly demonstrated in handedness research (Corballis, 1997; Jones and Martin, 2000), but have not been investigated thoroughly to date. These factors need to be explained in order to achieve a clearer understanding of the phenomenon of handedness.

The sex difference in praxic lateralisation is in fact one of the most important constraints shaping the theoretical understanding of human handedness, hence the large number of genetic models that have been proposed to explain it. At least three different explanations for a sex difference in handedness have been put forward within these models – the differential right-shift hypothesis of Annett (2002), the modifier-gene theory of McManus and Bryden (1992), and the recessive model of Jones and Martin (2000), as described earlier. Studying handedness phenotypes in the two sexes and in

particular reaching a reliable quantitative estimate of the magnitude of the sex difference is therefore necessary in order to inform the evaluation and refinement of these genetic models.

Considering that some of the genetic theories claim that handedness and language dominance are controlled by the same gene (Annett, 1972; Crow, 2002), the study of the genetics of handedness would also be making a substantial contribution towards the genetics of language. Moreover, since a number of other cognitive functions, apart from language, such as spatial-constructional abilities, are organised along the left-right axis in the human cerebral hemispheres, understanding the genetic contributions to the development of cerebral asymmetry has significant implications for the entire field of cognitive neuroscience (Geschwind et al., 2002). Besides, there is evidence that psychotic disorders might be associated with deviations from the normal pattern of right-handedness and left-cerebral dominance (Crow, 1990). This raises the possibility that handedness, cerebral asymmetry, and psychotic disorder may depend, at least in part, on the same genetic locus (Corballis, 1997). It has even been claimed that “finding the locus for the gene for cerebral dominance could unravel the genetic predisposition to schizophrenia” (Sommer et al., 2001).

Being able to reach a definite conclusion on whether a sex difference in handedness exists, as well as estimating the true size of this effect, is of great importance with respect to experimental study design as well. Individual differences in hand preference indicate subtle differences in performance in a variety of functions such as memory (McKelvie and Aikins, 1993; Martin and Jones, 1998; Martin and Jones, 1999a; Martin and Jones, 1999b), spatial ability (Annett, 1992), motion detection (de Sperati and Stucchi, 1997), hand representation (Gentilucci et al., 1998), divergent thinking (Coren, 1995), mathematical ability (Annett and Kilshaw, 1982), right-left discrimination (Ofte,

2002), motor performance (Nalcaci et al., 2001), and reading ability (Palmer, 1996). Martin and Jones (1999a) have even suggested the possibility of a chiral psychology of cognition that takes note of a person's handedness. Therefore, if males are more likely to be left-handed compared to females and at the same time there is evidence that handedness affects cognitive function, then handedness needs to be controlled in studies comparing the two sexes in cognitive function.

Praxic lateralisation, apart from being a biological marker for language lateralisation (Kimura, 1984; Knecht et al., 2000; Khedr et al., 2002), has also been related to the volume of brain structures like the corpus callosum, the hippocampus, and the amygdala (Witelson, 1985; Luders, 2003; Anstey, 2004). It has further been studied in relation to a number of psychiatric diseases, (Bishop, 1990; Grouios, 1999; Elias, 2001; Sommer, 2001; Buijsrogge, 2002; Delisi, 2002; Chemtob, 2003). In addition, evidence exists, albeit conflicting and confusing, that there are differences in the levels of T between right- and left-handers (Tan, 1991a; Moffat and Hampson, 1996). Therefore, determining whether there is a sex difference in praxic lateralisation will also be informative for neurological, neuro-anatomical, and psychoendocrinological research.

Understanding the quantitative relationships between language lateralisation, handedness, and demographic factors that influence these asymmetries of function in the normal population, such as sex, is also of clinical relevance for two reasons. Firstly, these relationships might be useful for predicting the risk of post-operative language disturbance in patients undergoing brain surgery for adult-onset disease. Secondly, such knowledge could lead to an improved understanding of the biological basis of language lateralisation, which might eventually result in novel therapeutic strategies for patients with impaired language processing (Szaflarski et al., 2002).

Overall, apart from its intrinsic interest, the study of sex differences in praxic and linguistic lateralisation is important because it contributes to the broader question of individual differences in brain organisation and abilities (Kimura and Harshman, 1984).

Chapter 2

Meta-analysis on the sex differences in praxic lateralisation

2.1 Introduction

Praxic lateralisation has attracted great research interest over the past decades, due to its intimate relationship with linguistic lateralisation (Knecht et al., 2000), along with the fact that the latter is difficult to study in large populations. A widely reported finding is a greater male tendency towards left-handedness (e.g., Perelle and Ehrman, 1994), even though not all studies point to this direction (e.g., Salmaso and Longoni, 1985). This chapter investigates this putative sex difference in praxic lateralisation by means of meta-analytic techniques.

Investigating whether the sex difference in praxic lateralisation is reliable and, if so, what the overall magnitude of the difference is, and what the systematic influences upon it are, is no easy task: the field is overwhelmed by the amount of published studies. In terms of the general area, McManus (1986) estimated that about 5000 papers had been published on lateralisation by 1985; updating the survey, McManus (1991) reported that between 1960 and 1989, 6564 papers were cited in *Psychological Abstracts* under the headings of "cerebral dominance", "handedness", and "lateral dominance", with 1047 being cited under the heading of "handedness" alone. The same search terms were

entered in PsycINFO and it was found that for the period 1989-2006, 8757 articles were cited under the search term "(cerebral dominance) OR handedness OR (lateral dominance)" and 2195 when "handedness" alone was used as a subject heading. This rapidly increasing body of published literature makes it increasingly difficult to have a clear picture of the research field.

A conventional literature review, valuable as it might be for the description of previous research, could only contribute in a subjective manner. More importantly though, a literature review could never hope to handle such an abundance of data. A meta-analysis, on the other hand, allows for the results of a large collection of studies to be analysed statistically in an integrated manner (Glass, 1976). It provides a discipline for summing up research findings using objective statistical methods similar to those used in primary data analysis for the collection, coding and interpretation of data. It also presents findings in a more sophisticated manner compared to conventional narrative reviews. Moreover, by summarising a research domain in a quantitative manner, meta-analysis protects against over-interpreting differences across studies. At the same time, it allows for even small and non-significant studies to contribute to the results of the analysis, by focusing on effect size rather than on sample size and significance thereby providing a safety net against wasting data. Furthermore, meta-analysis reduces the probability of false negative results. Lastly, meta-analysis allows for the detection of moderators as well as for the assessment of the presence of ascertainment bias, which can exist when significant results are produced by non-random sampling. While dealing effectively with these issues, meta-analysis still preserves the valuable aspects of narrative reviews (Egger et al., 1997; Rosenthal and DiMatteo, 2001).

In meta-analysis, the unit of observation is not the participant but rather the study. Hence, the place of the individual participant's data is taken up by the study's effect size. This is a measure of the strength of the relationship between

two variables and it can be any standardised index as long as (a) it is comparable across studies after standardisation, (b) it represents the magnitude and direction of the relationship of interest, and (c) it is independent of sample size (Lipsey and Wilson, 2001). Then, an estimate of the combined effect is calculated, which is the mean of the effects from the included studies, weighted according to the study size. Smaller studies contribute less than large studies, because smaller studies' results are more likely to be influenced by chance.

In the present meta-analysis, the measure of effect size used is the odds ratio, which is defined as the ratio of the odds of an event occurring in one group to the odds of it occurring in another group. In this case, the event would be left-handedness and the two groups would be the male and female populations. The main advantage of the odds ratio is that it is independent of the base rate of the event in question (i.e., left-handedness) within each study. In the context of the present meta-analysis, the base rate could, for example, be affected by the handedness instrument or the cut-off criteria used to determine left-handedness (e.g., the larger the number of items or the more stringent the criteria, the smaller the number of left-handers) or perhaps by the type of sample used (e.g., an East-Asian sample might include a smaller number of left-handers). Although the odds ratio has not generally been employed in theoretical accounts of handedness, it is straightforward to transpose quantitative formulations into this measure.

The study presented in this chapter is therefore a meta-analysis of studies that have assessed the incidence of handedness in males and females. The first goal is to provide a definitive test of the hypothesis that there is a sex difference in the incidence of handedness and to estimate the overall magnitude of this difference. The second goal is to assess whether systematic variation in the size of the sex difference between different studies occurs and, if so, to investigate the sources of any such variance. Possible sources include the

ancestry and the educational status of the participants, the instrument used, the number of questionnaire items, the type of response categories allowed, the year of publication of the study, whether the study's main purpose was to measure handedness and whether the data were collected by self-report. The hypothesis that the sex difference is a Type 1 error (Williams, 1991) will also be tested, by assessing the presence of ascertainment bias in the field.

2.2 Method

The studies that were entered into the meta-analysis were located using the following procedure. The computerised reference database Pubmed MEDLINE at PUBMED (NLM) was searched using the search terms (*handedness AND (sex OR gender)) NOT (animal OR child OR adolescen* OR infant OR imaging OR functional OR structural)* via the EndNote (v.8) citation management software package (Researchsoft, 2004) and the online database PsychINFO was searched using the terms *handedness OR hand*. The cited literature of all articles that were eligible for inclusion was scanned, and as more papers were obtained, their references were searched for pertinent articles as well. In addition, the bibliographies of six important books in the area of handedness were hand-searched in order to ensure that no major studies had been overlooked (Herron, 1980; Porac and Coren, 1981; Corballis, 1983; Annett, 1985; Beaton, 1985; McManus, 2002). Data collection ended in September 2007.

2.2.1 Study selection

The following criteria were set for inclusion of an individual study in the meta-analysis:

1. Participants: twin persons, persons with homosexual orientation, and persons with pathological conditions were excluded, but data from participants

acting as their controls were included (e.g., Cannon et al., 1995). Moreover, participants were required to be over the age of 16 years. Even though handedness is usually considered to be established around 3–7 years of age (Hardyck et al., 1975; McManus et al., 1998; Raymond and Pontier, 2004), this limitation was considered necessary in order to avoid possible developmental effects. An exception was made for a few studies that had grouped data across ages (such as “15-70”) where the majority of participants were over 16 (e.g., Ellis et al., 1988).

2. Reports had to be written in English. The Azémar and Stein (1994) study is the only exception, the data being extracted from Raymond et al. (1996).

3. Data were required to have been broken down by sex in a comprehensive way (i.e., in the text or in tables). In some cases the data reported could not be used, for example in studies in which handedness was reported only as laterality quotients (e.g., Merckelbach et al., 1989), when data were presented in an unsuitable way (e.g., Falek, 1959; Jones, 1980; Payne, 1987) or when only graphical representation was available, making the accurate extraction of data impossible (e.g., Provins et al., 1982).

4. Handedness was required to have been measured in terms of hand preference, not hand performance. Studies were included, however, if hand preference had been assessed by asking participants to perform an unskilled action in order to observe the preferred hand.

A number of studies included two or more samples from different geographical areas or from different age groups; in such cases the data sets were treated as separate. Where the sample was sub-divided into categories not meaningful for this meta-analysis (e.g., history of birth stress), then it was considered as a single data set. Several studies duplicated data already published (e.g., Annett, 1999). In those cases, care was taken to include each data set only once. Studies where participants had been selected or were

motivated to take part on the basis of their handedness (e.g., Lake and Bryden, 1976; Tan, 1983; Liederman and Healy, 1986; Casey et al., 1992), typically in order to increase the proportion of left-handed participants, were carefully excluded. An important problem that was encountered during data collection was the fact that some studies that found no significant sex difference reported only the results of statistical testing, without mentioning the actual incidence of handedness in the two sexes (e.g., Salmaso and Longoni, 1983). Those studies unfortunately could not be included, although formal tests of ascertainment bias were included to determine whether this resulted in a bias in the results.

Participants had been classified by the original authors primarily as right- or left-handed (R-L), as right-, mixed-, or left-handed (R-M-L), or as right- or non-right-handed (R-nonR). In a few studies, more complex classifications were used (i.e., right-, right mixed-, left mixed-, or left-handed; strong right-, mixed- or strong left-handed; strong right-, moderate right-, mixed-, moderate left-, or strong left-handed, as well as a 7-class classification). In the first case the results were converted to R-L, whereas in the rest of the cases they were converted to R-M-L. In the case of Salmaso and Longoni (1985), who provided 10 laterality classes, a cut-off point representing the middle of the continuum was introduced in order to classify the participants as R-L.

2.2.2 Moderators

The variables whose possible moderating effects were examined included:

Instrument. Handedness was mainly measured by means of handedness questionnaires and inventories, of writing hand, and by self-classification (by using some version of the question, “Do you consider yourself to be left-, (mixed-) or right-handed?”). In some studies observation of a certain action was employed (e.g., the hand holding the racket in tennis). In those cases where

percentages on a number of items were given, without reporting a laterality quotient, the information on writing hand was used (e.g., Merrell, 1957; McFarland and Anderson, 1980). For the Aggleton and Wood (1990) study, the information on the hand throwing a ten-pin bowling ball was used for both groups (professional bowling players and a control group), as information on writing hand were reportedly collected for the control group, but were not included in the paper. The studies were coded for instrument using seven different groupings, representing the most popular instruments used to measure handedness in the present data set: (a) writing hand, (b) the 10-item version of the EHI (Oldfield (1971), (c) the 4-items for handedness from the Lateral Preference Inventory by Porac and Coren (1981), (d) the 8-item, 10-item, 12-item, and 23-item versions of the AHPQ (Annett, 1970), (e) the Briggs and Nebes modification of the AHPQ (Briggs and Nebes, 1975),[6] (f) self-classification, and (g) observation of an action/information from official records.

Ancestry. A number of human population genetic studies have claimed that the genetic differentiation is greatest when defined on a continental basis (see Risch et al., 2002, for a review) and have suggested the categorisation of populations into five major groups: Caucasians, Africans, East Asians, Pacific Islanders, and Native Americans. Here only the three former groupings were used, as none of the studies included participants that would fall into the latter two groups. Participants from South America were not allocated to any of the groups, as individuals currently living in South America have a wide range of ancestries depending on the origins of their forebears. The Caucasian group included participants from Europe, North America, West Asia, and Australia.

[6] The modification that Briggs and Nebes introduced to the AHPQ is that they employ a wider response scale (5-point instead of binary forced choice or 3-point scale) for the same items as the AHPQ.

Rarely was information about ancestry reported, but rather it was inferred from the country in which the study took place.

Year of publication. For investigating possible moderation in terms of secular change, the year of publication was entered numerically for each study.

Educational status. Educational status was grouped at two levels, with the higher comprising individuals who had entered college (college students, faculty members, and professionals). Mixed samples (i.e., samples including both students and their family members) and samples for which no demographic information was given were not included in the analysis of the moderating effect of educational status.

Type of response categories. Four groupings were employed: (a) binary response formats (including right-left responses and the cases where participants had to tick a box next to a picture showing hand posture), (b) 3-point scale graded response formats, including variations of right/both/left, right/equally/left, right/ambidextrous/left, and always right/either right or left/always left, (c) 5-point scale graded response formats, and (d) the graphic graded response format, as employed by the original version of the EHI (Oldfield, 1971). This scheme features two columns labeled “right” and “left”. Participants are asked to indicate their preferences in the use of hands in the activities listed in the questionnaire by marking + in the appropriate column. Where preference is so strong that participants would never try to use the other hand unless absolutely forced to, they are asked to put ++. If it was the case that they are really indifferent they are asked to put + in both columns.

Other variables: Additionally, information on whether the measurement of handedness was the main purpose of the study and whether the data were collected by self-report were also extracted from the studies, using a “yes/no” coding. In order to test for the possible moderating effects of the number of

questionnaire items used, the number of questionnaire items used was entered numerically.

Not all the studies reported information for each of the above moderator variables. In the case of the mean age of the participants, this was reported in fewer than 25% of the data sets; hence mean age could not be used as a moderator variable.

2.2.3 Statistical analysis

Data were analysed using the Comprehensive Meta-Analysis (v.2; Borenstein et al., 2005) software package.

Analysing the data using different comparisons was deemed necessary in order to overcome the obstacle of the different handedness classifications employed by different researchers. Five 2 x 2 contingency tables were thus constructed, allowing for the primary analysis of sex by different conceptions of left-handedness. The first three adopted progressively more lax criteria for left-handedness; the fourth used the criterion of non-right handedness; and the fifth, termed left-handedness (total), was an inclusive analysis. These were as follows:

1. Left-handedness (extreme): extreme left-handers represent the participants who were classified as left-handers in data sets where an R-M-L classification was employed.

2. Left-handedness (forced choice): left-handers by forced choice represent the participants who were classified as left-handers in data sets where an R-L classification was employed.

3. Mixed-handedness: mixed-handers represent the participants who were classified as mixed-handers in studies where an R-M-L classification was employed.

4. Non-right handedness: non-right-handers represent the participants who were classified as non-right-handers in data sets where an R-nonR classification was employed.

5. Left-handedness (total): this comparison was designed to assess the overall presence of left-handedness. Information was extracted from the data sets that classified their participants in terms of R-L, R-nonR or R-M-L. In the last case, only the left-handers were included in the analysis, leaving the mixed-handers out. In those cases where the same participants were classified twice using more than one type of measurement (e.g., both by means of writing hand and of a handedness inventory), the information on the writing hand was preferred as it was the most popular way of measuring handedness in the present data set, therefore it would provide homogeneity in the meta-analysis. If information on writing hand was not one of the options, then data on self-classification were used (Reiss et al., 1998; Lippa, 2003). In the case of two studies where both the R-L and the R-M-L classifications were available for the same measures, information from the latter classification was used (Saunders and Campbell, 1985; Brito et al., 1989).

Male-to-female odds ratios (*OR*) and corresponding two-tailed 95% confidence intervals (*95% CI*) were calculated for each data set independently and were then combined using a fixed effect model to provide a pooled *OR* and a test for the overall effect (*Z*-statistic). An odds ratio value of 1.0 corresponds to the null hypothesis of no sex difference, whereas values greater than 1.0 indicate a larger proportion of male than female left-handers. Moreover, each comparison was tested for heterogeneity, using the homogeneity statistic *Q*, and for the extent of inconsistency among the data sets' results, using the I^2 index. The *Q* statistic is used to ascertain whether the primary level effect sizes estimate a common population effect size and the I^2 index can be interpreted as the percentage of total variation across studies that is due to heterogeneity

rather than chance. Higgins et al. (2003) have proposed that levels of 25%, 50%, and 75% may be described as low, moderate, and high, respectively. In the cases of significant heterogeneity between the data sets, the analysis was repeated using a random effects model. Fixed effects and random effects models are based on different assumptions. Whereas a fixed effects model assumes that all the data sets included in the meta-analysis come from a single population, the random effects model assumes that the included data sets are drawn from a distribution of populations. The two models therefore address different research questions: the fixed effects model asks what the best estimate of the true effect size (in the present case the odds ratio) of the population is, whereas the random effects model asks what the range and distribution of odds ratios in the sample of populations studied is. For both models the differences in the effect sizes across the data sets can be due to sampling error but only for the random-effects model the between-study heterogeneity can be a source of variance as well.

The data sets were also tested for ascertainment bias using the funnel plot graphical test, Egger's *t* statistical test and the fail-safe *N.* The rationale behind the funnel plot is that if all data sets come from a single population then the plot should resemble a funnel with the diameter of the funnel decreasing (i.e., effect-size estimates becoming more accurate) as the sample size increases. In the absence of ascertainment bias, one should expect a symmetrical funnel plot; asymmetry is therefore suggestive of the possibility of ascertainment bias. Egger's *t* provides an estimate of asymmetry of funnel plot, with positive values ($a > 0$) indicating a trend towards higher levels of test accuracy in studies with smaller sample sizes. The fail-safe *N* is the number of data sets with an odds ratio of one (i.e., zero effect) that would be needed to be added to the existing meta-analysis for it to be no longer significant at the conventional level of $p < .05$. Duval and Tweedie's (2000) trim-and-fill method of

correcting bias was also used. This method aims at making the funnel plot symmetrical by omitting and/or adding hypothetical data sets to the plot where necessary. Then, it provides an adjusted estimate of the effect size, including the added studies.

In examining the possible moderating effects of categorical moderator variables (i.e., instrument, ancestry, educational status, response categories, whether the main purpose of the study was to measure handedness, and whether data were collected by self-report) the effect sizes in the different subgroups that form the levels of each moderator were compared by means of the *Q* statistic. In examining the possible effects of the interval moderator variables (i.e., year of publication of the study and number of questionnaire items) meta-regression was performed; a random-effects model was used as recommended by Thompson and Higgins (2002), with evaluation again in terms of the *Q* statistic.

2.3 Results

A total of 144 studies were included in the analysis, comprising 208 separate data sets and totaling 1,787,629 individuals (831,537 male, 956,092 female). The details of all the studies used can be found in Appendix 2.1.

2.3.1 Handedness categorisation

Analyses were conducted first on each of the five different types of handedness categorisations previously outlined. The results are as follows:

Left-handedness (extreme). This comparison included k_d = 51 data sets, drawn from k_s = 42 studies, comprising up to n_t = 240,346 individuals (n_m = 127,516 male, n_f = 112,830 female). Fixed effects analysis gave a pooled *OR* = 1.22, *95% CI* = 1.19-1.25, Z = 14.39, $p < .01$. Significant heterogeneity was

found to exist among the data sets, Q (50) = 78.88, p < .01, with small-to-moderate inconsistency between studies, I^2 = 36.61%, indicating that one or more variables may moderate the relationship between sex and handedness. A random effects model was therefore employed, which revealed a clear difference in left-handedness (extreme) between the sexes, *OR* = 1.20, 95% *CI* = 1.11-1.29, indicating that the *OR* was significantly different from 1.0, Z = 4.62, p < .01.

Left-handedness (forced choice). This comparison included k_d = 137 data sets, drawn from k_s = 94 studies, comprising up to n_t = 358,602 individuals (n_m = 184,003 male, n_f = 174,599 female). Fixed effects analysis gave a pooled *OR* = 1.23, *95% CI* = 1.20-1.26, Z = 18.17, p < .01. Significant heterogeneity was found to exist among the data sets, Q (136) = 199.12, p < .01, with small-to-moderate inconsistency between studies, I^2 = 31.70%. A random effects model was therefore employed, giving a pooled *OR* = 1.24, *95% CI* = 1.19-1.30, indicating that the *OR* was significantly different from 1.0, Z = 10.30, p < .01.

Mixed-handedness: This comparison included k_d = 51 data sets, drawn from k_s = 42 studies, comprising up to n_t = 240,346 individuals (n_m = 127,516 male, n_f = 112,830 female). Fixed effects analysis gave a pooled *OR* = 1.16, *95% CI* = 1.09-1.23, Z = 5.10, p < .01. Significant heterogeneity was found to exist among the data sets, Q (50) = 152.80, p < .01, with moderate-to-large inconsistency between studies, I^2 = 67.28%. A random effects model was therefore employed, which revealed a clear difference in mixed-handedness between the sexes, *OR* = 1.31, *95% CI* = 1.16-1.48, indicating that the *OR* was significantly different from 1.0, Z = 4.28, p < .01.

Non-right-handedness. This comparison included k_d = 20 data sets drawn from k_s = 18 studies, adding up to n_t = 1,198,476 individuals (n_m = 524,611 male, n_f = 673,865 female). Fixed effects analysis gave a pooled *OR* = 1.31, *95% CI* = 1.29-1.32, Z = 46.23, p < .01. Significant heterogeneity was found to exist among the data sets, Q (19) = 43.61, p < .01, with moderate inconsistency

between studies, I^2 = 56.44%. A random effects model was therefore employed, which revealed a clear difference in non-right-handedness between the sexes, *OR* = 1.22, *95% CI* =1.10-1.36, indicating that the *OR* was significantly different from 1.0, Z = 3.72, p < .01.

Left-handedness (total). This comparison included k_d = 199 data sets drawn from k_s = 144 studies, adding up to n_t = 1,787,629 individuals (n_m = 831,537 male, n_f = 956,092 female). Fixed effects analysis gave a pooled *OR* = 1.28, *95% CI* = 1.27-1.30, Z = 51.40, p < .01. Significant heterogeneity was found to exist among the data sets, Q (198) = 329.10, p < .01, with small-to-moderate inconsistency between studies, I^2 = 39.84%. A random effects model was therefore employed, which revealed a clear difference in left-handedness between the sexes, *OR* = 1.23, *95% CI* = 1.19–1.27, indicating that the *OR* was significantly different from 1.0, Z = 13.17, p < .01. A forest plot of male-to-female odds ratios can be found in Appendix 2.2.

Interestingly, male-to-female *OR*s were numerically greater for comparisons using more lax criteria of left-handedness. Figure 2.1 summarizes graphically the *OR*s with their *95% CI*s for the left-handedness (extreme), left-handedness (forced choice), and mixed-handedness comparisons. These comparisons were visually represented because they include independent samples and they are also distinct conceptually from each other (as opposed to the non-right-handedness comparison, the place of which in a theoretical continuum from strict to lax criteria of left-handedness is not clear).

2.3.2 Ascertainment bias

The data sets that were included in the left-handedness (total) comparison were tested for ascertainment bias. No ascertainment bias was detected using Egger's Test, t (198) = 1.21, p = .23 or by visual inspection of the funnel plot graphical test (see Figure 2.2). Using Duval and Tweedie's trim-and-

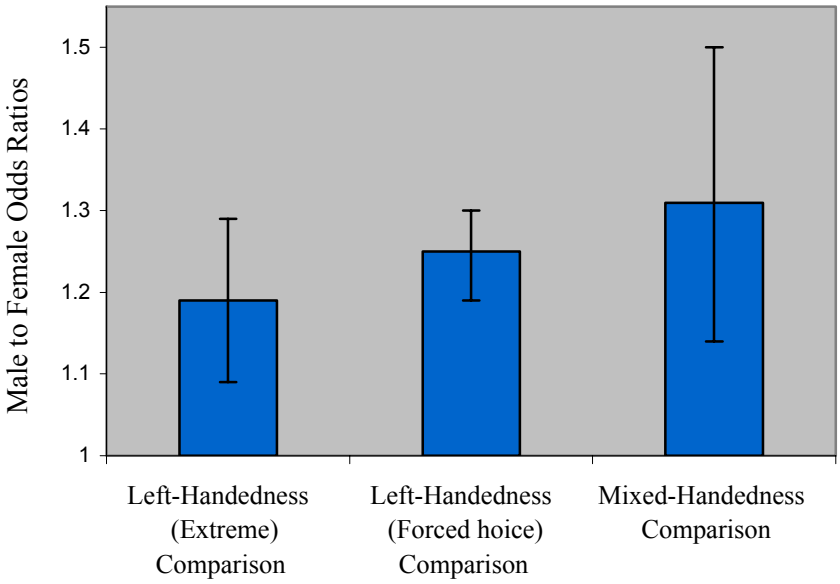

Figure 2.1. Graphic representations of the male-to-female odds ratios and the corresponding 95% confidence intervals for the left-handedness (extreme), left-handedness (forced choice), and mixed-handedness comparisons.

fill method for bias correction, for the random effects model, two data sets were "trimmed", no data sets were "filled" and the adjusted odds ratio was *OR* = 1.23, *95% CI* = 1.19-1.27, an estimation identical to the *OR* originally calculated (*OR* = 1.23, *95% CI* = 1.19-1.27). Finally, the fail-safe *N* was calculated, and found to be *N* = 17,408. The high value of *N* confirms the reliability of the observed effect.

2.3.3 Moderating variables

The moderating effects of the previously indicated variables were tested within the left-handedness (total) comparison. This comparison included data from all n_t = 1,787,629 participants within k_d = 199 independent data sets, and it is therefore the most representative as well as the most powerful one. Table 2.1 presents detailed statistics for each level of the categorical variables. Since the left-handedness (total) comparison included studies that had classified their

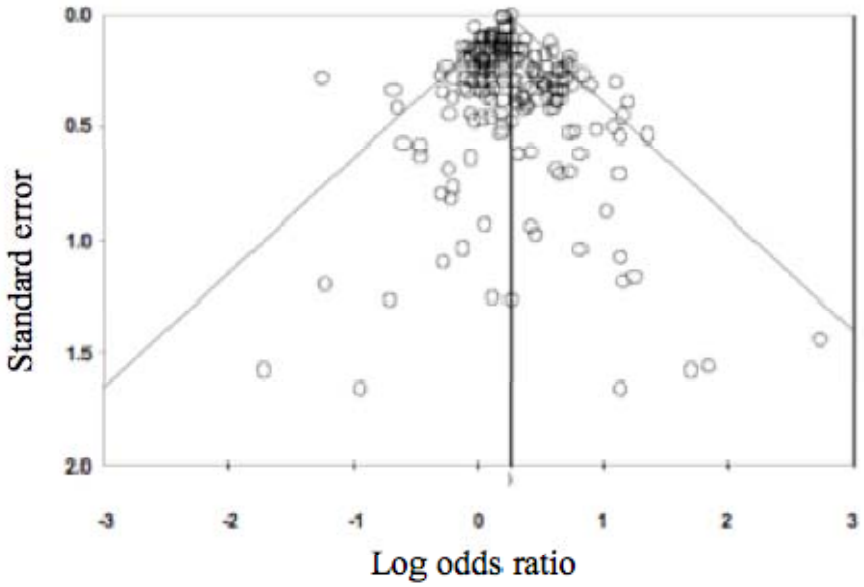

Figure 2.2. Funnel plot of standard error on log odds male-to-female ratio, for the left-handedness (total) comparison.

participants as either R-L, R-M-L, or R-nonR, it was first confirmed that these different classifications did not have a significant moderating effect on the sex difference in left-handedness, Q (2) = 1.50, p = .47, before investigating the presence of other possible moderator variables. For all analyses, only data sets in which pertinent information was reported were used.

Ancestry. Overall, there was significant heterogeneity among the studies, Q (180) = 298.29, p < .001, with small-to-moderate variation between studies, I^2 = 39.64%. It can be seen from Table 2.1 that the odds of being left-handed rather than right-handed were found to be 22%, 31%, and 60% higher for male than for female participants among the Caucasian, African, and East Asian samples, respectively; ancestry was found to exert a significant moderating effect on the size of the sex difference in handedness, Q (2) = 11.26, p = .011. Within groups exploration revealed that significant heterogeneity remained in the Caucasian group, Q (156) = 270.08, p < .001, I^2 = 42.24%, but not in the East

Table 2.1. Male-to-female left-handedness odds ratios (OR) and 95% confidence intervals (CI) for all levels of the moderator variables.

Moderator variable	Level	Number of data sets	OR	95%CI
Classification	Right-Left (R-L)	134	1.24	1.19-1.29
	Right-Mixed-Left (R-M-L)	49	1.19	1.10-1.28
	Right-non-Right (R-nonR)	16	1.29	1.16-1.44
Instrument	Writing Hand	54	1.16	1.10-1.23
	EHI	27	1.28	1.19-1.38
	Porac & Coren's	9	1.28	1.17-1.42
	AHPQ	4	2.28	1.07-4.86
	Briggs & Nebes	6	1.19	.97-1.47
	Self-Classification	18	1.17	1.07-1.27
	Specific Action	13	1.20	1.05-1.37
Ancestry	Caucasian	157	1.22	1.18-1.26
	East Asian	17	1.60	1.36-1.87
	African	7	1.31	1.02-1.65
Education	College	76	1.26	1.17-1.35
	Other	103	1.23	1.18-1.27
Response Categories	Binary	37	1.26	1.19-1.33
	3-Point Graded	68	1.24	1.16-1.33
	5-Point Graded	30	1.22	1.12-1.33
	Graphic Graded	8	1.34	1.17-1.53
Main Purpose	Yes	107	1.22	1.17-1.27
	No	91	1.26	1.20-1.32
Report	Self-Report	171	1.23	1.19-1.7
	Report by Others	26	1.29	1.16-1.43

Asian group, Q (16) = 17.68, p = .34, I^2 = 9.50%, or the African group, Q (6) = 3.26, p = .72, I^2 = .00%.

The Caucasian group was investigated for further moderator effects by contrasting North American samples (k_d = 79) with European samples (k_d = 57). Within this overall set of studies there was significant heterogeneity, Q (135) = 230.38, p < .001, I^2 = 41.40%, with a significant moderating contrast between North America and Europe, Q (1) = 4.66, p = .042; the odds ratio was higher for North America (*OR* = 1.25, *95% CI* = 1.20-1.31) than for Europe (*OR* = 1.14, *95% CI* = 1.07-1.23). However, there remained significant low to moderate levels of heterogeneity within both the North American group, Q (78) = 122.30, p = .001, I^2 = 36.22%, and the European group, Q (56) = 84.95, p < .01, I^2 = 34.08%. In the North American group, the contrast between USA (k_d = 58) and Canada (k_d = 21) was not significant, Q (1) = .93; significant heterogeneity remained within USA studies, Q (57) = 105.42, p < .001, I^2 = 45.93%, but not within Canada studies, Q (20) = 16.88, I^2 = .00%. In the European group, the contrast between Scandinavia (here Norway, Sweden, and Finland; k_d = 9) and the remaining group (k_d = 48) reached borderline significance, Q (1) = 3.51, p = .061. For Scandinavia, the magnitude of the odds ratio was below unity, though not significantly so, *OR* = .88, *95%CI* = .67-1.17, Z = .88, p = .38, and there was no significant heterogeneity, Q (8) = 4.51, I^2 = .00%. For the remaining group, the odds ratio was significantly above unity, *OR* = 1.16, *95%CI* = 1.08-1.25, Z = 4.04, p < .001, and there was significant heterogeneity, Q (47) = 75.39, p < .01, I^2 = 37.66%.

Instrument. The moderating effects of the instrument used to measure handedness also approached significance, Q (6) = 12.82, p = .081. Since the instrument used to measure handedness is of particular practical importance, this variable was examined further. An analysis of instrument with writing hand against all other instruments was performed. Writing hand is theoretically distinct

from all the other instruments, making such a comparison a rational choice. Moreover, it was the most frequent way to measure handedness in the present data set. The moderating effect of instrument when comparing writing hand (k_d = 51 data sets) with all the other instruments (k_d = 81 data sets) was significant, Q (1) = 8.36, p = .022, with the odds ratio for writing hand being OR = 1.16, *95% CI* = 1.10-1.23, and the odds ratio for the other measures combined being OR = 1.24, *95% CI* = 1.18-1.30. There remained moderate levels of heterogeneity within writing hand, Q (53) = 97.24, p < .001, I^2 = 45.50%, but no significant heterogeneity within the other measures, Q (80) = 88.27, p = .25, I^2 = 9.37%. As noted earlier, self-assessment can generally be assimilated to writing hand and thus these categories were also combined (k_d = 72) and contrasted with questionnaire studies (k_d = 46), yielding a significant effect, Q (1) = 5.93, p = .015; for writing hand and self-assessment, OR = 1.17 (*95% CI* = 1.12-1.22), and for the questionnaire measures, OR = 1.28 (*95% CI* = 1.21-1.35). Writing hand (and self-assessment), unlike questionnaire measures, lacks a bimanual component. Consistent with the lower odds ratio for writing hand (i.e., 1.17), a similar value was obtained when those studies (k_d = 11) employing a specific action which was unimanual were analysed, OR = 1.16 (*95% CI* = 1.01-1.34), with no significant heterogeneity, Q (10) = 5.90, p = .82, I^2 = .00%.

Publication year. Meta-regression of the year of publication of the studies revealed a significant linear trend in the size of the sex difference in handedness, Q (1) = 6.44, p = .010, (see Figure 2.3). The best-fitting linear relation between log odds ratio and year was:

$$ln(OR) = -.00199\ (year) + 4.213$$

equivalent to a decline in estimated odds ratio between 1927 and 2007 from 1.46 to 1.24.

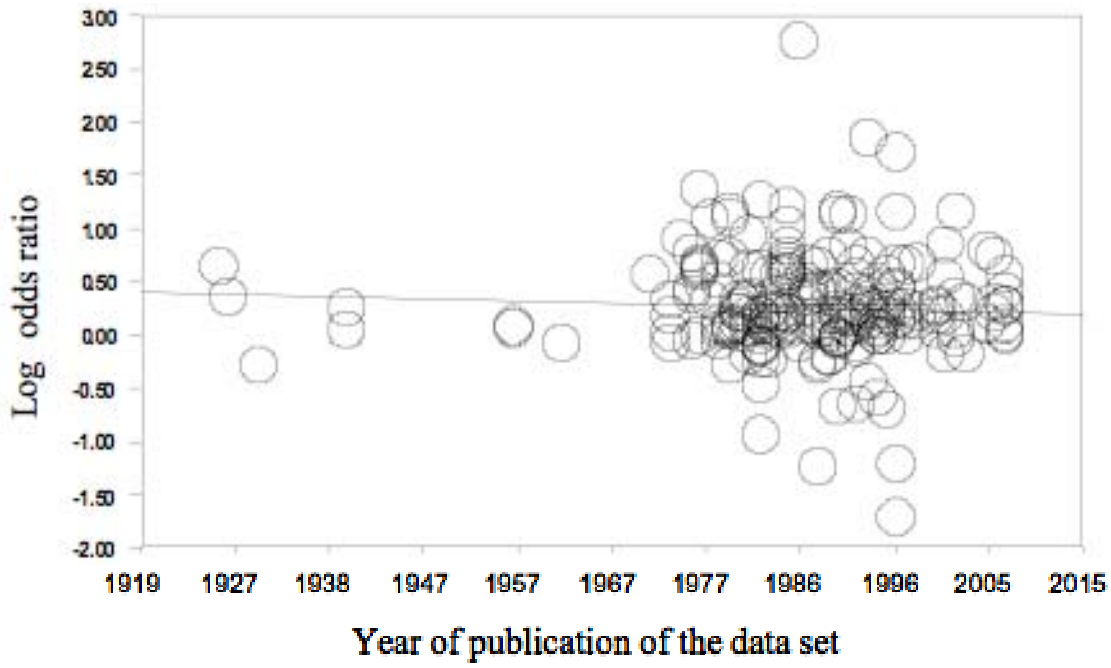

Figure 2.3. Meta-regression of the year of publication of the data set on log odds male-to-female ratio, for the left-handedness (total) comparison.

Other moderators. No significant moderating effects were found for the educational status of the participants, Q (1) = .57, p = .75; the type of response categories used, Q (3) = 2.37, p = .66; whether the main purpose of the study was to measure handedness, Q (1) = 1.02, p = .31; and whether the data were collected by self-report, Q (1) = 1.70, p = .43. Meta-regression on the number of questionnaire items did not reveal any significant effect either, Q (1) = .23, p = .63.

2.4 Discussion

The present meta-analysis includes data on 1,787,629 individuals (831,537 male, 956,092 female) extracted from 144 studies, divided into 208 separate data sets. Tests of ascertainment bias revealed that there was no evidence that the studies in the sample had been distorted by preferential reporting. The most comprehensive comparison, which included nearly all the

data sets, left-handedness (total), provided an estimate of 1.23 for the ratio of male-to-female left-to-right handedness odds, with a 95% confidence interval of 1.19 to 1.27. Moreover, a significant sex difference was detected in each of four other meta-analyses carried out on smaller sets of data. There was a trend towards the direction of the odds ratio increasing as the criterion for left-handedness becomes more lax, with estimates for male-to-female odds ratios ranging from 1.20 (95% *CI* 1.11-1.29) for the left-handedness (extreme) comparison (left-handers identified in data sets where an R-M-L classification was employed) to 1.24 (95% *CI* 1.19-1.30) for the left-handedness (forced choice) comparison (left-handers identified in data sets where an R-L classification was employed), and 1.31 (95% *CI* 1.16-1.48) for the mixed-handedness comparison (mixed-handers identified in data sets where an R-M-L classification was employed).

Over the whole sample, a small-to-moderate proportion of the variability across studies was found to be due to genuine heterogeneity rather than to chance. Three factors were found to significantly moderate the size of the sex difference odds ratio, namely, the way in which handedness had been assessed, the year of publication of the study, and the ancestry of the participants. The sex difference was larger when handedness was assessed using methods other than the recording of writing hand (or, equivalently, writing hand together with self-assessment); in earlier rather than later studies; and in East Asian rather than Caucasian and African samples.

The findings on the moderating effects on ancestry and publication year were not confounded, as all studies using oriental samples were published after 1976. Both results may be attributed to differential levels of cultural pressures (Harris, 1990; Provins, 1997), even though a genetic basis for the effect of ancestry cannot be precluded. Oriental cultures are known to exert strong pressures for social conformity, whereas Western societies are more tolerant

towards left hand use. The *OR*s here for the East Asian, Caucasian, and African groups were, respectively, 1.60, 1.22, and 1.31. The East Asian group comprised Japanese and Chinese participants, for whom pressure towards the use of the right hand has been previously reported (Medland et al., 2004). Additionally, across cultures, social pressures against the use of the left hand were stronger in past years than they are nowadays (see, e.g., Martin and Porac, 2007; Searleman and Porac, 2003).

However, for the results to be explained by social pressures, these would have to affect females more than males. This could be the case if (a) females are the recipients of stronger pressures or (b) females respond to these pressures differently and are more successful at switching over to the right hand (Harris, 1990). Further work may show whether such differences in response can be attributed to females either being generally more compliant than males (as shown by, e.g., Gabriel and Gardner, 1999; Van Vugt et al., 2007), or to females being more capable of switching, due to inherent properties related to their greater motoric maturity or to their underlying neurobiological organisation (as shown by, e.g., Boghi et al., 2006).

Further light may be thrown on the social pressure explanation by examining the odds ratios for different types of measuring instruments. Some activities are more likely to be the focus of social pressure than others. Writing with the left hand has been systematically discouraged, especially in the past (Hildreth, 1949), but possibly even today in some cultures. For the collection of other activities measured, not only is it unlikely that there is – or has been – any such prohibition, but there may even be encouragement to use the left hand. For example, in some sports such as cricket and baseball one could gain a competitive advantage as the opponent will have had less experience of left-handers. The effect is likely to be larger for males than females as more males engage in sport. Moreover, other activities included in handedness

questionnaires, in particular those involving both hands, are also unlikely to be influenced by social pressure. For example, sweeping with a broom, dealing playing cards, guiding a thread through the eye of a needle, and unscrewing the lid of a jar are all included in the AHPQ (1970, 2002). Thus, one might expect writing hand to show a lower odds ratio than other instruments that include a range of other activities, including sporting and bimanual activities. Indeed, when handedness is assessed by means of writing hand the sex difference takes its smallest value (male-to-female *OR* = 1.16) compared to the difference found by other instruments (male-to-female *OR* = 1.24). The present findings therefore suggest that it may be of future interest to compare explicitly the role of handedness in influencing the performance of unimanual versus bimanual activities in the two sexes. In addition to that, it could be the case that the lower odds ratio of the writing hand is due to the two types of hand use, verbal (writing and gesturing during speech) and nonverbal, resulting from separate etiologies, as suggested by Perelle and Ehrman (1983).

Other potential moderating factors that, despite their acclaimed effect in the incidence of handedness, do not seem to be sensitive with regards to sex differences, are: the educational status of the participants, the number of questionnaire items used, the type of response categories used, whether the main purpose of the study had been to measure handedness and whether the data were collected by self-report. No ascertainment bias was found to exist within the sex-difference literature, supporting the view that the cases where no difference is detected are not due to Type 1 errors, but rather that they should rather be attributed to the use of instruments that are not powerful enough to detect a sex difference in small samples.

The finding that only three variables account for all the heterogeneity among studies may seem counter-intuitive. Nonetheless, in examining meta-analytic data for effects of moderator variables the crucial characteristic is the

number of data sets (199 in this case for the left-handedness [total] comparison) and not the number of participants (over 1.5 million). This can result in a surprisingly low power of meta-analytic studies when it comes to examining moderating effects, despite the large numbers of participants (Hunter and Schmidt, 1990). Moreover, in examining the effect of each different moderator, not all data sets were included, but only those that reported pertinent information. Therefore, with the sample size of the present data set, only large effects could have been detected.

Only studies measuring hand preference were included in the present analysis. Studies measuring hand skill were excluded, as preference and skill represent two rather distinct concepts. Although there is a debate about the relative value of these two manifestations of handedness (Morgan and Corballis, 1978; Bishop, 1989), preference may be considered to be primary, because the presence of preference asymmetry in the absence of skill asymmetry has been demonstrated in children with autism (McManus et al., 1992). Moreover, there is some evidence of differences in hand preference but not in hand skill between individuals with schizophrenia or schizoaffective disorder and their unaffected relatives (DeLisi et al., 2002). Nevertheless, preference can be reliably correlated with measures of performance (Annett, 1976), even though these correlations are not perfect (.6 to .7; Todor and Doane, 1977); an upper limit on the magnitude of such correlations appears to be provided by the relatively low levels of reliability of measures of relative hand skill (Hiscock and Chapieski, 2004). This correlation does, however, allow for moderate assumptions that the results of the present meta-analysis can be informative with regards to sex differences in hand skill.

Another important distinction in handedness research is the distinction between direction versus degree of handedness (Dellatolas et al., 1997). Direction and degree of handedness have been given different biological and

psychological interpretations (McManus, 1983). The findings of a neuroimaging study using fMRI suggest that these aspects are independent and that they are coded separately in the brain (Dassonville et al., 1997). These two measures are, nevertheless, confounded in studies using statistical tests that are unable to differentiate between them, or that merely report the mean laterality score across their sample. Dissentagling direction from degree using meta-analytic methods would require studies using the same handedness questionnaires and reporting the number of females and males gaining each score. In the present meta-analysis, only direction of hand preference was taken into account, as limited information on the degree of hand preference was reported in the included studies. The closest the current meta-analysis approached the direction/degree question was the finding that the sex difference in left-handedness appears to lie upon a continuum; the stricter the criterion for left-handedness the lower the male-to-female odds ratio and thus the smallest the difference between the two sexes. Nevertheless, the *CIs* of these comparisons are largely overlapping, making it hard to draw conclusions.

Showing that a sex difference in handedness is present in every comparison representing different conceptions of left-handedness, as well as in all the levels of the different moderator variables, provides support for the theories that explain handedness with biological factors pertinent to sexual differentiation, namely genetic theories, hormonal theories, and theories on the rate of somatic maturation (see chapter 1 for a detailed description). Therefore, further investigation on the sex differences in handedness should be along the lines of those theories. It should be noted however, that genetic, maturational, and hormonal theories are not mutually exclusive. It could be the case that they focus on different aspects of the same phenomenon, maturation being intertwined with hormonal changes that are controlled by genetic factors, all resulting in the different neural organisation of the two sexes. Nevertheless,

suggesting that the sex differences are best explained by biological factors does not preclude the possibility that environmental factors could be moderating the size of male-to-female odds ratios in different populations. In fact, the findings of this meta-analysis provide evidence that social/cultural pressures do moderate the size of the sex differences in handedness.

Within the framework of the biological explanations of the sex effect in handedness considered earlier (i.e., genetic, maturational, and hormonal), the present findings could have deeper implications with regards to the genetic ones. The three genetic models of handedness that have made predictions for a sex difference are the differential RS hypothesis of Annett (2002), the modifier-gene theory of McManus and Bryden (1992), and the recessive model of Jones and Martin (2000).

The RS theory claims that the sex difference in handedness can be interpreted as due to the displacement of a chance distribution of asymmetry farther to the right in females than in males by about 20% (Annett, 1999). This estimate is indeed very close to the best estimate observed in the present meta-analysis coming from the left-handedness (total) comparison of 1.23 for the ratio of male-to-female left-to-right handedness odds, and falls within the *95% CI* of 1.19 to 1.27. Nevertheless, the sex difference is not integral in the RS theory, which could actually accommodate a sex difference of any degree, including none. Thus, insofar as the modifier-gene hypothesis makes an integral prediction of the occurrence of a sex-difference in handedness, it receives greater support from the present findings than does the differential RS theory. As noted by Roberts and Pashler (2000), the occurrence of observations that are consistent with a theory provides strong support for the theory only if the theory also prohibits the occurrence of alternative observations.

The present findings are particularly informative for the single-gene recessive model of Jones and Martin (2000). As with the modifier-gene

hypothesis, the recessive model's integral prediction of the existence of a sex difference receives significant support from the present findings. But for this model, there are quantitative as well as qualitative implications. The odds ratio predicted on the basis of the parameter values estimated for their recessive model by Jones and Martin (2000, 2001) takes the value of 1.70. Because the theoretical odds ratio lies outside the confidence intervals established here, it is apparent that reconsideration of this model is recommended.

Overall, the present meta-analysis provides a powerful test of the hypothesis of a sex difference in praxic lateralisation. It was shown using objective statistical procedures that the sex difference is robust for all the commonly used conceptions of left-handedness, with males having significantly greater odds of being left-handed than females (except, it appears, in Scandinavia). In addition, it has been shown that the possible range in the magnitude of the sex difference is sufficiently narrow to impose a significant new constraint on the quantitative genetic modeling of handedness. The size of the sex difference is moderated by means of the instrument used to measure handedness (writing hand or not), the ancestry of the participants, and the year of publication of the studies. The evidence reviewed here suggests that the sex difference in praxic lateralisation has its basis in innate biological differences between the two sexes but is also significantly modulated by environmental factors, such as culturally transmitted social influences.

The following chapters build upon the meta-analysis in the following ways: (a) by examining in an experimental manner another possible source of the sex difference in handendess which was not investigated directly in the meta-analysis, namely the claim that the two sexes have differential avoidance to extreme responses in hand preference inventories (chapter 3), (b) by studying the differential sensitivity of the different hand preference inventories in detecting the sex difference in praxic lateralisation, while including hand skill tests and

other LIs, such as footedness and eyedenss, the inclusion of which was beyond the scope of the meta-analysis (chapter 4), and (c) by investigating empirically the finding that the sex difference in lateralisation has its basis in innate biological differences between the two sexes, by focusing on the relationship of T levels with praxic and linguistic lateralisation (chapters 5 and 6).

Chapter 3

Psychometric properties of different response formats of hand preference inventories

3.1 Introduction

Handedness, the most important manifestation of manual praxic lateralisation and an indirect index of linguistic lateralisation in the brain, is sexually dimorphic as shown by the large-scale meta-analysis including over 1.7 million participants described in chapter 2. Males were found to have greater odds of being left-handed than females for all the commonly used conceptions of left-handedness, with the best estimate of a male-to-female odds ratio being 1.23.

One of the factors that have been suggested to produce this sex difference in handedness is the use of a graded response format in hand preference inventories, following the rationale that the two sexes have different reactions to the wording of the responses allowed (Bryden, 1977). Bryden studied 1107 undergraduate students (620 males and 487 females) using the 14-item Crovitz-Zener Questionnaire (Crovitz and Zener, 1962) with a 5-point graded response format as well as the 10-item EHI (Oldfield, 1971) in its original graphic graded response format. He found that males avoid giving extreme responses in hand preference inventories and that they are inclined to report to

“usually” do something with their right or left hand rather than “always”. Given that there are more right-handers than left-handers in the population, this criterion shift is suggested to produce the increase in the mean laterality score for females that generates the sex difference. However, Bryden’s conclusion did not fit with Lansky et al.’s (1988) data comparing 1741 Whites and 342 Blacks[7] for hand preference, except when looking at the Black participants alone. Lansky et al. (1988) used a 5-item questionnaire and the format of each of the questions was the following: “With which hand do you (e.g.) write with? Is it your left hand, right hand, or do you write equally often with either hand?” If the response was “right” hand or “left” hand, the second part of the question was: “Do you write with your right (left) hand most of the time, or all of the time?”. Bryden’s claim could further not explain the results, even for Black participants, of the Saunders and Campbell study of 281 American and Caribbean students at Howard University (Saunders and Campbell, 1985). These authors noted that the variances of the males’ scores were significantly larger than the females’ scores, with the female’s scores being more localised at the right end of the scale.

The possible moderating effects of the type of response categories employed by the different hand preference inventories were investigated in chapter 2’s meta-analysis. Four groupings were employed, namely binary response format, 3-point scale graded response format, 5-point scale graded response format, and the graphic graded response format. It was shown that the response category used does not significantly moderate the magnitude of the sex difference in a significant manner. Nonetheless, the claim that the two sexes have differential avoidance to extreme responses of a hand preference inventory was not directly investigated. This is a slightly, but essentially, different issue to

[7] *Whites* and *Blacks* are terms used by Lansky et al. in their 1988 paper.

comparing handedness incidences between studies that employed questionnaires using different response formats.

One might argue that if the studies using inventories with a 5-point graded or the graphic graded response format (both of them providing 5 response choices) are found to produce a lower male-to-female odds ratio of left-handedness, compared to the inventories using a binary response format, this might be enough evidence that males avoid giving extreme responses. However, this comparison would have been problematic using the data sets of chapter 2's meta-analysis, the reason being that the majority of the data sets that used a binary response format corresponded to participants having been classified according to writing hand (k_d = 22 data sets) or by self-classification (k_d = 4 data sets), or to participants having been observed while carrying out an action, like playing tennis (k_d = 4 data sets). In other words, for the most part, the binary response group of the meta-analysis consisted of studies which had not used hand preference inventories. Even if the latter were the case, a conclusion with regards to males avoiding giving extreme responses could still not have been reached by means of the moderator analysis of the meta-analysis, as the odds ratio of the binary response format (*OR* = 1.26) lies between the OR for the 5-point graded response format (*OR* = 1.22) and the graphic graded response format (*OR* = 1.34).

Moreover, the crucial characteristic for the moderating variables' analysis within the meta-analytic framework as mentioned in chapter 2 is the number of included data sets and not the number of participants in the included studies (Hunter and Schmidt, 1990). Additionally, when examining the moderating effect of each different moderator, not all data sets can be included, but only those that report pertinent information. Thus, in the case of the moderating effects of the response category used, only 143 data sets were used out of the 208 data sets of the meta-analysis in question. Therefore, only large effects could have

reached significance. Moreover, in the meta-analysis the male-to-female odds ratios were compared between studies, each study employing only one of the response formats, thereby possibly allowing other moderators, such as length or type of questionnaire used to confound the results. A within-subjects design would be more suitable for comparing the different reactions of the two sexes to the wording of a hand preference questionnaire.

Apart from having been proposed as a contributing factor to the sex differences in handedness, another interesting property of different response formats is the way they translate into each other. McMeekan and Lishman (1975), for example, compared the 10-item EHI using its original graphic graded response format, with the 12-item AHPQ using a 3-point graded response format. They employed a within-subjects design with 617 participants, even though the order of presentation of the two questionnaires does not appear to have been counterbalanced across the sample. McMeekan and Lishman (1975) found that a number of participants who had answered “right” or “left” on the AHPQ put the equivalent of “either” against the same item on the EHI. They claimed that this is due to the different instructions given in the two questionnaires, with the AHPQ discouraging an “either” response by asking “Which hand do you use?”, whereas the EHI, states “… if in any case you are really indifferent put + in both columns”. Williams (1991) also compared the 10-item EHI, which was administered to 161 students in the University of Sussex, with the 12-item AHPQ, which was administered to 111 students at the University of Ulster. Similarly to McMeekan and Lishman (1975), Williams found that more “either” responses and fewer “left” responses were given for the EHI than for the AHPQ. Williams used a between-subjects design, whereby he did not directly compare the responses of the same participants.

Response schemes have also been shown to yield different reactions between handedness groups. Peters (1998) reanalysed data from the Peters

and Murphy (1993) paper and focused on the responses that the participants made in a binary response format against the same items for which they gave an "either" response when the same inventory was administered using a 5-point graded response format. The clear majority (78.85%) of the 525 right-handed writers who answered "either" hand on the 5-point scheme chose "right" on the binary response format. Similarly, the majority (81.81%) of the 74 left-handed writers preferred to choose a "left" in the place of an "either" response. Based on the above findings, it could be claimed that Bryden's (1977) finding could actually be due to the fact that it is left-handers of both sexes who avoid giving extreme answers and at the same time there are more left-handers within the male population.

Surprisingly, no studies to date have systematically investigated the effect of different response formats of hand preference inventories, while controlling for both handedness and sex. The present study was designed to do just that. Moreover, previous studies had small samples of left-handed participants. For example, Bryden in his 1977 study used a random sample, where only 14.68% of the male participants and 11.91% of the female participants were left-handed. Here, left-handers were specifically encouraged to participate, resulting in a large sample of left-handed participants.

The primary interest was to directly test the claim that the two sexes have different reactions to graded response formats. A number of other effects pertinent to the response format of a hand preference questionnaire were also investigated. More specifically, it was investigated whether an "either" response is translated differently into a binary response format according to the handedness and/or the sex of an individual. It was further investigated whether the EHI in its 5-point graded response format differs significantly in producing "either" responses to the EHI in its graphic graded response format. The graphic graded response format of the EHI has been directly compared in the past only

to the AHPQ using a 3-point graded response format (Williams, 1991). Hence, comparing the two response formats under the same set of questions seems to be filling another gap in the literature.

A within-subjects design was employed here, an improvement to the methodology used by Bryden (1977). It has been claimed that such a design may diminish real differences between questionnaires, following the rationale that participants will strive for consistency in their responding (Williams, 1991). However, consistency is not an issue when investigating the way an “either” response is translated into a binary response questionnaire, because both possible responses (“left” or “right”) are equally consistent. Similarly, if one chooses a “right” answer in the binary response format, then any response among “either”, “usually right”, and “always right” are equally consistent, as long as one does not go all the way to “usually left” or “ always left” (and vice versa for a “left” response in a binary response questionnaire). Moreover, in order to control for the possible effects of order of testing, the order of the two versions of the questionnaire was counterbalanced across participants, which was not the case for all the previous studies (e.g., McMeekan and Lishman, 1975).

The following hypotheses were tested:

(a) There is no sex difference in the avoidance of extreme responses.

(b) Left-handers avoid giving extreme responses compared to right-handers.

(c) Left-handers prefer to use a “left” response in a binary response format in the place of an “either” response in a 5-point graded response format and right-handers prefer to use a “right” instead of an “either” response regardless of their sex.

(d) The graphic graded response format of EHI produces more “either” responses than the 5-point graded response format.

3.2 Method

The study was reviewed by, and received ethics clearance through the Central University Research Ethics Committee (CUREC) of the University of Oxford. Maintenance of confidentiality of information is subject to normal legal requirements.

3.2.1 Participants

Two hundred volunteers (50 male right-handers, 50 female right-handers, 50 male left-handers, and 50 female left-handers; handedness groups according to writing hand) took part in the present study. Participants were undergraduate and graduate students enrolled in the University of Oxford (*mean age* = 22 years., *SD* = 3, *range* = 18-31). Participants were reimbursed for their time with either course credit (Research Participation Scheme [RPS][8] participants) or with 5 pounds in cash (all the rest).

3.2.1.1 Inclusion/Exclusion criteria

All participants underwent screening before being enrolled in the study. Exclusion criteria included participants being free of any neurological problems (e.g., epilepsy, meningitis, encephalitis, multiple sclerosis, stroke) and of any medical conditions interfering with hand function (e.g., arthritis), and to be native, monolingual English speakers. Screening was done by e-mail, using a short questionnaire, which was send as an e-mail attachment (see Appendix 3.1).

[8] The RPS is an on-line system that allows researchers to list the experiments on offer, display times of availability, credit students for taking part in their experiments, etc. Likewise, participants/students can view the details of experiments, book to take part in experiments, view their existing experimental credits and engagements, etc.

Participants completed the questionnaire in their own time and e-mailed it back to the researcher.

3.2.1.2 Recruitment

Participants were recruited in the following ways:

(i) Through the Department of Experimental Psychology's RPS.

(ii) Through posters that were be put up throughout the University campus.

(iii) Through e-mails sent to different mailing lists of the University's Departments and Colleges.

(iv) Through advertisements placed on the web pages *www.dailyinfo.co.uk* and *www.facebook.com*.

When the potential participants contacted the researcher declaring their interest to participate, they were sent the information sheet for the study (see Appendix 3.2) and were screened for suitability to participate via the e-mail questionnaire described above. The day and time of testing was then agreed upon.

3.2.2 Instruments

Two versions of the same inventory were administered to the participants (see Appendix 3.3 for the full list of items). The inventory included the items from the 12-item AHPQ (Annett, 1970), the 10-item EHI (Oldfield, 1971), the 68-item Waterloo Handedness Questionnaire (WHQ; Steenhuis and Bryden, 1989), and the 55-item Healy, Liederman, and Geschwind Inventory (HLGI; Healy et al., 1986). The first version of the inventory also included the graphic graded response format version of the EHI (see Appendix 3.4). The original wording of the items was retained except where too much repetition would have occurred due to the overlap of content among questionnaires.

The first version of the inventory had a binary response format, whereby participants were asked to indicate which hand they habitually use for each of the listed activities by circling *R* (for right hand) or *L* (for left hand). The second version used a 5-point graded response format, whereby participants were asked to choose between the following options: If they always use one hand to perform the described activity, they were asked to circle *Ra* or *La* (for right always and left always). If they usually use one hand they were asked to circle *Ru* or *Lu* (for usually right or usually left), as appropriate. If they use either hand equally often, they were asked to circle *Ei.*

The following instructions were given to the participants in writing, but were also verbally repeated by the researcher:

> Please take your time to read the instructions carefully and answer the following questions. Do not simply circle one answer for all questions, but imagine yourself performing each activity in turn, then mark the appropriate answer. If necessary, stop and pantomime the activity.

3.2.3 Procedure

Participants were tested individually in a quiet room. The study was explained as soon as they arrived and they were encouraged to ask questions. They gave written informed consent before taking part in the study, but were explicitly told they remained free to leave at any time and without having to give any reason for doing so. The consent form was signed in two copies so that the participants could keep one for their own records. Testing took place in the Department of Experimental Psychology, University of Oxford.

Participants filled out the two inventories in the company of the experimenter and were instructed to take as much time as they needed, but not to think too much about each item. The two versions were completed one after

the other with the order of administration counterbalanced within sex and handedness groups.

All participants were debriefed after the completion of the study.

3.2.4 Scoring

For the binary response format version of the inventory, hand preference scores were derived by calculating the percentage of right hand responses, therefore giving a laterality index (LI) varying from 0 (extreme left-handedness) to 100 (extreme right-handedness). For the 5-point graded response format version, the score was calculated by giving a value of 0 to an “always left”, 1 to a “usually left”, 2 to a “both equally”, 3 to a “usually right”, and a value of 4 to an “always right” response, adding up the score for all items for each participant, dividing by the maximum score and multiplying by 100. A LI ranging from 0 (extreme left-handedness) to 100 (extreme right-handedness) was obtained for each participant. The graphic graded response format version of the EHI was scored separately following the procedure described by Oldfield (1971): the crosses under the “left” and the “right” columns were added up and then the score for the left hand was subtracted from the score for the right hand, divided by the sum of both and multiplied by 100, thus giving a LI varying from -100 (extreme left-handedness) to 100 (extreme right-handedness).

3.2.5 Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) v.14. The correlation coefficients between the different questionnaires were calculated using Spearman’s rank correlation coefficient, r_s, (formerly rho [ρ]), the non-parametric equivalent of Pearson’s *r,* as the data did not follow a normal distribution. Spearman’s r_s addresses how well an arbitrary monotonic function could describe the relationships between two variables without

making any assumptions about the frequency distributions or the variables. In order to investigate the working hypotheses, analysis of variance (ANOVA) was performed as the number of data points was sufficient for parametrical testing (n_m = 100 for males and n_f = 100 for females; MacCallum et al., 2001). Sex and handedness for writing hand were the between-subjects factors. The following variables were employed as within-subjects factors for different analyses: questionnaire type, percentage of "either" or "extreme" responses, direction of translation between the two response formats, and responses category. The partial eta squared (η^2) statistic was used as the effect size measure. The η^2 statistic describes the proportion of total variability attributable to a factor, by dividing the sum of squares between groups by the sum of squares total.[9] Post-hoc tests were run using pairwise comparisons with the Least Significant Difference (LSD) adjustment. Moreover, chi-square (χ^2) analysis was performed, crosstabulating the number of extreme responses for the EHI graphic graded response format with sex or handedness for writing hand. All *p*-values were two-tailed and the *a*-level was set at .05.

3.3 Results

One person failed to complete the graphic graded response EHI. The count of the participants classified as left- and right-handers by the different questionnaires for both response formats is shown in Table 3.1. A participant with a LI score of less than or equal to 50 was classified as left-handed and a participant with a LI greater than 50 was classified as right-handed. Table 3.2 shows the distribution of the graded responses for both sexes.

[9] If there is no error variance, then the sum of squares between equals the sum of squares total and η^2 = 1. If all the groups means are equal, then sum of squares between groups equals zero and η^2 = 0. In the former case, 100% of the variance is explained by the factor; in the latter case, 0% of the variance is explained by the factor.

Table 3.1. Number of participants classified as left- and right-handers by the different questionnaires for both the binary and the graded response formats.

	Binary response format				Graded response format			
	Males (n_m = 100)		Females (n_f = 100)		Males (n_m = 100)		Females (n_f = 100)	
Questionnaire	**Left-handed (LQ≤50)**	**Right-handed (LQ>50)**	**Left-handed (LQ≤50)**	**Right-handed (LQ>50)**	**Left-handed (LQ≤50)**	**Right-handed (LQ>50)**	**Left-handed (LQ≤50)**	**Right-handed (LQ>50)**
AHPQ	43	57	43	57	43	58	43	57
EHI	47	53	44	56	48	52	46	54
WHQ	40	60	39	61	41	59	42	58
HLGI	40	60	42	58	48	52	46	54

Table 3.2. Distribution of responses on the different handedness questionnaires using the 5-point graded response format.

	Males (n_m = 100)					Females (n_f = 100)				
Questionnaire	**% left always**	**% left usually**	**% either**	**% right usually**	**% right always**	**% left always**	**% left usually**	**% either**	**% right usually**	**% right always**
AHPQ	23.83	15.17	7.00	20.58	33.33	26.17	12.08	6.92	21.58	33.08
EHI	25.70	13.40	6.70	19.90	31.20	28.10	10.10	6.50	19.00	36.2
WHQ	14.94	19.82	15.88	30.25	18.76	14.19	16.06	15.21	28.19	26.09
HLGI	20.76	16.16	9.31	26.42	27.07	19.51	12.49	9.96	25.24	32.67
Mean	21.31	16.14	9.72	24.29	27.59	21.99	12.68	9.65	23.50	32.01

	Males (n_m = 99)					Females (n_f =100)				
Questionnaire	**++ left column**	**+ left column**	**+ right and left columns**	**+ right column**	**++ right column**	**++ left column**	**+ left column**	**+ right and left columns**	**+ right column**	**++ right column**
EHI graphic	17.27	22.02	9.60	28.18	22.93	16.70	19.60	9.20	29.90	24.60

3.3.1 Relationships between different questionnaires

The correlation coefficients between the different questionnaires were calculated using Spearman's r_s. Correlations varied from .88 to .98 and were all highly significant (all $p < .001$). The average correlation between the two versions of the same questionnaire (average $r_s = .93$, $SD = .01$, $n_q = 4$) was comparable to the average correlation among the binary response versions of all four questionnaires (average $r_s = .93$, $SD = .03$, $n_q = 6$) and all the 5-point graded response versions of the four questionnaires (average $r_s = .94$, $SD = .03$, $n_q = 6$). Thus, the rank order of participants in terms of their hand preference score was not significantly dependent upon the questionnaire used or upon the response format employed.

3.3.2 Translation of "either" responses to the binary response format

Table 3.3 summarizes the way right- and left-handers translated "either" responses in a 5-point graded response format questionnaire to "right" or "left" responses in a binary response format questionnaire. A 4 x 2 x 2 x 2 repeated measures ANOVA was performed with percentage of "either" responses for each questionnaire type (AHPQ, EHI, WHQ, and HLGI) and direction of translation ("either to left" and "either to right") as the within-subjects factors. Sex (male or female) and handedness for writing hand (right or left) were the between-subjects factors. There was a significant main effect of questionnaire type, F (3,196) = 84.18, $p < .001$, $\eta^2 = .30$. The WHQ produced more "either" responses (mean percentage of "either" responses = 15.55%, $SE = .82$) compared to the AHPQ (mean percentage of "either" responses = 6.92%, $SE = .63$), EHI (mean percentage of "either" responses = 6.60%, $SE = .62$) and the HLGI (mean percentage of "either" responses = 9.62%, $SE = .57$). Pairwise comparisons using the LSD adjustment revealed that the difference in means

Table 3.3. Translation of "either" responses to binary "right" or "left" responses.

	Left-handers (n_l = 100)		Right-handers (n_r = 100)	
Questionnaire	**Either to left (%)**	**Either to right (%)**	**Either to left (%)**	**Either to right (%)**
AHPQ	4.42	3.08	1.50	4.92
EHI	4.10	3.30	1.30	4.50
WHQ	11.97	5.69	0.94	12.37
HLGI	6.78	5.02	1.09	6.25

between all questionnaire pairs was significant (all $p < .001$) except for the two shortest questionnaires' pair, the AHQP and EHI pair ($p = .39$). Moreover, there was a significant main effect of handedness, F (1,196) = 7.05, $p = .011$, $\eta^2 = .04$, with left-handers giving more "either" responses (mean percentage of "either" response = 11.10%, $SE = .77$) than right-handers (mean percentage of "either" responses = 8.24%, $SE = .77$). A significant interaction between questionnaire type and handedness was also found, F (3,196) = 3.96, $p = .008$, $\eta^2 = .02$ (see Figure 3.1). There was also a main effect of direction of translation, F (3,196) = 10.81, $p = .001$, $\eta^2 = .05$, with more "either" responses being translated into "right" ones (5.64%, $SE = .43$) than "left" ones (4.01%, $SE = .29$). Moreover, there was a significant interaction between direction of translation and handedness, F (3,196) = 70.93, $p < .001$, $\eta^2 = .27$, as well as 3-way interaction of Questionnaire Type x Direction of Translation x Handedness, F (3,196) = 45.81, $p < .001$, $\eta^2 = .19$ (see Figure 3.2). No other main effects or interactions were significant (all $p > .10$).

The 3-way interaction was further investigated by running two 4 x 2 repeated measures ANOVAs with questionnaire type (AHPQ, EHI, WHQ, and HLGI) and direction of translation ("either to left" and "either to right")

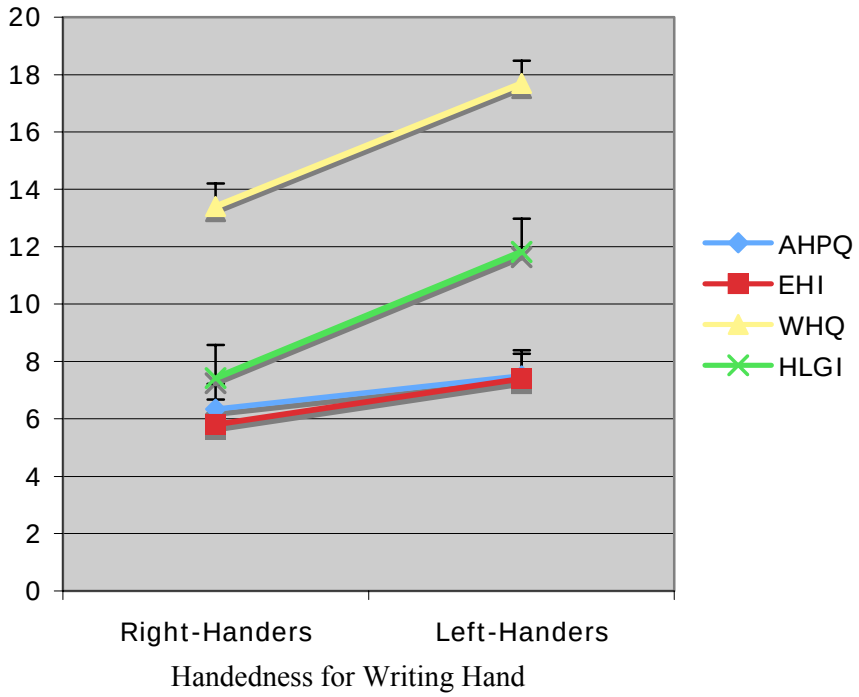

Figure 3.1. Schematic representation of the two-way interaction of Questionnaire Type x Handedness for percentage of "either" responses. Error bars show the standard error (σ_M).

separately for right- and left-handers.

For right-handers, there was a significant main effect of questionnaire type, F (3,99) = 31.61, p < .001, η^2 = .24, with the EHI having the lowest percentage of "either" responses (2.90%, SE = .44), followed by the AHPQ (3.21%, SE = .45), the HLGI (3.67%, SE = .40) and the WHQ (6.65%, SE = .58). Pairwise comparison using the LSD adjustment, showed that the WHQ was significantly different from the other three questionnaires with regards to the mean percentage of "either" responses produced (all p < .001), whereas the rest of the questionnaire pairs were not significantly different from each other (all p > .06). There was a further significant main effect of direction of translation, F (3,99) = 85.47, p < .001, η^2 = .47, with significantly more "either" responses in a 5-point graded response format being translated into a "right" response in a

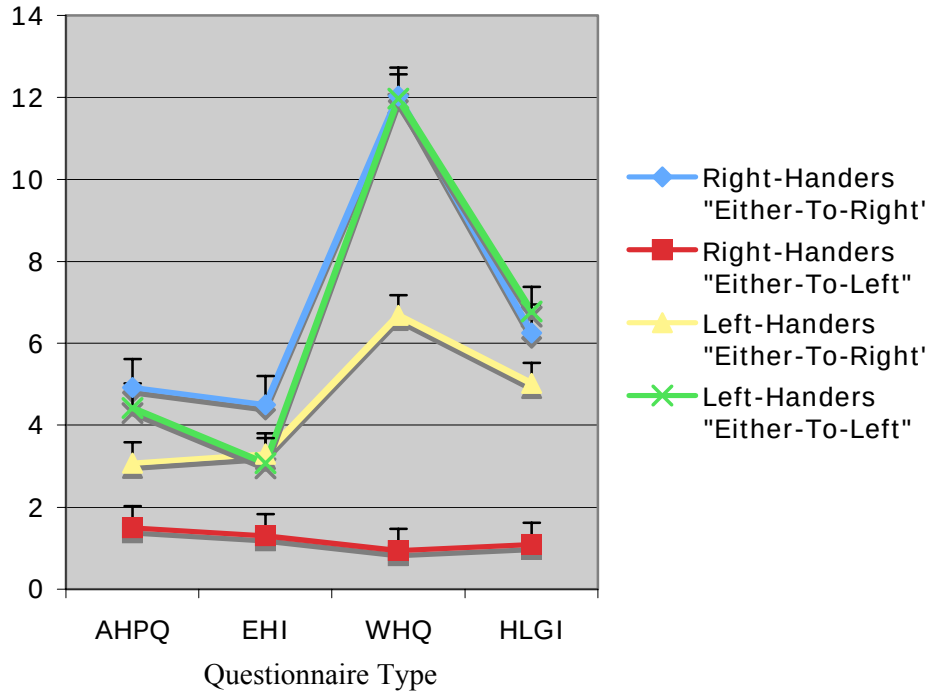

Figure 3.2. Schematic representation of the three-way interaction of Questionnaire Type x Direction of Translation x Handedness for the translation of "either" responses to the binary response format. Error bars show the standard error (σ_M).

binary questionnaire (7.01%, *SE* = .63) than into a "left" response (1.21%, *SE* = .22). Moreover, there was an interaction between questionnaire type and direction of translation, F (3,99) = 46.81, $p < .001$, $\eta^2 = .32$. The interaction was followed up with two one-way ANOVAs with four levels, with questionnaire type (AHPQ, EHI, WHQ, and HLGI) as the within-subjects factor, separately for the two directions. Results were not significant for the "either to left" direction (p = .39), but they were significant for the "either to right" direction, F (1,99) = 46.09, $p < .001$, $\eta^2 = .32$. Pairwise comparisons using the LSD adjustment showed that the mean difference in producing "either" responses that were translated into "right" ones was significant for all questionnaire pairs (all $p < .047$), apart from the two shortest ones' pair, the AHPQ and the EHI pair (p = .33).

For left-handers, results were similar: There was a significant main effect of questionnaire type, F (3,99) = 55.48, p < .001, η^2 = .36, with the EHI having the lowest percentage of "either" responses (3.70%, *SE* = .45), followed by the AHPQ (3.75%, *SE* = .44), the HLGI (5.95%, *SE* = .44) and the WHQ (8.83%, *SE* = .62). Pairwise comparisons using the LSD adjustment showed that the mean difference in producing "either" responses was significantly different for all questionnaire pairs (all p < .001), apart from the two shorter ones, the AHPQ and EHI pair (p = .85). There was further a significant main effect of direction of translation, F (3,99) = 11.00, p = .001, η^2 = .10, with more "either" responses being translated into a "left" response (6.82%, *SE* = .55) than a "right" response (4.27%, *SE* = .57) in a binary questionnaire. Moreover, there was an interaction between questionnaire type and direction of translation, F (3,99) = 11.22, p < .001, η^2 = .10. The interaction was followed up with two one-way ANOVAs with four levels, with questionnaire type (AHPQ, EHI, WHQ, and HLGI) as the within-subjects factor, separately for the two directions. Results were significant for both the "either to left" direction, F (3,99) = 43.32, p < .001, η^2 = .31, and the "either to right" direction, F (1,99) = 8.74, p < .001, η^2 = .08. Pairwise comparisons using the LSD adjustment showed that, for the "either to left" direction, the mean difference in producing "either" responses that were translated into "left" ones was significant for all questionnaire pairs (all p < .001), apart from the two shortest ones, the AHPQ and EHI pair (p = .51). For the "either to right" direction, the mean differences were significant for all pairs (all p < .01), apart from the two shortest ones, the AHPQ and the EHI pair (p = .49) and the two longer ones the WHQ and HLBI pair (p = .15).

In summary, left-handers produced more "either" responses (mean "either" responses = 11.10%) than right-handers (mean "either" responses = 8.24%). The two handedness groups further differed with regards to the way "either" responses were translated into a binary format: right-handers gave

significantly more “right” responses (7.01%) than “left” responses (1.21%), whereas left-handers gave more “left” responses (6.82%) than “right” responses (4.27%). This effect seems to be much stronger for right-handers (η^2 = .47) compared to left-handers (η^2 = .10). In other words, it is not unlikely for left-handers to give a “right” response in the place of an “either“ response, but is rather unlikely for right-handers to give a “left” response in the place of an “either” response. This was tested statistically with a univariate ANOVA, comparing the mean percentage of responses in a 5-graded response format questionnaire that were “either” hand and were subsequently translated into a “left” response for right-handers to mean percentage of responses in a 5-graded response format questionnaire that were “either” hand and were subsequently translated into a “right” response for left-handers. There was a significant difference, F (1, 199) = 36.75, p < .001, η^2 = .16. When testing the difference in the way the two handedness groups translate “either” responses in favour of their writing hand (i.e., right-handers to “right” and left-handers to “left”), no difference was found, F (1.99) < .01. p = .96, η^2 < .01.

3.3.3 Extreme responses

“Always right” and “always left” were considered to be extreme responses in the 5-point graded response format. They were added up and a percentage of extreme responses was calculated for each questionnaire. A 4 x 2 x 2 repeated measures ANOVA was performed with percentage of “extreme” responses for each questionnaire type (AHPQ, EHI, WHQ, and HLGI) as the within-subjects factor and sex (male or female) and handedness for writing hand (right or left) as the between-subjects factors. There was a significant main effect of questionnaire type, F (3,196) = 284.84, p < .001, η^2 = .59, in the percentage of extreme responses. The EHI produced more extreme responses (mean

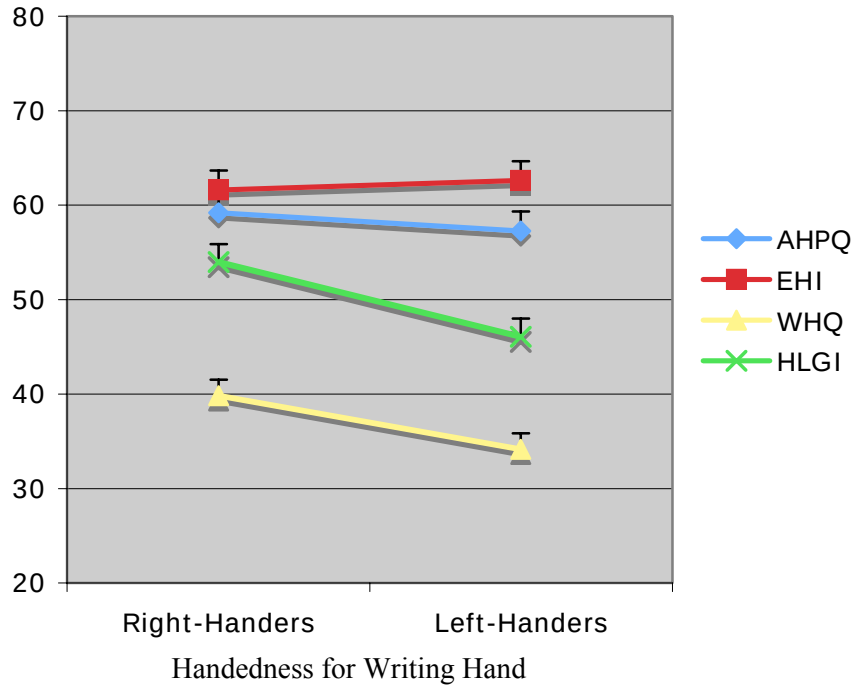

Figure 3.3. Schematic representation of the two-way interaction of Questionnaire Type x Handedness for percentage of "extreme" responses. Error bars show the standard error (σ_M).

percentage of extreme responses = 62.10%, *SE* = 1.45) compared to the AHPQ (mean percentage of extreme responses = 58.21%, *SE* = 1.47), the HLGI (mean percentage of extreme responses =50.01%, *SE* = 1.36), and the WHQ (mean percentage of extreme responses = 36.99%, *SE* = 1.21). Pairwise comparisons showed that all questionnaires differed significantly from each other (all $p < .001$). A significant interaction was also found for questionnaire type and handedness, F (3,196) = 8.96, $p < .001$, $\eta^2 = .04$ (see Figure 3.3). No other main effects or interactions were significant (all $p > .15$).

The interaction was followed up with four univariate ANOVAs, run separately for each questionnaire type with handedness (right or left) as the between subjects factor. Handedness was not found to be significant for the AHPQ ($p = .52$) and the EHI ($p = .73$), but it was significant for the longer questionnaires, the WHQ, F (1,198) = 5.38, $p = .021$, $\eta^2 = .03$ (mean percentage

of “extreme” responses for right-handers = 39.82%, *SE* = 1.72; for left-handers = 34.16%, *SE* = 1.72) and the HLGI, F (1,198) = 8.38, p = .004, η^2 = .04 (mean percentage of “extreme” responses for right-handers = 53.95%, *SE* = 1.93; for left-handers = 46.07%, *SE* = 1.93).

3.3.4 EHI graphic graded response format

The number of “always left” and “always right” responses given for the EHI graphic graded responses format were added up to form the “extreme” responses category and the number of “usually left” or “usually right” responses were added up to form the “less extreme” responses category. A 2 x 2 x 2 repeated measures ANOVA was performed with response category (“extreme” or “less extreme”) as the within-subjects factor and sex (male or female) and handedness for writing hand (right or left) as the between-subjects factors. There was a significant main effect of response category, F (1,195) = 128.69, p < .001, η^2 = .40. The “extreme” responses category had a significantly larger count (mean number of “extreme” responses = 6.21, *SE* = .15) than the “less extreme” responses category (mean number of “less extreme” responses = 3.12, *SE* = .13). No other main effects or interactions were found (all p > .10).

Results were further analysed following Bryden’s (1977) methodology,[10] in order to see if his results can be replicated in the present data set. Bryden run χ^2 analysis with the “extreme” response category crosstabulated with sex separately for each of the items. It was found that on five items females were more likely to use extreme response categories than were males, namely on the

[10] Bryden (1977) analysed separately each of the 16 items he used in his study (based on the 10-item EHI and the 14-item Crovitz-Zener questionnaires, which nevertheless had most of their items overlapping). His paradigm was followed only for the 10 items of the EHI (in the graded responses format as used by Bryden) and not for the whole 100 items used in the present study. This was considered necessary in order to avoid possible Type 1 errors, stemming from the huge number of statistical comparisons.

use of scissors, toothbrush, knife without fork, striking a match, and opening the lid of a box. On four items males were more likely to use extreme categories, namely writing, throwing, using a spoon, and upper hand on broom. For one item, drawing, both sexes gave the same number of extreme responses. Only for two of the items were these differences statistically significant: scissors, χ^2 (1) = 16.86, p = .002 (with 33% of males and 62% of females giving extreme responses), and throwing, χ^2 (1) = 10.17, p < .001 (with 50% of males and 28% of females giving extreme responses).

The same type of analysis was then run, this time crosstabulating the number of "extreme" responses with handedness, in order to test the hypothesis that it is left-handers of both sexes that avoid giving extreme responses. On 6 items, right-handers were more likely to use the extreme categories than were left-handers, namely writing, throwing, scissors, knife without a fork, striking a match, and opening the lid of a box. On 3 items left-handers were more likely to use extreme categories, namely drawing, using a spoon, and upper hand on broom. For one item, toothbrush, both handedness groups gave the same number of extreme responses. For four of the items these differences were statistically significant, all of the items describing actions for which right-handers are more likely to give extreme responses: throwing, χ^2 (1) = 5.38, p = .025 (with 47% of right-handers and 31% of left-handers giving extreme responses), scissors, χ^2 (1) = 4.51, p = .047 (with 55% of right-handers and 40% of left-handers giving extreme responses), knife without a fork, χ^2 (1) = 7.88, p = .008 (with 45% of right-handers and 26% of left-handers giving extreme responses), and sticking a match, χ^2 (1) = 6.83, p = .014 (with 33% of right-handers and 17% of left-handers giving extreme responses).

3.3.5 Comparison between EHI graphic graded and 5-point graded response formats

Table 3.4 compares the number of "either" responses produced by each item for the EHI using the 5-point graded response format and for the EHI graphic graded response format (i.e., the number of times a cross was placed under both the "left" and "right" columns). A 2 x 2 x 2 repeated measures ANOVA was performed with percentage of "either" responses for each questionnaire type (EHI graded response or EHI graphic graded response formats) as the within-subjects factor and sex (male or female) and handedness for writing hand (right or left) as the between-subjects factors. There was a significant main effect of questionnaire type, F (1,195) = 13.52, $p < .001$, $\eta^2 = .07$, in the count of "either" responses. The EHI in its graphic graded response format produced significantly more "either" responses (mean percentage of "either" responses = 9.50%, SE = .81) than the EHI with a 5-point graded response format (mean percentage of "either" responses = 6.58%, SE = .62). Moreover, there was a marginal main effect of sex, F (1,195) = 3.91, $p = .049$, $\eta^2 = .02$, with males producing more "either" responses (mean percentage of "either" responses = 9.23%, SE = .85) than females (mean percentage of "either" responses = 6.85%, SE = .85) and a significant main effect of handedness, F (1,195) = 5.91, $p = .016$, $\eta^2 = .03$, with left-handers producing more "either" responses (mean percentage of "either" responses = 9.50%, SE = .85) than right-handers (mean percentage of "either" responses = 6.58%, SE = .65). Furthermore, there was an interaction of questionnaire type and sex, F (1,195) = 7.82, $p = .006$, $\eta^2 = .04$ (see Figure 3.4). No other main effects or interactions were significant (all $p > .11$).

The interaction was followed up with two univariate ANOVAs, run separately for the EHI in its 5-point graded response format and the EHI in the graphic graded response format, with sex (male or female) as the fixed factor.

Table 3.4. Number of "either" responses to each item of the EHI in its graphic graded and 5-point graded response formats.

Item	Edinburgh Graphic Graded Response Format	Edinburgh 5-Point Graded Response Format
Writing	0	0
Throwing	9	5
Match	14	10
Scissors	11	10
Broom	51	43
Toothbrush	21	21
Lid	59	25
Draw	0	1
Knife	10	9
Spoon	12	8

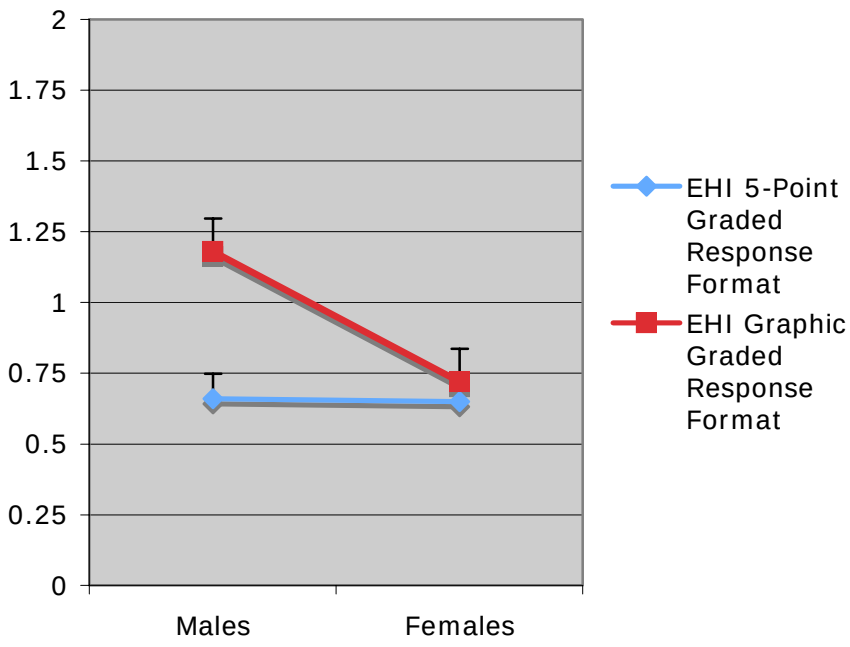

Figure 3.4. Schematic representation of the two-way interaction of Questionnaire Type x Sex for count of "either" responses. Error bars show the standard error (σ_M).

Sex was found to be significant only for the EHI in its graphic graded response format, F (1,197) = 7.95, p = .005, η^2 = .04, (EHI 5-point graded response format: p = .87), with males giving more either responses (mean number of "either" responses = 1.18, SE = .12) than females (mean number of "either" responses = .72, SE = .11).

3.4 Discussion

The psychometric properties of the different response formats of hand preference inventories were the focus of this chapter. Findings clearly demonstrate that both the translation of an "either" response into a binary response questionnaire and the reluctance to give extreme responses are subject to one's handedness and not to one's sex. An interesting new finding is that, irrespective of sex, right-handers tend to choose a "right" response in the place of an "either" response more often than left-handers choose a "left"response in the place of an "either" response. Moreover, the rank order of participants in terms of degree of handedness was not significantly dependent upon the questionnaire or upon the response format used.

Looking at the results in more detail, no sex difference was found to exist in avoiding giving an extreme response in a 5-point graded responses format. Rather, reaction to extreme responses was found to be contingent on handedness, with left-handers being the ones avoiding giving extreme responses, even though this was found to be statistically significant only for the longer rather than the shorter questionnaires. A complementary finding is that left-handers give proportionally more "either" responses than right-handers, especially in the longer questionnaires (i.e., the HLGI and the WHQ). It is therefore argued that the sex difference in hand preference is not artificially produced by the different reactions of the two sexes to the wordings of the response format of handedness questionnaires, as suggested by Bryden (1977). Bryden's findings should be rather ascribed to the fact that left-handers of both

sexes avoid giving extreme responses and at the same time there are more left-handers within the male population than the female population (Papadatou-Pastou et al., 2008).

The 10 items of the EHI were also analysed individually following Bryden's (1977) methodology, in order for a direct comparison between the results of the two studies to be feasible. The results of Bryden were not replicated here, as only two out of ten items were significantly different between the sexes in terms of the number of extreme responses they produced, one item favouring males (throwing) and the other favouring females (using scissors). On the contrary, four items were found to favour right-handers (throwing, scissors, knife without a fork, and sticking a match) and no item was found to favour left-handers. The finding that males give significantly more extreme responses when it comes to throwing, is particularly interesting, as it is in line with the suggestion made in chapter 2 that the sex difference in handedness might be mediated by the encouragement of the use of the left hand in some sports, with males being the primary recipients of such encouragement. Throwing might be subject to this kind of social pressure, as it is an action that is very common in sporting activities.

The translation patterns between graded response and binary response formats confirmed the hypothesis that left-handers prefer to translate "either" responses into "left" responses and right-handers prefer to translate "either" responses into "right" responses, with no sex difference in this behaviour. More importantly, right-handers are significantly more reluctant to give a "left" response in the place of an "either" response than left-handers are to give a "right" response in the place of an "either" response. It is here argued that this finding, together with the finding that left-handers give in total more "either" responses compared to right-handers, does not depict just a different pattern of reactions between handedness groups to the wording of the response format of

hand preference inventories, but that it supports the notion that left-handers are less lateralised and more widely dispersed than their right-handed counterparts (Borod et al., 1984).

Results further replicated the observations of Williams (1991) and McMeekan and Lishman (1975) that the graphic graded response format of the EHI encourages the equivalent of an “either” response compared to a 5-point graded response format. These researchers had compared the 12-item AHPQ using a 3-point graded response format with the graphic graded version of the EHI. Here, the graphic graded version of the EHI was directly compared to the EHI 5-point graded response format version. The same 10 items were therefore compared, whereas the previous researchers had only compared six, which is the overlap between the AHPQ and the EHI. The comparison was also stricter here, since participants had 5 options instead of 3 in the graded response format. A within-subjects design was employed and the two orders were counterbalanced throughout the sample, correcting methodological flaws of the previous two studies.

The finding that putting a cross in both the “left” and the “right” column is preferred to selecting the middle point of a Likert scale, may not be due to the nature of this response scheme, but rather due to the instructions given in the original version of the EHI as argued by McMeekan and Lishman (1975), or to a combination of both factors. The importance of the instructions of the EHI has also been pointed out by Messinger and Messinger (1995), who argue that the presence or absence of what they call the “Oldfield admonition” (i.e., the phrasing “the preference is so strong that you would never use the other hand unless absolutely forced to”) for instructing the participants when they should put two crosses under the same column, has significant impact on item responses. Nevertheless, this finding suggests that clinicians and researchers who need to

detect any trace of sinistrality in right-handers should prefer the use of the graphic graded response format of the EHI.

The greater use of “either” responses in a graphic graded rather than a 5-point graded response format was further found to be stronger for males compared to females. It is not clear why this might be the case. It may well be that males react differently to the wording of the instructions of hand preference inventories. Nevertheless, this finding reached only marginal significance.

This study dealt with the psychometric properties of different response formats. It did not focus on their relative strengths and weaknesses, which have been debated upon in the past. Peters (1998) has suggested that a 5-point graded response format is a workable compromise between a binary response format, which does not give the possibility of a differentiated answer, and a range of other answering options, which are either impractically large or methodologically questionable. Bishop et al. (1996) argued against a graded response format, as the quantifiers used (e.g. “most of the time” or “usually”) have no absolute interpretation, therefore people may vary in how they understand and react to them (Moxey and Sanford, 1993). Beaton and Moseley (1984) have even claimed that graded responses introduce the confounding variable of the extent to which a person avoids or prefers extreme responses. Moreover, Bishop et al. (1996) pointed out that graded response formats produce problems in scoring the degree of hand preference, as a weak preference on the one side could be equivalent to a mixture of right- and left-handed responses. She finally showed that the distinction between “usually” and “always” does not correspond to a distinction in the relative skill of the two hands (even thought Peters [1998] did find that gradation in strength of preference has meaningful performance correlates). Nevertheless, it was shown here that the rank order of participants in terms of their hand preference score was not significantly dependent upon the response format employed. Thus, graded

response formats classify participants in a way that is highly correlated with the way in which they are classified when using a binary response format. It is therefore here argued that a 5-point graded response format would be preferable for a hand preference questionnaire, since – even though some complexity is introduced – results with regards to hand preference are comparable to the results obtained using a binary response format, and – more importantly – no information is lost.

The present findings have implications for study design. It has been shown that the graphic graded response format of the EHI is more sensitive to tracing sinistrality than its 5-point graded responses counterpart, by encouraging "either" responses. It was also shown that the rank order of participants in terms of their handedness was not significantly dependent upon the questionnaire used or upon the response format employed. Moreover, it was shown that left- and right-handers have different reactions towards different response formats of hand preference questionnaires and it is known that males tend to be more left-handed than females. Thus, one should control both sex and handedness when conducting research on the neurological and cognitive correlates of handedness or research on the sex differences in cognition. For example, it is argued that Bryden's (1977) conclusion that the sex difference in handedness is due to the different reactions the two sexes have to the wording of hand preference questionnaire, stems from the fact that he had not controlled for handedness when making claims about sex differences.

It would be interesting to investigate whether the difference between left- and right-handers in avoiding extreme responses is specific to hand preference inventories. Bishop et al. (1996) studied the use of quantifier terms between handedness groups using a "Daily Rhythms Questionnaire", in which participants checked "never", "seldom", "sometimes", usually", and "always" for items about eating and sleeping patterns and found no differences in the

frequency of “always” responses. Nevertheless,, Bishop et al. compared the responses of three groups of right-handers (strong exclusive, weak exclusive, and predominant right-handers) without including groups of left-handers in the analysis. It is here suggested that a future study should test this hypothesis using groups of both left- and right-handers.

Overall, it has been shown that there is a sex difference in manual praxic lateralisation (chapter 2) and hand preference inventories are the most popular way to determine this form of lateralisation. One of the factors that have been suggested to produce the sex difference, but which was not adequately dealt with in the meta-analysis presented in chapter 2, is the response format used in hand preference inventories. It was here shown that Bryden’s suggestion (1977) that the sex difference is artificially produced by the different reactions of the two sexes to the wording of the response format of handedness questionnaires is questionable. Rather, it was here shown that it is handedness for writing hand and not one’s sex that moderates the reactions of an individual towards the wording of different response formats.

Chapter 4

Discriminatory properties of different tests of praxic lateralisation with regards to detecting sex differences

4.1 Introduction

Meta-analytic investigation of the factors that systematically influence the magnitude of the sex difference in praxic lateralisation revealed that – apart from environmental factors – the magnitude of the sex difference in handedness is moderated by the instrument used to measure handedness (Papadatou-Pastou et al., 2008). In particular, the sex difference was found to be larger when handedness is assessed using methods other than the recording of writing hand (or, equivalently, writing hand together with self-assessment).

However, the crucial characteristic of the moderating variables' analysis within the meta-analytic framework is the number of data sets reporting pertinent information and not the number of participants included (Hunter and Schmidt, 1990). Thus, in the case of the moderating effects of the instrument used to measure handedness, only 131 out of the 208 data sets were used. Therefore, only large effects could have been reliably detected. Still, the meta-analysis gave some information as to which of the hand preference questionnaires might be more discriminating when it comes to detecting the sex difference in handedness. In particular, the AHPQ was found to have the largest male-to-

female odds ratio (2.28), followed by the EHI and the 4 items for handedness from the Lateral Preference Inventory by Porac and Coren (1981) (both *ORs* = 1.28; see Table 2.1), even though the odds ratios produced by the different instruments were not found to be significantly different from each other.

While the meta-analysis gave an indication as to which questionnaires might be more discriminating, this was nonetheless an indirect test. Moreover, any meta-analysis is only as good as the primary studies used to carry it out. If the studies have methodological and analytical limitations then in turn the meta-analysis would not be all inclusive. For example, chapter 2's meta-analysis could only exploit information reported in studies that had reported hand preference data broken down by sex. This resulted in the under-reporting of some of the hand preference instruments. For example, the AHPQ – one of the most popular questionnaires for measuring handedness (Bishop, 1990) – was used only in four of the data sets that were eligible for inclusion in the meta-analysis, thereby producing a wide 95% *CI* (1.07-4.80) around its odds ratio. In addition, in the meta-analysis the male-to-female odds ratios were compared between studies, each study employing only one of the instruments, thereby possibly allowing other moderators to confound the results. A within-subjects design would therefore be more suitable for comparing different instruments in their discriminating ability with regards to sex differences.

The meta-analysis described in chapter 2 was moreover constrained by the fact that it did not include studies using relative hand skill tests, but it only included studies having assessed handedness in terms of preference. Hand skill tests (also known as performance measures), are nevertheless widely used both in research and clinical practice (e.g., Corey et al., 2001; Francks et al. 2002). Moreover, such tests have the advantage of overcoming some of the inherent limitations of hand preference measures, most importantly their subjectibility (Brown et al., 2006). Preference measures indeed rely on the participant's or the

patient's interpretation of the question, as well as the ability to imagine oneself performing the particular task (Bryden et al., 1996). Hand preference questionnaires are further particularly unreliable when administered to special populations such as the elderly or children, because individuals in these populations may have difficulty remembering which hand they use to perform certain tasks and/or may have difficulty judging which hand is used in certain circumstances (Bryden et al., 2000). In contrast, performance measures have an important objectivity embedded in the procedure of their administration, as well as in the tasks they sample (ibid.). Preference and performance are often interpreted as though they were interchangeable, but, even though they might be indicators of common underlying factors (Bishop, 1989), they are still two rather distinct concepts that are imperfectly correlated (.6-.7; Todor and Doane, 1977) and that have notably different distributions: whereas preference measures typically exhibit a bimodal distribution with two handedness groups, performance measures tend to be distributed unimodally (Annett, 2002). An investigation into the sex differences in handedness excluding hand skill measures would therefore be incomplete.

Apart from handedness, which is by far the most popular behavioural asymmetry, other asymetries have also been studied, such as footedness (e.g., Brown and Taylor, 1988), eyedness (e.g., Jackson, 2005), eardness (e.g., Coren, 1993), chewing preference (e.g., Hoogmartens and Caubergh, 1987), head turning asymmetry (e.g., Güntürkün, 2002), and rotational movement (e.g., Bracha et al., 1987), but were not included in the meta-analysis either. Footedness, defined as the preferential use of one foot in various voluntary motor activities such as kicking a ball to hit a target (Gabbard, 1997; Elias and Bryden, 1998) and eyedness, defined as the preference for using one eye for sighting tasks, or for carrying out monocular activities such as looking down a

microscope or through a telescope[11] (Bourassa, 1996), are the most studied among these behavioural asymmetries. Both footedness and eyedness are concerned with activities that are usually less complex and receive less influence, if any, by culture or practice compared to handedness (Searleman, 1980; Peters, 1988; Peters, 1990; MacNeilage, 1991).[12] Foot preference is indeed somewhat influenced by social training, as in sporting activities, but nevertheless not to the degree that handedness is influenced by parents, schooling, or by other environmental effects, such as living in a "right-handed world" (Elias and Bryden, 1998; Chapman, 1987). Peters (1988, 1990) has even argued that footedness should be considered part of the standard neuropsychological assessment because of the sensitivity of the feet in reflecting certain maturational and functional characteristics of the motor system.

Footedness is further interesting because it has been repeatedly reported to be a better predictor of right-ear advantage in DL tests (Rasmussen and Milner, 1977; Searleman, 1980; Strauss, 1986; Day and MacNeilage, 1996; Elias and Bryden, 1998), which in turn is considered indicative of language dominance (Bryden, 1986, 1988). Hence, footedness may actually be a better predictor than handedness of linguistic laterality. Similar results were obtained when using the sodium amytal method (Wada and Rasmussen, 1960) to determine linguistic lateralisation. For example, Strauss and Wada (1983) reported that right-

[11] Sighting dominance (the usual sense of the term eyedness, as described earlier) should be distinguished from sensory dominance (concerned with binocular rivalry) and acuity dominance (concerned with differences between the eyes in visual acuity), with both of which sighting dominance is uncorrelated (Coren and Kaplan, 1973; Bourassa, 1996).

[12] The notion of a "global" lateral preference for performing skilled motoric activities, had led to the conclusion that footedness may be providing a more pure measure of "sidedness" than handedness. Unfortunately, an environmental or cultural explanation may help explain why a fraction of the right-handed population is left-footed, but it does not account for the higher prevalence of "crossed" lateral preference in the left-handed population. The very existence of left-handed, right-footed individuals contradicts the hypothesis that people have global lateral preferences (Elias and Bryden, 1998).

handed, right-footed people have a higher prevalence of left-hemispheric language representation than those who were left-handed and left-footed, whereas Watson et al. (1993) reported that right language dominance is more closely associated with non-right footedness than it is with non-right handedness. However, both of these studies' findings are restricted by their small sample sizes and the fact that participants were candidates for temporal lobe surgery.

Keeping in mind that the instrument used to assess handedness is of particular practical importance for research as well as for clinical assessment, further investigation on the discriminating properties of the different instruments was deemed necessary. Moreover, in order to pursue possible biological explanations of the aetiology of the sex difference in handedness (see chapter 2) in the following studies of the present thesis, an instrument sensitive in detecting the sex difference needed to be identified. Thus, the present chapter reports a novel study comparing different hand preference questionnaires and hand skill tests. Previous work has compared different preference and performance measures (e.g., Todor and Doane, 1977; Borod et al., 1984; Rigal, 1992; Brown et al., 2006), but to date none of these studies has focused on the discriminatory properties of these tests with regards to detecting sex differences. The study presented here will further includes other behavioural asymmetries such as footedness and eyedness.

The hand preference questionnaires compared here are the following: the AHPQ (Annett, 1970), the EHI (Oldfield, 1971), the WHQ (Steenhuis and Bryden, 1989), and the Healy, Liederman, and Geshwind's Inventory (HLGI; Liederman, 1986). While the EHI was selected because it was the most popular questionnaire used to measure handedncess amongst the studies included in the meta-analysis (k_d = 27), the AHPQ was included because it was under-

represented (k_d = 4).[13] The WHQ and the HLGI, on the other hand, were selected on the basis of their greater length, comprising 68 and 55 items respectively, thus providing a large pool of hand preference items.

Moreover, Bishop et al.'s (1996) Quantification of Hand Preference Test (QHPT) was included, as it provides a promising tool for quantifying hand preference using card reaching in different locations. This test has the advantage of measuring preference in terms of an internally consistent continuum, rather than giving equal weight to preference responses for an arbitrary collection of different activities, which could be influenced by tool use and which may load on different factors, as is the case for hand preference questionnaires (Steenhuis and Bryden, 1989; Bishop et al., 1996).

With regards to the assessment of hand performance, this cannot depend on a single measure, but it should include different relative hand skill tests (Rigal, 1992). Performance measures have very low correlations with each other (Borod et al., 1984), mostly because there are many different underlying components of hand performance, such as proximal versus distal musculate, and fine versus gross control (Corey et al., 2001). Barnsley and Rabinovich (1970) have even claimed to have found, using factor analysis, nine different factors related to performance, namely reaction time, dexterity, stated hand preference, wrist finger speed, aiming, hand stability, arm-movement stability, finger tapping, and grip strength. In the study presented here (apart from stated hand preference measured as described earlier), three of these factors, namely aiming, finger dexterity, and tapping, which are known to differentiate between right- and left-handers (Bishop et al., 1996), were considered. Aiming was assessed by means of the Dot-Filling test (Tapley and Bryden, 1985), finger dexterity by the Peg-Moving test (Annett, 1976), and tapping by the Tapping

[13] According to Steenhuis et al. (1990) the EHI and the AHPQ are two of the most popular hand preference inventories.

Speed test as described by Bishop (1996).

This study is a direct investigation, employing a within-subjects design, of whether different praxic laterality tests have different sensitivity levels when it comes to sex differences. It is an investigation using a population that is homogeneous (as opposed to the heterogeneous samples of the meta-analysis) and that is further relevant to subsequent studies presented in this thesis. The present study also provides the opportunity to investigate possible mechanisms producing a sex difference.

Furthermore, given there is accumulating evidence in support of the notion that endogenous estrogen (the concentrations of which flucutate during the menstrual cycle) and exogenous estrogen (which is the main substance administered in oral contraceptives) have activational effects on overt motor behaviour (for a review see Hampson and Kimura, 1992; Sommer, 1992; Szekely et al., 1998), it was considered vitally important to include female participants who were not taking the contraceptive pill and to control for menstrual cycle phase. Therefore, all female participants were tested at menses, as this is a reliably identified point in the cycle.

It has additionally been suggested that not only the nature of the task, but also the age of the participants may be crucial to the direction of any sex by handedness interaction. For example, Kilshaw and Annett (1983) examined participants from 3½ to older than 50 years of age and found that females tended to be faster with the right hand up to 10 years of age but males then equalled and surpassed females, to be faster in most older groups. This supports the use of undergraduate and graduate students as participants. Moreover, rather than using a sample representative of the population with approximately 90% right-handers and 10% left-handers, an equal number of right-handed and left-handed individuals was tested in order to increase the power to find a relationship between sex and handedness.

The rationale of the study is that, if different instruments of measuring handedness are indeed differentially sensitive in capturing a sex difference, then they will produce significantly different mean scores for the two sexes. Conversly, if the different instruments are not differentially sensitive to sex differences (consistent with the meta-analysis for the hand preference questionnaires), then there will be no significant differences in mean scores between the two sexes. This test between hypotheses is not watertight; one might fail to find differences because the instruments here used are irrelevant. They are nevertheless, amongst the most popular instruments in the literature of handedness (Bryden et al., 2007). Another possibility is that one might find differences between the sexes that are not theoretically interesting, but simply reflect differential practise of the two sexes. However, by focusing on tasks that are either relatively unpractised (e.g., tapping) or in which both sexes are likely to have had similar amounts of practice (e.g., dotting using a pen), this latter possibility should be minimised.

The purpose of this study is therefore twofold. Firstly, it compares, in a direct manner and using a homogenous population, a number of hand preference questionnaires, hand skill measures as well as foot and eye preference questionnaires on their sensitivity when it comes to capturing sex differences in praxic lateralisation. Secondly, it aims to inform subsequent studies of this thesis as to which instrument should be employed for the experimental study of the sex differences in praxic and linguistic lateralisation.

The following predictions were made:

(a) Amongst hand preference inventories, the AHPQ will be the most sensitive one with regards to sex differences, as shown by the findings of the meta-analysis.

(b) Hand skill measures will be more sensitive to sex differences than hand preference measures, according to findings by Annett and Kilshaw (1993),

who did not find any significant differences between the two sexes in hand preference as measured by the AHPQ, but did find significant differences in Peg-Moving performance.

4.2 Method

The study was reviewed by, and received ethics clearance through the CUREC of the University of Oxford. Maintenance of confidentiality of information is subject to normal legal requirements.

4.2.1 Participants

Two hundred volunteers[14] (50 male right-handers, 50 female right-handers, 50 male left-handers, and 50 female left-handers; handedness groups according to writing hand) took part in the present study; 120 participants (30 male right-handers, 30 female right-handers, 40 male left-handers, and 20 female left-handers[15]) were administered all laterality tests whereas 80 participants (20 male right-handers, 20 female right-handers, 10 male left-handers, and 30 female left-handers[16]) were administered only the questionnaire-based tests. Participants were undergraduate and graduate students enrolled in the University of Oxford (*mean age* = 22 years., *SD* = 3, range = 18-33). Participants were reimbursed for their time with either course

[14] These are the same participants as the ones participanting in the study presented in chapter 3.

[15] The sample of female left-handers being only half the size (n_f = 20) compared to the sample of male left-handers (n_m = 40), was due to the extra constraints placed on the recruitment of female participants. Left-handers are more difficult to recruit than right-handers in the first place (with left-handers for writing hand representing only about 10% of the population; Papadatou-Pastou et al., in preparation). In the case of female left-handers they also (a) had to be off the pill for at least six months previous to the testing, and (b) had to be at menses at the time of the testing.

[16] In the case of the participants who were administered only the questionnaire-based tests, an effort was made to recruit female left-handers, in an attempt to increse the power to find a sex by handedness interaction.

credits (RPS participants) and with either 5 pounds in cash (non-RPS participants who were administered only the questionnaire-based tests) or 10 pounds in cash (non-RPS for participants who were administered all the laterality tests).

4.2.1.1 Inclusion/Exclusion criteria

All participants underwent screening before being enrolled in the study. Exclusion criteria included having used any medication that affects the central nervous system, as well as the contraceptive pill or hormonal replacements, in the previous six months. All participants had to be free of any neurological problems (e.g., epilepsy, meningitis, encephalitis, multiple sclerosis, stroke) and of any medical condition interfering with hand function (e.g., arthritis) and to be native, monolingual English speakers. Screening was done by e-mail, using a short questionnaire, which was send as an e-mail attachment (see Appendix 4.1). Participants completed the questionnaire in their own time and e-mailed it back to the researcher.

4.2.1.2 Recruitment

Participants were recruited in the following ways:

(i) Through the Department of Experimental Psychology's RPS.

(ii) Through posters that were put up throughout the University campus.

(iii) Through e-mails sent to different mailing lists of the University's Departments and Colleges.

(iv) Through advertisements placed on the web pages *www.dailyinfo.co.uk* and *www.facebook.com.*

When the potential participants contacted the researcher declaring their interest to participate in the research study, they were sent the information sheet (see Appendix 4.2 for the information sheet sent to the participants who were

administered all laterality tests and Appendix 3.2 for the information sheet sent to the participants who were administered only the questionnaire-based tests) and were screened for suitability to participate via the e-mail questionnaire described earlier. The day and time of testing was then agreed upon.

4.2.2 Instruments

4.2.2.1 Preference tasks

Hand preference: The two versions of the hand preference questionnaire described in chapter 3 were used (see Appendix 3.3). Briefly, the first version of the questionnaire had a binary response format, whereby participants were asked to indicate which hand they habitually use for each of the listed activities by circling *R* (for right hand) or *L* (for left hand). The second version used a 5-point graded response format, whereby participants were asked to choose among the following options: If they always use one hand to perform the described activity, they were asked to circle *Ra* or *La* (for right always and left always). If they usually use one hand they were asked to circle *Ru* or *Lu* (for usually right or usually left), as appropriate. If they use either hand, they were asked to circle *Ei.* The questionnaire included the items from the 12-item version of AHPQ (Annett, 1970), the 10-item EHI (Oldfield, 1971), the 68-item WHQ (Steenhuis and Bryden, 1989), and the 55-item HLGI (Healy, 1986). The first version of the questionnaire also included the original version of the EHI, which uses a graphic response scheme whereby one or two crosses are put under the columns “right” and “left” according to the hand used for each of the actions listed.

Footedness: Footedness was assessed by means of the “Waterloo Footedness Questionnaire” (WFQ; Steenhuis and Bryden, 1989).[17] Two versions

[17] The WFQ includes the three items on footedness included in the Coren and Porac Lateral Preference Inventory (Coren, 1993).

of the WFQ using the two different response formats (i.e., binary response and 5-point graded response formats) were administered, corresponding to the two versions of the hand preference questionnaires. The following items were used: foot used for kicking a ball, hopping, smoothing sand, crossing one's legs, picking up a marble, stepping up onto a chair, writing one's name in the sand, stepping on a shovel, standing on one foot, and stomping on a bug.

Eyedness: Eyedness was assessed by means of the four items on eyedness included in the Coren and Porac's Lateral Preference Inventory (Coren, 1993; from now on referred to as Eyedness from the Lateral Preference Inventory; ELPI). Again, two versions of the ELPI using the two different response formats (i.e. binary response and 5-point graded response formats) were used, corresponding to the two versions of the hand preference questionnaires. The following items were used: eye used to look through a telescope, eye used to look into a dark bottle to see how full it is, eye used to peep through a keyhole, and eye used to sight through a rifle.

Quantification of Hand Preference Test (QHPT; Bishop et al., 1996): This is a behavioural test measuring strength of hand preference through card reaching in different locations. A cardboard template was used to mark seven positions, each at a distance of 40 cm from the mid-point of a baseline, at successive 30-degree intervals (see Figures 4.1 and 4.2). Three playing cards were placed at each position. The participant stood at the baseline and was asked to pick up a given card and place it in a box positioned at the midline, in one's own time. The card order was random, but kept the same for all participants. The hand used to pick up each card was recorded. The following instructions were given:

Now I want you to pick up the card I ask you to and place it in the box positioned in front of you, at your own time. Please place in front of you the card numbered [...].

4.2.2.2 Hand skill tests

Relative hand skill was measured using the following tests:

Peg-Moving test (Annett, 1985): This task uses 10 small cylindrical pieces (i.e., pegs) and a pegboard (see Figure 4.3). The board was placed parallel to the edge of a desk, which was suitable for the height of the participants. Participants stood in front of the pegboard facing the board on its longest dimension and were asked to move all the pegs one by one in sequence from the back row of holes to the front row as fast as possible using one hand. Three trials were given with each hand, starting with the right hand and then alternating, according to the original instructions by Annett (1985). A trial consisted of a perfect run of ten peg placements, without dropping a peg or any other significant distraction taking place. If any disruption occurred, the trial was discarded and replaced. The accuracy of the timing of the start was assured by the experimenter placing a finger on top of the first peg while saying “ready, steady, go”, releasing the peg, and starting the watch on “go”. The right hand worked from right to left and the left hand from left to right. The following instructions were given:

The task is to move the pegs from the top row to the bottom row like this, as fast as you can (the experimenter here demonstrated the task, moving the pegs as in a trial). It does not matter if you drop a peg. We will just start the trial again. The idea is to be as quick as you can, trying each hand in turn. Do not talk while moving the pegs because that slows you up.

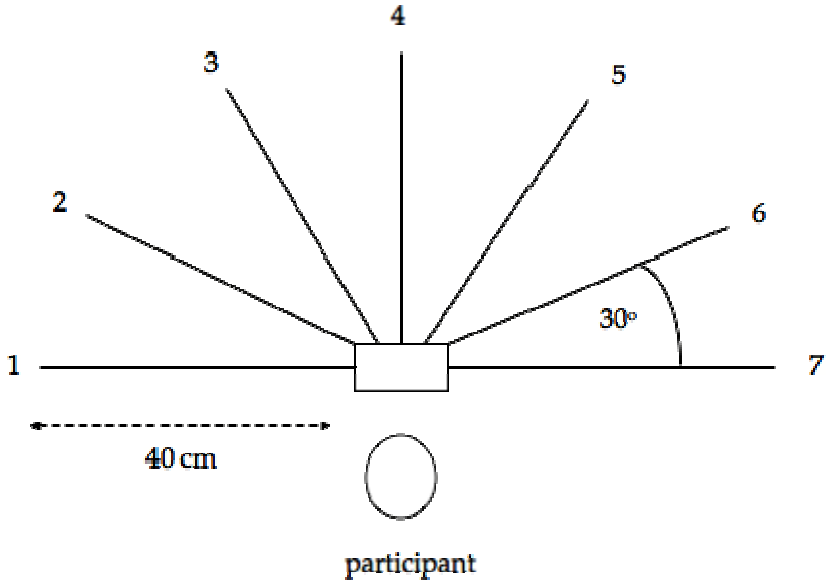

Figure 4.1. Set-up for the Quantification of Hand Preference Test (QHPT).[18]

Figure 4.2. The experimental set-up of the present study for the Quantification of Hand Preference Test (QHPT). The participant stands before the cardboard, reaches for three cards at each of the numbered locations, and places them in the central box.

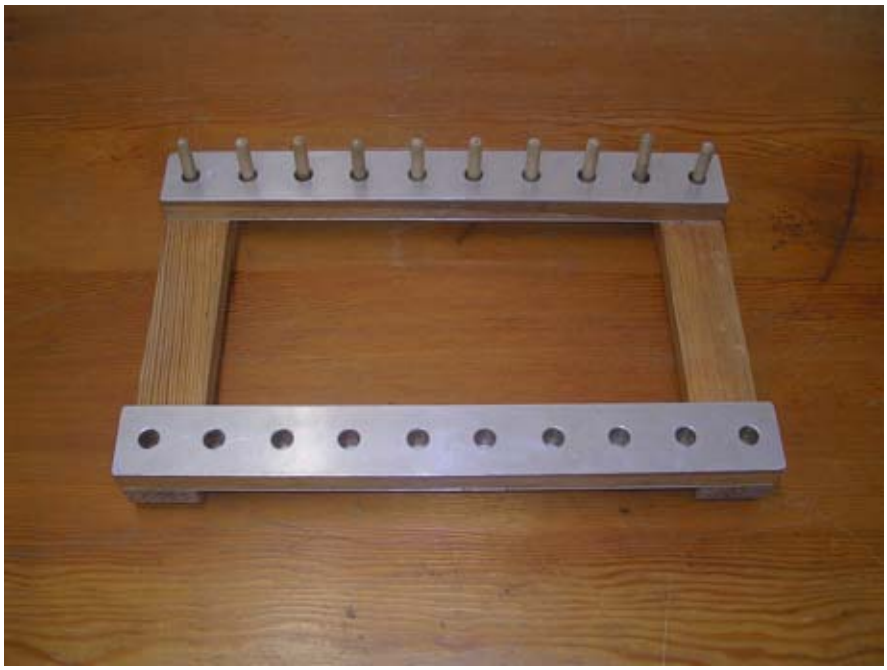

Figure 4.3. The pegboard with the 10 pegs.

Dot-Filling test (Tapley and Bryden, 1985): This is the group version of the test employed by Stott et al. (1972). Participants were presented with a paper on which there were circles arranged in a particular pattern (see Figure 4.4 for a smaller version of the sheet provided; the test sheet was A4 paper size). They were asked to make a dot in the middle of each circle, following the pattern, as quickly as they could. It was pointed out that the dot must be *in* the circle, not on the edge or outside of it in order to be scored. The participants were given four trials and 20 s were allowed for each trial. Participants used their preferred hands on the first and fourth trials and their non-preferred hands on the seconds and third trials. Only trials in which the dot did not touch the borders of the circles were counted as valid. The following instructions were given:

[18] Figure reproduced based on the figure in Bishop et al. (1996).

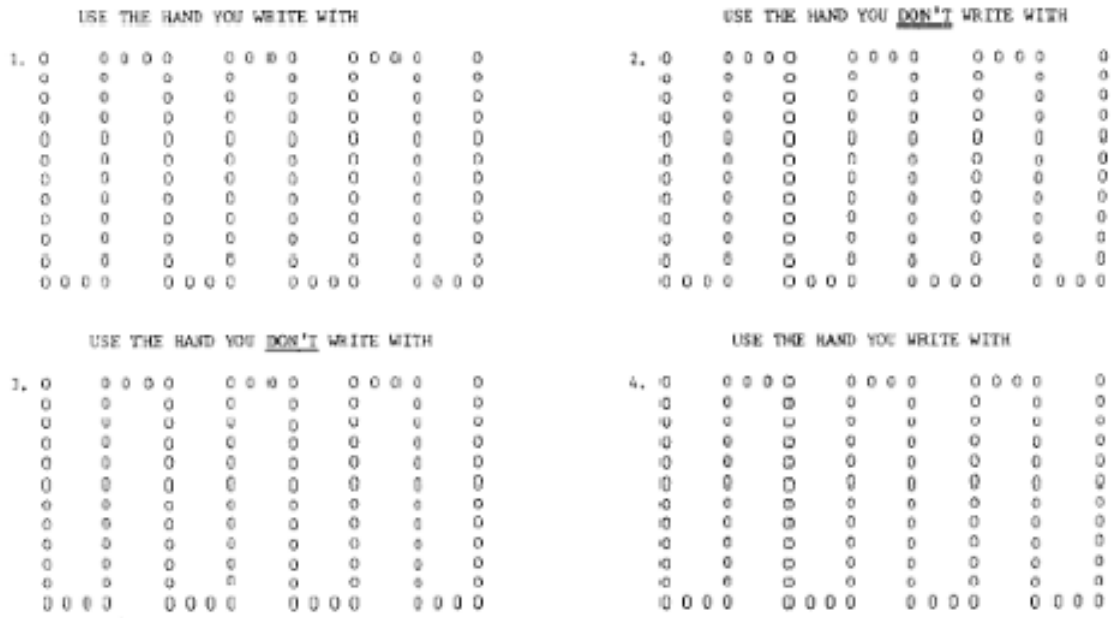

Figure 4.4. The test sheet used for the Dot-Filling test.

Now please make a dot in the middle of each circle, following the pattern as quickly as you can. The dot must be in the circle, not on the edge or outside of it. You will be given 20 seconds for each trial.

Tapping Speed test: For this task the procedure described in Bishop (1989) was followed. A commercially available tally counter was used (see Figure 4.5), which the participant held in one hand, using the thumb to depress the key that advances the counter. After a practice period during which participants familiarised themselves with the counter, there were given three trials with each hand. The starting hand was counter-balanced within each handedness group, in order to control for fatigue or practice effects. On each trial, participants were instructed to tap as fast as possible for 20 seconds. The instructions given were “please tap as fast as possible for 20 seconds.”

Figure 4.5. The tally counter used for the Tapping Speed test.

4.2.3 Procedure

Participants were tested individually in a quiet room. The study was explained as soon as they arrived and they were encouraged to ask questions. They gave written consent before taking part in the study, but were explicitly told they remained free to leave at any time and without having to give any reason for doing so. The consent form was signed in two copies so that the participants could keep one for their own records. Testing took place in the Department of Experimental Psychology, University of Oxford.

In the case of the 80 participants who were administered only the hand preference questionnaires, the two versions were completed one after the other with the order of administration counterbalanced across participants. Participants filled out the questionnaires in the company of the experimenter and were instructed to take as much time as they needed, but not to think too much about each item.

In the case of the 120 participants who were administered all laterality tests, the procedure was different. Straight after signing the consent form, the

participants performed the QHPT, while they were still relatively naïve to the purposes of the experiment.[19] One version of the hand preference questionnaire was then completed. The hand skill tests (Peg-Moving, Dot-Filling, and Tapping Speed) followed, with their order counterbalanced. Neuropsychological testing described in chapter 5 was then performed and finally the other version of the hand preference questionnaire was completed. The order of administration of the two questionnaires was counterbalanced. All female participants were tested in the same phase of the menstrual cycle (menses).

All participants were debriefed after the completion of the study.

4.2.4 Scoring

4.2.4.1 Questionnaire-based preference tests

The procedures described in chapter 3 were followed. For the binary response format version of the questionnaire, hand preference scores were derived by calculating the percentage of right-hand responses. A LI ranging from 0 (extreme left-handedness) to 100 (extreme right-handedness) was therefore calculated for each participant. For the 5-point graded response format, the score was calculated by giving a value of 0 to an “always left” response up to a value of 4 to an “always right” response, adding the score for all questions for each participant, dividing by the maximum score and multiplying by 100. A LI ranging from 0 (extreme left-handedness) to 100 (extreme right-handedness) was obtained for each participant. The EHI with the graphic graded response scheme was scored separately, as placing one or two crosses under the appropriate columns is somewhat different to a 5-point Likert scale response

[19] Even though it was clearly stated in the information sheet that the study is about handedness, by the time the QHPT was administered, participants had still not completed the long hand preference questionnaires asking them to think actively about their hand preference for different activities, neither had they performed any of the hand skill tasks.

format. In order to score the graphic graded responses of the EHI, the procedure described by Oldfield (1971) was used: the crosses under the “left” and the “right” columns were added and then the score for the left hand was subtracted from the score for the right hand, divided by the sum of both and multiplied by 100, thus giving a LI varying from -100 to 100 (extreme left-handedness to extreme right-handedness).

4.2.4.2 Hand skill tests

Peg-Moving: The mean time needed to move all 10 pegs was calculated for each hand. Time taken was measured from the participant’s touching of the first peg to the releasing of the last peg. Hand differences were then expressed as the difference between the right- and left-hand scores, divided by the total, using the formula:

$$LI = (RH-LH) / (RH+LH)$$

where RH = mean time needed to move the pegs with right hand and LH = mean time needed to move the pegs with the left hand. This score represents the difference in rate between the two hands expressed as a proportion of the overall rate. A positive value indicates a right-hand advantage and a negative value a left-hand advantage.

Dot-Filling: The mean number of circles properly filled was counted for each trial. Hand differences were then expressed as the difference between the right- and left-hand scores, divided by the total, using the formula:

$$LI = (RH-LH) / (RH+LH)$$

where RH = mean number of dots written by the right hand and LH = mean number of dots written by the left hand. A positive value indicates a right hand advantage and a negative value a left hand advantage.

Tapping Speed: The mean number of taps was calculated for each hand. Hand differences were then expressed as the difference between the right- and left-hand scores, divided by the total, using the formula

$$LI = (RH-LH) / (RH+LH)$$

where RH = mean number of taps produced by the right hand and LH = mean number of taps produced by the left hand. A positive value indicates a right-hand advantage and a negative value a left-hand advantage.

4.2.4.3 Quantification of Hand Preference Test (QHPT)

QHPT: The proportion of cards picked up with the right hand served as the LI for this test. A LI ranging from 0% (extreme left-handedness) to 100% (extreme right-handedness) was therefore calculated for each participant.

4.2.5 Statistical analysis

All analyses were performed using the SPSS v.14. ANOVAs were performed as the number of data points was sufficient for parametrical testing (n_m = 100 for males and n_f = 100 for females; MacCallum et al., 2001). The different LIs were the dependent variables, and sex and handedness for writing hand were the between-subjects factors. The partial eta squared (η^2) statistic was used as the effect size measure. Post-hoc tests were run using paiwise comparisons with the LSD adjustment. All *p*-values were two-tailed and the *a*-level was set at .05.

4.3 Results

4.3.1. Questionnaire-based preference tests

Classification as a left- or right-hander according to writing hand was the same as self-classification for all participants (i.e., all right-handers for writing hand were self-classified as right-handers and the same for left-handers). Descriptive statistics for each of the preference tests broken down by sex are given in Tables 4.1 and 4.2. One participant failed to complete the EHI in the graphic graded response format. For all preference tests the median score for males was smaller than the median score for females, except for the HLGI (5-point graded response format), where the median for males was greater than the median for females (57.82 vs. 57.09 respectively) and the ELPI (binary response format), where the median was the same for the two sexes.[20]

4.3.1.1 Hand preference tests

A 4 x 2 x 2 x 2 repeated measures ANOVA was performed with questionnaire type (AHPQ, EHI, WHQ, or HLGI) and response format (binary response or 5-point graded response format) as the within-subjects factors. Sex (male or female) and handedness for writing hand (right or left) were the between-subjects factors. Male (mean score = 56.20, *SE* = 1.46) and female (mean score = 56.75, *SE* = 1.46) participants were not found to differ significantly in their mean scores for the different questionnaires, F (1,196) = .07, p = .79, $\eta^2 < .01$. Handedness, as expected, did have a significant main effect, with left-handers having a lower mean score (mean score = 25.59, *SE* = 1.46) than right-handers (mean score = 87.37, *SE* = 1.46), F (1,196) = 900.12, p < .001, η^2 = .82. The mean scores for the different questionnaires were significantly different from each other, F (3,196) = 34.97, p < .001, η^2 = .15. The

[20] For the ELPI only 5 scores were possible, though: 0, 25, 50, 75, 100.

Table 4.1. Descriptive statistics for the preference tests using both binary response and 5-point graded response formats for males (M) and females (F).

Hand Preference Questionnaire	Sex	N	Mean	SD	Range	Median
AHPQ (binary)	M	100	57.23	4.01	0-100	70.83
	F	100	59.68	4.08	0-100	83.33
AHPQ (graded)	M	100	56.11	3.30	2-100	66.67
	F	100	55.84	3.36	0-100	70.83
EHI (binary)	M	100	56.07	4.08	0-100	70.00
	F	100	58.36	4.11	0-100	80.00
EHI (graded)	M	100	55.03	3.42	0-100	66.25
	F	100	54.23	3.53	0-100	71.25
WHQ (binary)	M	100	60.57	3.77	1-99	80.15
	F	100	61.54	3.93	0-100	86.66
WHQ (graded)	M	100	56.78	2.51	11-99	68.20
	F	100	56.11	2.75	5 - 99	67.83
HLGI (binary)	M	100	61.46	3.81	2 - 100	80.00
	F	100	62.17	3.96	0-100	89.09
HLGI (graded)	M	100	46.38	2.38	8-80	57.82
	F	100	46.10	2.52	3-80	57.09
EHI (graphic graded)	M	99	11.64	7.62	(-100)-100	25.00
	F	100	15.83	7.93	(-100)-100	50.00

Table 4.2. Descriptive statistics for the foot and eye preference tests using both binary response and 5-point graded response formats for males (M) and females (F).

Preference test	Sex	N	Mean	SD	Range	Median
WFQ (binary)	M	100	59.80	3.67	0-100	70.00
	F	100	62.77	3.62	0-100	80.00
WFQ (graded)	M	100	55.90	2.00	8-100	61.25
	F	100	55.83	1.99	15-90	62.50
ELPI (binary)	M	100	53.75	4.57	0-100	75.00
	F	100	58.50	4.44	0-100	75.00
ELPI (graded)	M	100	53.94	3.19	0-100	56.25
	F	100	55.31	3.06	0-100	59.38

WHQ had the highest mean score (58.75, *SE* = 1.10), followed by the AHPQ (57.21, *SE* = 1.19), the EHI (55.92, *SE* = .95), and the HLGI (54.02, *SE* = 1.02). Moreover, the binary response format gave a significantly higher mean score (59.64, *SE* = 1.23) than the 5-point graded response format (53.32, *SE* = .87), F (1,196) = 138.87, $p < .001$, $\eta^2 = .42$.

A number of significant two-way interactions were detected: (i) Questionnaire Type x Response Format, F (3,196) = 293.02, $p < .001$, $\eta^2 = .60$, (ii) Questionnaire Type x Handedness, F (3,196) = 104.90, $p < .001$, $\eta^2 = .35$, (iii) Response Format x Sex, F (1,196) = 3.87, $p = .051$, $\eta^2 = .02$, and (iv) Response Format x Handedness, F (1,196) = 251.14, $p < .001$, $\eta^2 = .56$. There was also a significant three-way interaction of Questionnaire Type x Response Format x Handedness, F (3,196) = 83.21, $p < .001$, $\eta^2 = .30$ (see Figure 4.6) and a marginal three-way interaction of Questionnaire Type x Sex x Handedness, F

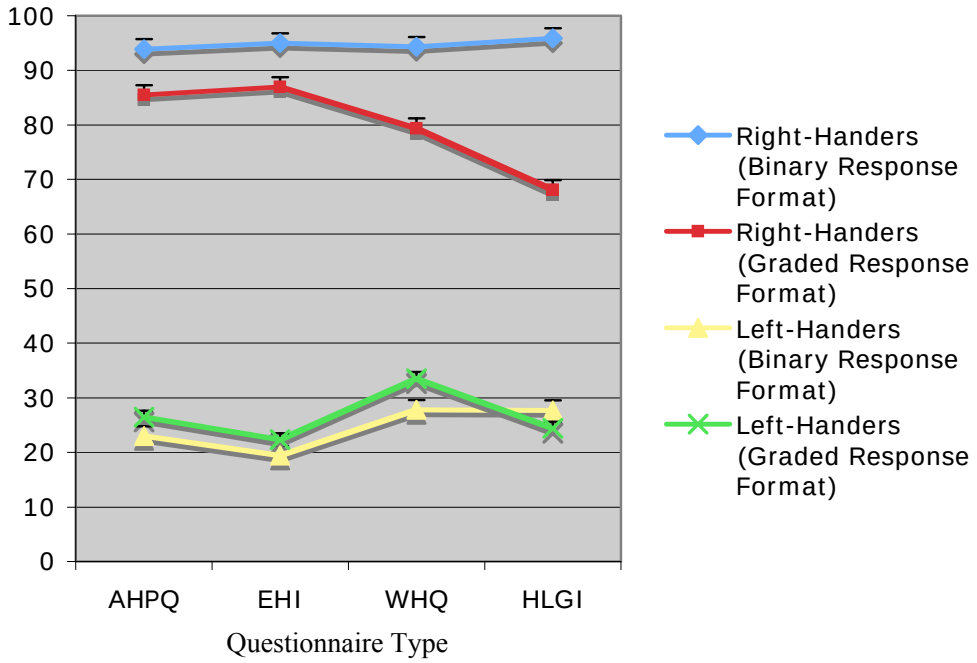

Figure 4.6. Schematic representation of the three-way interaction of Questionnaire Type x Response Format x Handedness. Error bars show the standard error (σ_M).

(3,196) = 2.55, p = .055, η^2 = .01 (see Figure 4.7). No other main effects or interactions were significant (all p > .16). The above interactions were further investigated.

Questionnaire Type x Response Format x Handedness: In order to investigate this three-way interaction, two 4 x 2 repeated measures ANOVAs with questionnaire (AHPQ, EHI, WHQ, or HLGI) and response format (binary response or 5-point graded response format) as the within-subjects factors were performed separately for right- and left-handers.

(i) For right-handers, the means for the different questionnaires were significantly different from each other, F (3,297) = 115.89, p < .001, η^2 = .54. The EHI had the highest mean score (90.95, SE = .64), followed by the AHPQ (89.69, SE = .80), the WHQ (86.85, SE = .68), and the HLGI (81.98, SE = .56). Moreover, the binary response format gave a significantly higher mean score

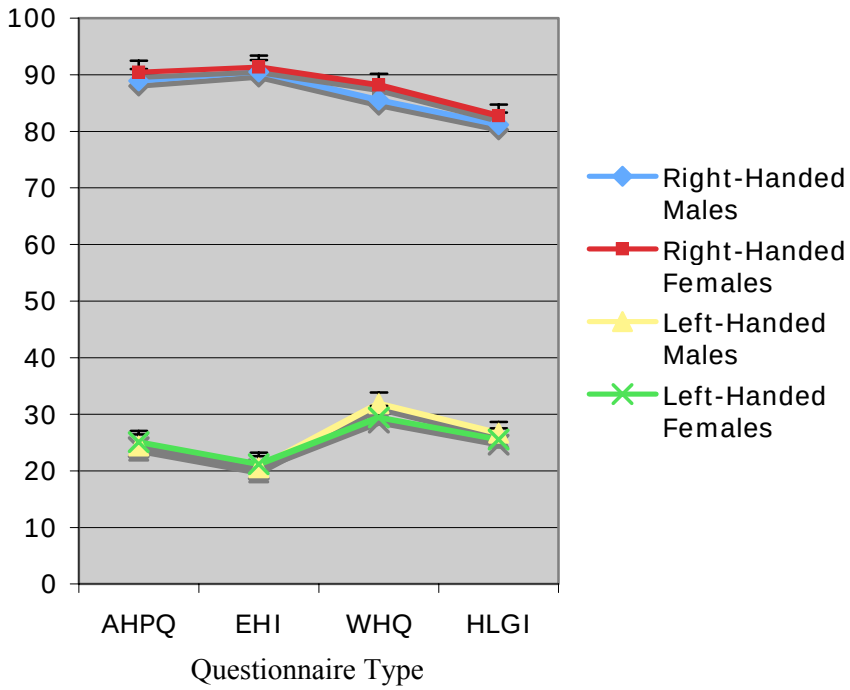

Figure 4.7. Schematic representation of the three-way interaction of Questionnaire Type x Sex x Handedness. Error bars show the standard error (σ_M).

(94.77, *SE* = .68) than the 5-point graded response format (79.96, *SE* = .63), F (1,99) = 742.72, $p < .001$, $\eta^2 = .88$. There was also a significant two-way interaction between questionnaire type and response format, F (3,297) = 581.78, $p < .001$, $\eta^2 = .86$. The interaction was followed up with two one-way ANOVAs with four levels with questionnaire (AHPQ, EHI, WHQ, or HLGI) as the within-subjects factor, performed separately for the binary response and the 5-point graded response formats.

For the binary response format, there was a significant main effect of questionnaire, F (3,297) = 4.06, $p = .008$, $\eta^2 = .04$. Pairwise comparisons using the LSD adjustment revealed that the difference in means between the AHPQ and the EHI (mean difference = 1.08, $p = .008$), the AHPQ and the HLGI (mean difference = 2.01, $p = .006$) as well as the WHQ and the HLGI (mean difference = 1.60, $p < .001$) were significantly different from each other (all other $p > .16$).

For the 5-point graded response format there was a significant main effect of questionnaire type, F (3,297) = 468.10, p < .001, η^2 = .83. Pairwise comparisons using the LSD adjustment revealed that the difference in means was significantly different for all questionnaires (all p < .001), with the HLGI having the greatest mean score differences from the rest of the questionnaires (mean score difference between EHI and HLGI = 18.87; AHPQ and HLGI = 17.43; WHQ and HLBQ = 11.34), the AHPQ and EHI pair having the smallest mean score difference (1.44), and the difference of the WHQ and EHI pair (5.54), and the WHQ and AHPQ pair (6.09) falling in-between.

(ii) For left-handers, there was a significant main effect of questionnaire type, F (3,297) = 50.04, p < .001, η^2 = .37. The WHQ had the highest mean score (30.65, SE = 2.09), followed by the HLGI (26.08, SE = 1.96), the AHPQ (24.74, SE = 2.24), and the EHI (20.89, SE = 1.78). Moreover, the binary response format gave a significantly higher mean score (26.68, SE = 1.61) than the 5-point graded response format (24.50, SE = 2.35), F (1,99) = 5.48, p = .021, η^2 = .05. There was also a significant two-way interaction between questionnaire type and response format, F (3,297) = 743.44, p < .001, η^2 = .28. The interaction was followed up with two one-way ANOVAs with four levels of questionnaire type (AHPQ, EHI, WHQ, or HLGI), performed separately for the binary response and the 5-point graded response formats.

For the binary response format, there was a significant main effect of questionnaire type, F (3,297) = 30.27, p < .001, η^2 = .23. Pairwise comparisons using the LSD adjustment revealed that all the mean differences between the questionnaires were significant (p < .001) except for the WHQ and HLGI pair (mean difference = .07, p = .91). The mean score difference between the EHI and WHQ pair (8.35) was the largest followed by the EHI and HLGI pair (8.28), the AHPQ and EHI pair having the smallest mean score difference (3.56) and the difference of AHPQ and WHQ (4.78) falling in-between.

For the 5-point graded response format there was a significant main effect of questionnaire type, F (3,297) = 77.92, p < .001, η^2 = .44. Pairwise comparisons using the LSD adjustment showed that all mean differences between the different questionnaires were significant (all p < .01) with the WHQ having the greatest mean score differences from the rest of the questionnaires (mean score difference between WHQ and EHI = 11.17; WHQ and HLGI = 9.08; WHQ and AHPQ = 7.04), the AHPQ and HLGI pair having the smallest mean score difference (2.04) and the difference of AHPQ and EHI (4.13), and EHI and HLGI (2.08) falling in-between.

Thus, the Questionnaire Type x Response Format effect appears greater for right-handers (η^2 = .88) than left-handers (η^2 = .28). For right-handers, the difference in the means of the different questionnaires seems greater for the 5-point response format (η^2 = .83) than the binary response format (η^2 = .04), and similarly so for left-handers, even though the difference is smaller (η^2 = .44 vs. η^2 = .23 respectively). All mean differences between the different questionnaire pairs were significant for the 5-point response format, for both handedness groups (all p < .001), whereas for the binary response format, all mean differences were significant at the a = .05 level, apart from the mean differences between AHPQ and WHQ, EHI and WHQ, and EHI and HLGI (all p > .16) for right-handers, and the mean difference between WHQ and HLBQ (p = .91) for left-handers.

Questionnaire Type x Sex x Handedness: In order to investigate this three-way interaction, a mean score for each questionnaire was first computed, by adding up the scores for its two formats (binary response and 5-point graded response formats) and dividing the total by two. Two 4 x 2 repeated measures ANOVAs, with the mean score for each questionnaire (AHPQ, EHI, WHQ, or HLGI) as the within-subjects factor and sex (male or female) as the between-subjects factor, were then performed separately for right- and left-handers.

(i) For right-handers, the means for the different questionnaires were significantly different from each other, F (3,294) = 115.93, $p < .001$, $\eta^2 = .54$. The EHI had the highest mean score (90.95, SE = .64), followed by the AHPQ (89.69, SE = .80), the WHQ (86.85, SE = .67), and the HLGI (81.98, SE = .55). There was no main effect of sex, F (1,98) = 1.96, $p = .16$, $\eta^2 = .02$, nor an interaction between sex and handedness, F (3,294) = 1.04, $p = .37$, $\eta^2 = .01$. Pairwise comparisons using the LSD adjustment showed that all mean differences between the different questionnaires were significant (all $p \leq .001$) with EHI and HLGI having the largest mean score difference (8.97), followed by AHPQ and HLGI (7.71). The AHPQ and the EHI had the smallest mean score difference (1.26) and the differences between AHPQ and WHQ (2.84), EHI and WHQ (4.10), and WHQ and HLGI (4.87) were found falling in-between.

(ii) For left-handers, results were similar. The means for the different questionnaires were significantly different from each other, F (3,294) = 50.39, $p < .001$, $\eta^2 = .34$. The WHQ had the highest mean score (30.65, SE = 2.09), followed by the HLGI (26.08, SE = 1.97), the AHPQ (24.74, SE = 2.25), and the EHI (20.89, SE = 1.79). There was no main effect of sex, F (1,98) = .02, $p = .88$, $\eta^2 < .01$, nor an interaction between sex and handedness, F (3,294) = 1.69, $p = .17$, $\eta^2 = .02$. Pairwise comparisons using the LSD adjustment showed that all mean differences between the different questionnaires were significant (all $p < .001$) except for the mean difference between AHPQ and HLGI (mean difference = 1.34, $p = .08$). The greatest mean score difference comes from EHI and WHQ (9.76), followed by AHPQ and WHQ (5.91), EHI and HLGI (5.18), and AHPQ and EHI (3.85).

Thus, for neither handedness group is there a significant main effect of sex (both $p > .16$) nor an interaction between sex and questionnaire type (both $p > .17$), but only a main effect of questionnaire type (both $p < .001$) as previously shown.

Response Format x Sex: In order to investigate this two-way interaction, a mean score was computed for each response format, by adding up the scores of the four different questionnaires for each response format and dividing the total by four. Two univariate ANOVAs were then performed, with the mean score for each response format (binary response or 5-point grade response format) as the dependent variable, and sex (male or female) as the fixed factor. For both ANOVAs the difference in mean scores between males and females was not significant (all $p > .77$, $\eta^2 < .01$). The interaction is probably driven by the fact that females have both a lower hand preference score for the 5-point graded responses format (53.07% vs. 53.57% for males) as well as a higher one for the binary response format (60.44% vs. 58.83% for males).

In summary, sex does not appear to affect the performance of the participants in hand preference questionnaires in a significant manner, whereas questionnaire type, response format, and handedness do affect performance significantly. Hence, no hand preference questionnaire can be claimed to be more sensitive in capturing the sex difference in handedness.

4.3.1.2 EHI graphic graded response format

A univariate ANOVA was performed with the score of the EHI in its graphic graded response format as the dependent factor, with sex (male or female) and handedness for writing hand (right or left) as the between-subjects factors. Male (11.64, *SE* = 2.59) and female (15.85, *SE* = 2.57) participants were not found to differ significantly in their mean scores, F (1,195) = .90, p = .34, $\eta^2 <$ .01. Left-handers had a significantly lower mean score (-58.72, *SE* = 2.57) than right-handers (86.95, SE = 2.59), F (1,195) = 1592.74, $p < .001$, $\eta^2 = .89$. No interaction between handedness and sex was found, F (1,195) = .44, p = .51, η^2 < .01.

4.3.1.3 Footedness and eyedness

A 2 x 2 x 2 x 2 repeated measures ANOVA was performed with laterality questionnaire (WFQ or ELPI) and response format (binary response or 5-point graded response format) as the within-subjects factors. Sex (male or female) and handedness for writing hand (right or left) were the between-subjects factors. Male (55.85%) and female (58.10%) participants were not found to differ significantly in their mean scores, F (1,196) = .57, p = .45, $\eta^2 < .01$. Handedness did have a significant main effect, with left-handers having a lower mean score (38.86, SE = 2.11) than right-handers (75.09, SE = 2.11), F (1,196) = 147.17, p < .001, $\eta^2 = .43$. The binary response format had a higher mean score (58.71, SE = 1.88) than the 5-point graded responses format (55.24, SE = 1.20), F (1,196) = 11.69, p < .01, $\eta^2 = .06$.

A number of significant two-way interactions were found: (i) Laterality Questionnaire x Handedness, F (1,196) = 4.86, p = .031, $\eta^2 = .02$, (ii) Response Format x Handedness, F (1,196) = 63.42, p < .01, $\eta^2 = .06$, and (iii) Laterality Questionnaire x Response Format, F (1,196) = 4.84, p = .029, $\eta^2 = .02$. There was also a significant three-way interaction of Laterality Questionnaire x Response Format x Handedness, F (1,196) = 28.36, p < .001, $\eta^2 = .13$ (see Figure 4.8). No other main effects or interactions were significant (all p > .12). The above interactions were further investigated.

Laterality Questionnaire x Response Format x Handedness: In order to investigate this three-way interaction, a 2 x 2 repeated measures ANOVA with laterality questionnaire (FWQ or ELPI) and response format (binary response or 5-point graded response format) as the within-subjects factors was performed, separately for right- and left- handers.

(i) For right-handers, the WFQ (79.34, SE = 1.21) had a significantly higher mean score than the ELPI (70.84, SE = 3.15), F (1,99) = 7.75, p = .006, $\eta^2 = .07$. Moreover, the binary response format (80.85, SE = 2.33) gave a higher

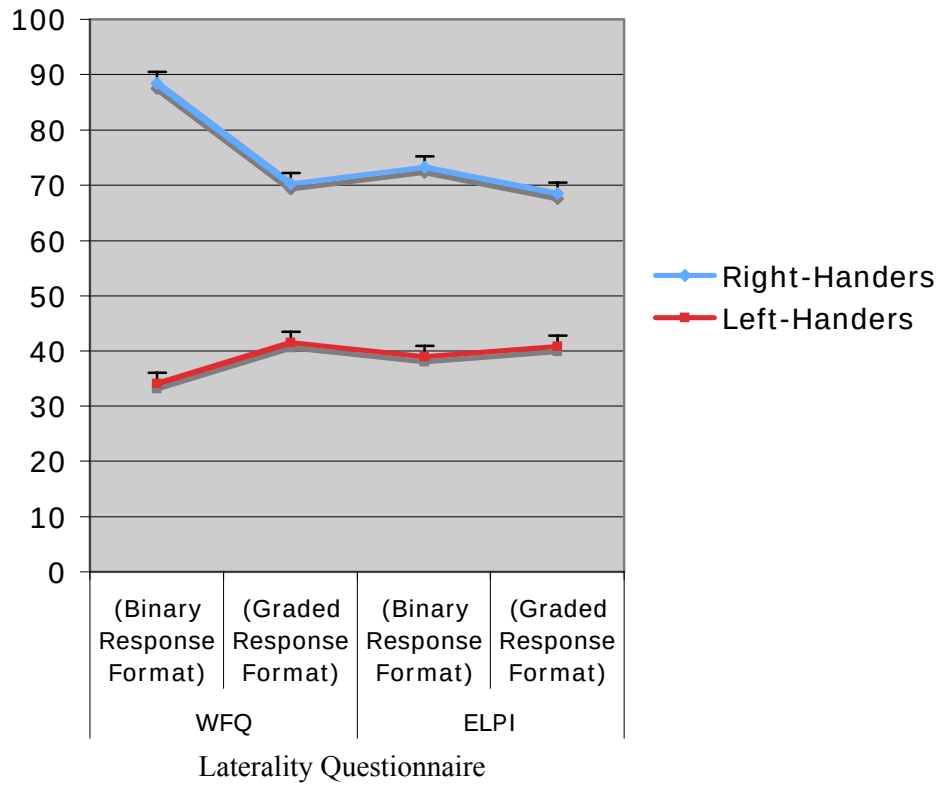

Figure 4.8. Schematic representation of the three-way interaction of Laterality Questionnaire x Response Format x Handedness. Error bars show the standard error (σ_M).

mean score than the 5-point graded response format (69.33, *SE* = 1.53), *F* (1,99) = 65.15, $p < .001$, $\eta^2 = .40$. There was also a significant two-way interaction between laterality questionnaire and response format, *F* (1,99) = 29.95, $p < .001$, $\eta^2 = .23$, which was followed up with paired samples *t*-tests. The difference in means between the two response formats was significantly different for the WFQ ($t = 15.28$, $df = 99$, $p < .001$) and only marginally significant for the ELPI ($t = 2.02$, $df = 99$, $p = .046$).

(ii) For left-handers, the 5-point graded response format (41.16, *SE* = 1.85) had a significantly higher mean score than the binary response format (36.56, *SE* = 3.57). Moreover, there was a main effect of response format, *F*

(1,99) = 10.21, p = .002, η^2 = .09, but no main effect of laterality questionnaire, F (1,99) = .32, p = .57, η^2 < .01. There was also a significant two-way interaction between Laterality Questionnaire x Response Format, F (1,99) = 4.12, p = .033, η^2 = .05, which was followed up with paired samples t-tests. The mean scores between the two response formats for the WFQ were significantly different from each other (t = -4.35, df = 99, p < .001), whereas this was not the case for the two response formats of the ELPI (t = -.85, df = 99, p = .40).

In summary, results are similar to the hand preference questionnaires' results, in that the laterality questionnaire by response format effect appears greater for right-handers (η^2 = .23) than left-handers (η^2 = .05). For both handedness groups, this interaction seems to be driven by the WFQ scores. Again, sex was not found to affect the perfor mance of the participants in a significant manner, whereas laterality questionnaire, response format, and handedness do affect performance significantly. Hence, none of the two laterality questionnaires can be claimed to be more sensitive in capturing sex differences in handedness.

4.3.2 Hand skill tests

One hundred and twenty participants were tested for relative hand skill. Table 4.3 gives the descriptive statistics. A 3 x 2 x 2 repeated measures ANOVA was performed with hand skill test (Tapping Speed, Dot-Filling, or Peg-Moving) as the within-subjects factor. Sex (male or female) and handedness for writing hand (right or left) were the between-subjects factors. Male (48.58, SE = .83) and female (47.95, SE = .99) participants were not found to differ significantly in their mean scores (transformed to a scale of 0 to 100), F (1,116) = .24, p = .63, η^2 < .01. Handedness did have a significant main effect, with left-handers having a lower mean score (41.46, SE = .94) than right-handers (55.07, SE = .89), F (1,116) = 111.39, p < .001, η^2 = .49. The means for the different hand skill tests

Table 4.3. Descriptive statistics for the hand skill tests.

Hand Skill Test	Sex	Handedness	N	Mean	SD	Range	Median
Peg-Moving (ms)	M	right	30	-2.40	.57	(-8.46) -3.82	-2.38
		left	40	2.80	.60	(-8.71)-12.31	2.81
	F	right	30	-4.41	.42	(-8.39)-(-1.23)	-4.16
		left	20	3.32	.62	(-2.10)-7.47	3.99
Dot-Filling (number of dots)	M	right	30	28.97	1.71	12.00-49.00	27.00
		left	40	-27.95	1.64	(-53.00) -1.00	-28.00
	F	right	30	29.13	1.48	.00-41.00	29.00
		left	20	-27.35	2.81	(-7.00) -1.00	-27.50
Tapping Speed (number of taps)[21]	M	right	30	4.24	.72	(-5.65) -11.18	4.16
		left	40	-0.46	.55	(-7.78) -7.42	-.46
	F	right	30	7.29	1.04	(-10.96)-21.89	7.41
		left	20	-2.50	1.33	(-17.07)-6.08	-1.69

[21] The Tapping Speed test score was multiplied by 100 for all participants, in order to make the results clearer.

were significantly different from each other, F (2,116) = 37.07, $p < .001$, $\eta^2 = .24$, with the Dot-Filling test having the highest mean score (54.86, SE = .88), followed by the Tapping Speed (49.32, SE = 1.23) and the Peg-Moving test (40.61, SE = 1.41). Moreover, there was a significant interaction of Hand Skill Test x Handedness, F (2,116) = 318.48, $p < .001$, $\eta^2 = .73$, and a three-way interaction of Hand Skill Test x Handedness x Sex, F (2,116) = 7.13, $p < .01$, $\eta^2 = .06$ (see Figure 4.9).

In order to investigate the three-way interaction, two 3 x 2 repeated measures ANOVAs with hand skill test (Tapping Speed, Dot-Filling, or Peg-Moving) as the within-subjects factor and sex (male or female) as the between-subjects factors were performed, separately for right- and left-handers.

(i) For right-handers, the scores of the different hand skill tests were significantly different from each other, F (2,58) = 349.57, $p < .001$, $\eta^2 = .86$. The Dot-Filling test (81.36, SE = 1.06) had the highest mean score, followed by the Tapping Speed test (58.63, SE = 1.62) and the Peg-Moving test (25.24, SE = 1.69). A significant two-way interaction was also found between hand skill test and sex, F (2,58) = 8.36, $p < .001$, $\eta^2 = .13$, but no main effect of sex, F (1,58) = .10, $p < .75$, $\eta^2 < .01$. The interaction was followed up with three univariate ANOVAs, run separately for the three hand skill tests (Tapping Speed, Dot-Filling, and Peg-Moving), with sex (male or female) as the between-subjects factor. Sex turned out to have a significant effect for the Peg-Moving, F (1,58) = 8.07, $p = .010$, $\eta^2 = .12$, and the Tapping Speed tests, F (1,58) = 5.89, $p = .019$, $\eta^2 = .09$, but not for the Dot-Filling test, F (1,58) = .01, $p = .94$, $\eta^2 < .001$. Thus, male right-handers had significantly higher scores (30.02, SE = 2.38) than female right-handers (20.45, SE = 2.38) in the Peg-Moving test, and female right-handers had significantly higher scores (62.55, SE = 2.29) in the Tapping Speed test than male right-handers (54.70, SE = 2.29).

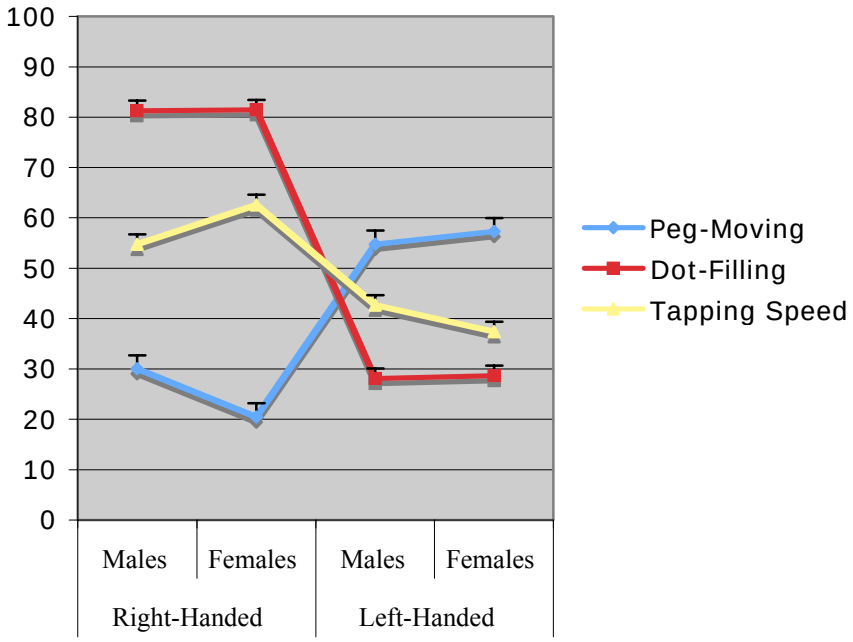

Figure 4.9. Schematic representation of the three-way interaction of Hand Skill Test x Sex x Handedness. Error bars show the standard error (σ_M).

(ii) For left-handers the scores of the different hand skill tests were significantly different from each other, F (2,58) = 57.82, p < .001, η^2 = .50. The Peg-Moving test (55.99, SE = 2.28) had the highest score, followed by the Tapping Speed test (40.01, SE = 1.56) and the Dot-Filling test (28.36, SE = 1.43). There was no significant main effect of sex, F (1,58) = .13, p = .72, η^2 < .01, nor an interaction between hand skill test and sex, F (2,58) = 1.22, p = .30, η^2 = .02.

In summary, the effect of hand skill test appears to be greater for right-handers (η^2 = .86) compared to left-handers (η^2 = .50). Moreover, sex was found to have a significant effect for right-handers when handedness was assessed by means of the Tapping Speed test as well as by means of the Peg-Moving test (with female right-handers achieving higher scores than male right-handers).

Higher scores for the Tapping Speed test mean that the mean difference in the number of taps produced by the right hand vs. the number of taps

produced by the left hand was significantly higher in right-handed females compared to right-handed males. Higher scores for female right-handers in the pegboard mean that the absolute mean difference in the time needed to move the pegs with the right hand compared to the time needed to move them with the left hand was greater for right-handed females (R mean time - L mean time for females = -4.41 ms), compared to right-handed males (R mean time - L mean time for males = -2.40 ms).

Could these results be attributed to the right hand being more skilful, or are they due to the left hand being less skilful (or both) in right-handed females compared to right-handed males? With regards to the Tapping Speed test, right-handed females produced significantly fewer taps with the right hand (mean number of taps = 88.77) than right-handed males (mean number of taps = 98.53 taps), F (1,59) = 12.66, $p < .01$, $\eta^2 = .18$, as well as fewer taps with the left hand, (mean number of taps = 76.7) compared to right-handed males (mean number of taps = 90.41), F (1,59) = 37.35, $p < .01$, $\eta^2 = .39$. With regards to the Peg-Moving test, right-handed females were faster with the right hand (9.81 ms) compared to right-handed males (10.13 ms), F (1, 59) = 2.37, $p = .13$, $\eta^2 = .04$, as well as slower with the left hand (10.72 ms) compared to right-handed males (10.63 ms), F (1.59 = .15, $p = .71$, $\eta^2 < .01$. Even though these differences did not reach significance when considering the difference separately for the right and the left hands.

4.3.3 Quantification of hand preference test

One hundred and twenty participants were administered the QHPT. Table 4.4 gives the descriptive statistics. A univariate ANOVA was performed with QHPT as the dependent factor. Sex (male or female) and handedness for writing hand (right or left) were the between-subjects factors. Male (47.30, SE = 2.39) and female (49.21, SE = 2.86) participants were not found to differ

Table 4.4. Descriptive statistics for the QHPT.

Sex	Handedness	N	Mean	SD	Range	Median
	right	30	60.32	3.17	38.10-100	57.14
M	left	40	34.29	3.14	0-100	42.86
	right	30	70.32	3.18	47.62-100	66.67
F	left	20	28.10	5.78	0-100	28.57

significantly in their mean scores, F (1,116) = .26, p = .61, η^2 < .01. Left-handers had a significantly lower mean score (31.19, SE = 2.71) than right-handers (65.32, SE = 2.56), F (1,116) = 83.68, p < .001, η^2 = .42. An interaction between handedness and sex was found, F (1,116) = 4.71, p = .032, η^2 = .04 (see Figure 4.10). Separate ANOVAs for right- and left-handers revealed that right-handed females had significantly higher scores (70.32, SE = 3.62) than right-handed males (60.32, SE = 3.62), F (1,58) = 4.97, p = .028, η^2 = .08, but the mean scores between left-handed females (28.10, SE = 4.43) and left-handed males (34.28, SE = 3.13), were not significantly different, F (1,58) = 1.06, p = .31, η^2 = .02.

Higher scores for the QHPT mean that the percentage of cards preferentially reached by the right hand was higher for right-handed females than for right-handed males. Taking into account both the results for the hand skill test and the results for the QHPT, it seems that right-handed females are more skilful with the right hand compared to the left hand (or to prefer the right rather than the left hand for reaching actions) as opposed to right-handed males. Overall, this sex effect in right-handers seems slightly greater for the Peg-Moving test (η^2 = .12) compared to the Tapping Speed test (η^2 = .09) and to the QHPT (η^2 = .08).

Figure 4.10. Schematic representation of the two-way interaction of Sex x Handedness for the Quantification of Hand Preference Test (QHPT). Error bars show the standard error (σ_M).

4.4 Discussion

The study presented in this chapter confirmed the findings of the meta-analysis in that the hand preference questionnaires do not significantly differentiate amongst them with regards to their sensitivity in capturing the sex difference in handedness. The foot and eye preference questionnaires also failed to produce significantly different scores between the sexes. The QHPT, though, a behavioural test of hand preference employing card reaching at different locations, did prove to be sensitive in capturing sex differences, at least for right-handed participants. Similar results were obtained for two of the hand skill tests: the Peg-Moving and the Tapping Speed test. For all these three tests, right-handed females were found to have a significant difference in skill between their right and left hands (or to prefer the right rather than the left hand for

reaching actions) as opposed to right-handed males. These findings lead to the conclusion that behavioural tests of handedness, and specifically the QHPT, the Peg-Moving test, and the Tapping Speed test, are more sensitive tools than hand preference inventories when it comes to the study of sex differences in handedness and its correlates.

Looking at the results more closely, a number of other interesting conclusions can be drawn. Questionnaire type, response format, and handedness are all factors that affect the scores of the participants in hand preference questionnaires in a significant manner. Moreover, for right-handers the questionnaire and response format interaction was found to be greater than for left-handers. For both handedness groups, and especially for right-handers, the difference in the mean scores produced by the different questionnaires was greater for the 5-point response format than the binary response format. Results are similar for the footedness and eyedness questionnaires. These findings point once again towards the need to reach a consensus amongst laterality researchers about the hand preference questionnaires and inventories that they employ. If questionnaire type and response format can artificially produce different laterality scores, and if they affect right-handers more than they affect left-handers, then comparison among studies that have not employed the same laterality measurements can produce misleading conclusions.

When it comes to hand skill tests, the effect of using different instruments was found to be greater for right-handers compared to left-handers, similarly to hand preference tests. Again, this suggests that comparing among studies that have employed different hand skill instruments should be done with caution. Moreover, sex was found to have a significant effect for right-handers for the Tapping Speed test as well as for the Peg-Moving test. These results might either be due to the right hand being more skilful, or to the left hand being less skilful, (or to both), in right-handed females compared to right-handed males.

With regards to the Tapping Speed task, this result was found to be due to right-handed females producing significantly fewer taps with both their right and left hands compared to the right and left hands of right-handed males, but the difference was greater for the left hand. Looking at the mean times needed to move the pegs in the Peg-Moving test, right-handed females were both faster with the right hand as well as slower with the left hand compared to right-handed males, even thought these differences did not reach significance between the right or left hands of the two sexes. In addition to these results, the QHPT showed that the percentage of cards preferentially reached by the right hand was higher for right-handed females than for right-handed males.

Taking into account both the results for the relative hand skill tests and the results for the QHPT, it seems that right-handed females are more skilful with the right hand compared to the left hand (or to prefer the right rather than the left hand for reaching actions) as opposed to right-handed males. This finding is in line with the results of Rigal (1992) who similarly found that right-handed females are better than right-handed males with their preferred hand. Rigal used a dexterity task, in which the participant takes a block from a hole, turns it over, and puts it back in the same hole using only one hand and repeats the procedure for 40 blocks, while the time necessary to turn over all blocks is recorded. Annett has also found that, within right-handers, females are more strongly right-handed on manual skill tasks than males (Annett, 1980). Annett and Kilshaw (1983) have further reported that, for a sample where no sex difference was found in hand preference (Kilshaw and Annett, 1983), the difference between right and left hand skill was more biased to the right in females than in males, and that this difference in skill was significant only for consistent right-handers. The present findings are moreover in agreement with data provided by Gardner and Broman (1979) for performance on the Purdue Pegboard that show that the superiority in fine dexterity tasks shown by girls is

greater for the preferred compared to the non-preferred hand, and further consistent with adult findings of a wider difference between the hands of females than of males (e.g., King et al., 1978; Curt et al., 1995). In line with these findings, Tan (1990a, 1990b) reported that only the right-hand skill showed a direct correlation and an inverse correlation with serum T concentration for males and females respectively.

This finding gives rise to two questions: (a) why is this sex effect only found in right-handers, and (b) why is this sex effect found only for the right hand, that is the preferred hand for right-handers? The first question may be relevant to Inman's remark that "a curious feature about left-handedness is that it is rarely as complete as right-handedness" (Inman, 1924). A number of authors seem to agree with this remark (Humphrey, 1951; Benton et al., 1962; Steenhuis and Bryden, 1989; Rigal, 1992). Inman's remark could be argued to have received some support from the results of the study presented in chapter 3 as well, whereby right-handers were found to be significantly more reluctant to give a "left" response in the place of an "either" response than left-handers were to give a "right" response in the place of an "either" response. In other words, it could be argued that left-handers are less lateralised than right-handers, which might result in sex differences being exaggerated amongst right-handers.

The second question might be answered by previous findings that the right hand (of dextrals) is usually faster and more accurate than the left on tasks requiring speeded actions such as aiming at a target, placing pegs in holes, or finger-tapping (Beaton, 2003). Moreover, on the Peg-Moving and Tapping Speed tests, right-handed adults tend to show greater variability of the left than of the right hand (e.g., Peters and Durding, 1978; Peters and Durding, 1979; Todor et al., 1982; Carlier et al., 1993). In addition, Tan (1991c) reported that the negative linear relationship he found between serum T concentrations

and Peg-Moving times was more pronounced for the right than the left hand in males.

It might be of interest to further contemplate on the reasons why the Peg-Moving and the Tapping Speed tests detected sex differences in hand skill, whereas the Dot-Filling test did not. This finding could be explained by the finding of the meta-analysis that writing hand gives the smallest male-to-female left-handedness odds ratio when compared to hand preferences tests, which include a number of other activities. The Dot-Filling test is clearly influenced by writing, thus it could share its smaller sensitivity with regards to sex differences. Another possibility is that the findings might be explained by the fact that the Dot-Filling test, again through its proximity with writing, is the test most influenced by training. In other words, the fact that the participants routinely write with one hand adds a component of differential experience between the hands to the task performance, skewing the outcome distribution in favour of the preferred hand (Peters, 1998). This skewing might be concealing underlying sex differences, by means of a ceiling effect for both sexes. A third possibility may be related to the fact that the three hand skill tasks employ different types of movement and there is evidence that different types of movements rely on different underlying neural systems, at least to some degree (Szekely et al., 1998). It might thus be claimed that the fact that the Dot Filling test was the least powerful in detecting sex differences might be due to sex difference in the neural substrate underlying the hand movements pertinent to aiming.

The present findings lead to the conclusion that behavioural tests of handedness and specifically the QHPT, the Peg-Moving test, and the Tapping Speed test, should be preferred when it comes to the study of sex differences in handedness and its correlates, as they were found to be the most sensitive ones with regards to capturing sex differences. It should be noted, however, that it is

not here assumed that the method that produces the biggest sex difference is the most valid one, as it may not reflect underlying reality but instead it may be producing an overestimate.

Among the behavioural tests that were used here, the Peg-Moving test was found to have the largest effect size within right-handers (η^2 = .12) compared to the Tapping Speed test (η^2 = .09), and the QHPT (η^2 = .08), even though all three effect sizes are small. In practical terms though, it may be the case that the Tapping Speed test is more convenient for use in large groups of participants: as long as each participant has his/her own tally-counter, the experimenter can just set the starting and finishing time (by saying 'go' and 'stop') and the participants can make a note of the number of taps they have produced, as written on the counter. Nevertheless, it would be recommended that when doing research on handedness, one should provide information on the writing hand and the score of the participants on the EHI in addition to their score on any behavioural task, for comparison purposes between studies. Both writing hand and the EHI are quick and easy to record and administer, and they are moreover the most popular hand preference instruments used in the literature, providing a solid basis for comparison.

Overall, the study presented in this chapter provided evidence that the most sensitive instruments for the study of sex differences in praxic lateralisation are the Peg-Moving test, the Tapping Speed test and the QHPT. Further studies presented in this thesis will be employing these three instruments, as well as writing hand and the EHI, for investigating the hormonal correlates of praxic and linguistic lateralisation.

Chapter 5

Relationships of adult T and C concentrations with praxic and linguistic lateralisation

5.1 Introduction

Praxic and linguistic lateralisation are two sexually dimorphic traits, which are intimately linked, with the incidence of right hemisphere language dominance increasing linearly with the degree of left-handedness (Knecht et al., 2000). The findings of chapter 2's meta-analysis provide support for the sex difference in praxic lateralisation having its basis in innate biological differences between the two sexes, namely differences in their genetic make-up (e.g., McManus and Bryden, 1992; Jones and Martin, 2000; Annett, 2002), in their rate of somatic maturation (e.g., Maehara et al., 1988), and in their hormonal environment (e.g., Geschwind and Galaburda, 1987). The present chapter investigated the hormonal theories of the sex difference in praxic and linguistic lateralisation.

The underlying concept is that sex differences in praxic and linguistic lateralisation are, at least in part, controlled by the same hormone, namely prenatal T. At least three different theories have been proposed within this framework (see chapter 1 for a detailed description). Briefly, the Geschwind and Galaburda hypothesis (Geschwind and Galaburda, 1985a, 1985b, 1985c, 1987;

Galaburda et al., 1987), suggests that prenatal T acts so as to increase the probability of right-hemispheric dominance by disrupting left hemisphere growth. Taking into account that the developing male brain is exposed to higher T concentrations than the female brain, increased left-handedness and atypical dominance in males is to be expected. The callosal hypothesis (Witelson, 1991), on the other hand, claims that it is actually low T levels exposure in early brain development that may contribute to the development of reduced linguistic lateralisation and greater left-handedness, at least in males, by reducing cell death and axonal pruning in the corpus callosum and the temporo-pariental cortex. Finally, the sexual differentiation hypothesis (Hines and Shipley, 1984) is based on data showing neural and behavioural masculinisation when exposing animals prenatally to androgens (Goy, 1980) and suggests that higher levels of prenatal T could be related to left-handedness and greater cerebral language dominance.

5.1.1 Hormonal assessment

Even though the sex difference in praxic and linguistic lateralisation is accounted for by theories implicating prenatal T concentrations, only limited work has been carried out involving the actual measurement of prenatal hormonal levels (e.g., Grimshaw, 1995). The bulk of the research on the relationships between hormonal levels and lateralisation in healthy individuals has actually studied adult hormonal levels, mostly because pre-natal T is very hard to measure. Nevertheless, there is reason to expect that T differences obtained in adulthood are at least moderately representative of individual differences in early life T secretion (Meikle et al., 1988; Jamison et al., 1993). An advantage of measuring T levels in adults is that it provides the means to test hormonal levels specifically in selected populations such as left-handers.

The measurement of adult T concentrations can be done by sampling saliva (e.g., Moffat and Hampson, 2000), blood (serum or plasma; e.g., Hausmann et al., 2002), or urine (e.g., Ward, 1972). For the purposes of the present investigation, T concentrations were determined from saliva, as sampling saliva has several advantages over sampling blood or urine: it is non-invasive, painless, and less stressful for the participants (Neave and Menaged, 1999). Moreover, saliva collection procedures allow for repeated sampling over the course of minutes, hours, days, or longer (Dabbs, 1990b; Malamud and Tabak, 1993). Researchers and participants themselves with minimal training can easily collect saliva samples. Also, the reliability, precision, accuracy, and analytical recovery of immunoassays designed to measure salivary T are now well documented (Granger et al., 1999).

Further to the above practical considerations, salivary T is optimal for bio-behavioural research, as only free or bioavailable T is present in saliva,[22] and, unlike bound T, it can pass the blood-brain barrier and thereby potentially influence cognitive processing (Vermulen and Verdonck, 1972; Shute et al., 1983). Another reason for using saliva is that, in females, T levels in the blood are 10 to 20 times lower than in males, making the determination of T concentrations by conventional immunoassays very difficult. Recently published articles have actually stated that results from blood samples have been

[22] Between 95% and 99% of the total T present in serum or plasma is bound to various binding proteins such as the sex hormone binding globulin (SHBG). The bound fraction is biologically incactive and is sometimes described as a reservior of T. The biologically active hormone is a small fraction of free steroid hormone that represents between 1% and 5% of the total concentration of T in serum. Therefore, measurement of T in serum or plasma will be mainly a reflection of the inactive hormone, as there is currently no reliable immunoassay available for the measurement of the free hormone fraction in serum. Salivary T, on the other hand, is derived primarily from the free, or non-SHBG-bound, or bioavailable T in plasma and therefore directly represents that fraction of T that is biologically active and available to tissue for metabolic purposes (IBL Laboratories, 2004).

incorrect, especially when measured by fully automated systems (Herold and Fitzgerald, 2003; Taieb et al., 2003). In saliva the concentration of free T in females is 3 to 5 times lower compared to males. Nevertheless, high correlations between salivary and serum free T concentrations have been reported (r = 0.91 to r = 0.97; Vittek et al., 1985; Dabbs and De La Rue, 1991).

Salivary cortisol (C) was also measured as a control hormone in order to be able to test for the specification of any obtained relationships to T. C was chosen, because it is another saliva steroid that displays similar diurnal variation. A strong correlation has been reported between salivary and serum levels for C (Kirschbaum and Hellhammer, 1994a, 1994b) and it is believed that similar genetic influences, such as the ones described for T, exist for baseline C levels (Kirschbaum et al., 1992). Indeed previous studies on hormonal levels and lateralisation have similarly used C as their control hormone (e.g., Moffat and Hampson, 2000).

5.1.2 Praxic lateralisation assessment

For the purposes of the present investigation, the tests with the greatest sensitivity with regards to capturing the sex difference in praxic lateralisation as identified in the study presented in chapter 4 were employed: the Peg-Moving test (Annett, 1985), the Tapping Speed test (Tapley and Bryden, 1985), and the QHPT (Bishop, 1989). Regarding hand preference questionnaires, none of the different questionnaires investigated in chapter 4 appeared to be differentially sensitive to sex differences. Thus, the EHI (Oldfield, 1971) was used, as this is the most popular hand preference inventory in the literature.

5.1.3 Linguistic laterality assessment

For the measurement of linguistic lateralisation a number of neuropsychological tests have been developed. Two tests that tap into two

different modalities (auditory and visual) were used here: the Consonant-Vowel Dichotic Listening test (CV-DL) and the Visual Half-Field Lexical Decision test (VHLD). These two tests are sensitive to many developmental, physiological, and behavioural factors, which makes them suitable for use in the investigation of individual differences in linguistic lateralisation (Cowell and Hugdahl, 2000; Cowell et al., 2003). They are, moreover, the most commonly used tests in the assessment of hemispheric performance differences (Stephan et al., 2007).

The DL test is a non-invasive behavioural test that assesses brain asymmetry by focusing on the left-right differences in the perception of auditory stimuli (Bryden, 1988b; Hugdahl, 1995). It was initially developed for the study of selective attention (Broadbent, 1952) but since its application to the research of cerebral dominance (Kimura, 1961), it has become the most popular non-invasive method for the study of temporal lobe function with regards to laterality (Hugdahl, 1996). In the DL situation, participants are simultaneously presented with two different stimuli via headphones to the right and left ears and they are asked to report what they heard. The stimuli are typically computer generated to allow for optimal synchronisation between the output channels. Thus, the basic feature of the dichotic situation is to provide more stimuli at any moment in time than the brain is capable of processing. The question then becomes which stimulus will be selected to be processed by the brain and therefore reported by the participant. A typical finding is the so-called right-ear advantage (REA), which means that more items heard from the right ear than the left ear are correctly reported (Foundas et al., 2006) and which reflects the standard left-hemispheric dominance for language. Conversely, the absence of an REA (i.e., symmetry) or the presence of a left-ear advantage (LEA) may indicate either symmetrical or right-hemispheric language dominance.

There are a number of theories that have been developed to account for the way the DL test reflects linguistic lateralisation. These theories include a

combination of anatomical, perceptual, and cognitive operations (Gadea et al., 2000; Foundas et al., 2006). Kimura's (1961) model postulates that the ear advantage reflects the physiology and anatomy of the auditory system and has been termed the "classical" or "structural" model. Although each ear has auditory connections to both cerebral hemispheres, it appears that the contralateral pathway has more fibres and greater cortical representation than the ipsilateral one (Rosenzeig, 1951; Celesia, 1976). Thus, the typical REA is induced by a left hemisphere processing advantage for verbal auditory stimuli in the following manner: the signal from the left ear reaches the right hemisphere and has to be transferred across the corpus callosum to the left hemisphere to be processed. The right ear signal, on the other hand, has a more direct route to the left hemisphere and so it could have an advantage over the left ear signal (Kimura, 1961, 1967; Berlin et al., 1973; Satz et al., 1975; Strauss et al., 1987; Strauss, 1988; Wexler and King, 1990; Cowell and Hugdahl, 2000).

The callosal relay model is another explanation based on anatomical connections (Beaton, 2003). According to this model, contralateral auditory pathways suppress ipsilateral input at the level of the brainstem, thereby inducing a left-hemisphere advantage (for the majority of the population) for auditory processing of verbal input. The corpus callosum inhibits information therefore allowing the two hemispheres to function in relative isolation (Cowell and Hugdahl, 2000).

An alternative hypothesis is that the ear bias is attentional ("attention model"). Kinsbourne (1970, 1975) has suggested that in free recall conditions the dominant hemisphere priming plays a role in the ear advantage, when verbal stimuli are used. According to Kinsbourne, each hemisphere primarily attends to the opposite perceptual field. Thus, anticipation that the task requires processing of verbal stimuli may preferentially activate the hemisphere dominant for language functions, with attention being directed to the contralateral ear. This

attentional bias may result from either or both of two processes: facilitation of report from the attended ear or suppression of reports from the non-attended ear.

Ipsilateral blockage and callosal transfer are supported by clinical studies of callosotomised patients, who show a dramatic REA under dichotic (but not monaural) stimulation (Bradshaw et al., 1986). However, an REA has also been found when stimuli are presented through loudspeakers for both callosotomised and normal participants (Tweedy et al., 1980). This suggests that the assumption of ipsilateral sensory pathway suppression during DL is not justified (Geffen and Quinn, 1984). On the other hand, the attentional model has received some experimental support. Hugdahl and Andersson (1986) showed that directing attention to the right or left ear during dichotic stimulus presentations had clear effects on the ear advantage in adult subjects. Other researchers have reported similar results when manipulating attention (Hiscock and Stewart, 1984; Mondor and Bryden, 1991). Nevertheless, many studies have failed to demonstrate such a priming effect. Although the attentional hypothesis can explain the lack of stable effects across many studies, it may be that the effects of vigilance and of attentional shifts reflect the adaptability of the auditory system. The most recent conceptualisations acknowledge that attentional factors can modulate a structurally-based ear advantage (Clarke and Zaidel, 1998; Gadea et al., 2000).

A number of stimuli have been used in DL situations, including different tonal sequences (Bryden et al., 1982), monosyllabic numbers (Cohen-Bendahan et al., 2004), etc. The present study employed a consonant-vowel (CV) paradigm, since presentation of CV stimuli gives the most robust REA (Foundas et al., 2006). The CV-DL paradigm is moreover the most reliable paradigm one can use to estimate laterality effects (r = .80; Voyer, 1998) and it has further been validated both through a comparison with the Wada technique (Wada and

Rasmussen, 1960) and through a H_2 ^{15}O-PET study on brain activation during CV-DL. The first study revealed that the DL scores based on the direction of ear advantages led to correct classification of hemispheric language dominance according to the Wada results in 92% of the participants (Hugdahl et al., 1997). The second study found that the CV-DL paradigm elicited neural activation in the left temporal lobe and a right ear superiority in response accuracy (Hugdahl et al., 1999).

Voyer (1998) suggests that it is the task demands underlying the CV-DL paradigm that are responsible for its high reliability and validity. The CV-DL task does not involve words which might vary in terms of their frequency of use, phonological regularity, etc., which are factors that are likely to affect word recognition performance (see Besner and Johnston, 1987). It rather involves a combination of basic speech sounds, which are essentially meaningless. Even though some letter combinations are likely to be more common than others, the influence of factors such as word frequency and regularity should be minimal. The CV-DL paradigm thus allows for the investigation of linguistic lateralisation, while minimizing the influence of extraneous factors, which are inherent to words (Voyer, 1998).

Linguistic lateralisation was furher investigated through the VHLD test. The visual half-field technique involves the tachistoscopic projection of stimuli to either the left or right visual field in order to ensure that stimuli reach only, or are at least initially processed only by, one of the two cerebral hemispheres. Participants must maintain fixation on the central point of a monitor screen while stimuli are presented to the right or left visual field centre at a rate too fast for the eye to saccade. Performance differences (i.e., accuracy and relative speed of responses) are interpreted as evidence of the relative specialisation of one or the other hemisphere. Similarly to the DL test where a REA is the most frequent finding, a right visual field advantage (RVFA) is the most frequent finding of

visual field studies using verbal stimuli, and it is similarly interpreted as indicative of left-hemispheric language dominance. (McKeever, 1971; McKeever and Hulling, 1971; Hines, 1976; Leiber, 1976; Bradshaw and Gates, 1978; Boles, 1983; Chiarello, 1985; Boles, 1987; Boles, 1990; Nicholls and Wood, 1998; Olk and Hartje, 2001; Weems and Reggia, 2004). The RVFA appears to be true across languages (Babkoff and Ben-Uriah, 1983; but also see Melamed and Zaidel, 1993) and it is commonly observed for word stimuli but not for non-word stimuli (Chiarello, 1985; Iacoboni and Zaidel, 1996; Weems and Zaidel, 2004), for both number of correct responses and reaction times (Krach et al., 2006).

It should be noted, however, that although the RVFA is a robust finding of group studies, the degree of visual field asymmetry is highly variable and does not reliably indicate left-hemisphere language dominance when considering individual participants (Chiarello et al., 1984; Kim and Levine, 1991). In order for this variability to be reduced, the “bilateral presentation mode” has been introduced: this refers to the simultaneous bilateral presentation of two different stimuli, one as the target to be processed and the other as a distractor to be ignored by the participant (Olk and Hartje, 2001). Using this method, larger and more reliable visual field asymmetries are obtained with both verbal and nonverbal stimuli (Hines, 1975; Boles, 1983, 1987, 1990, 1994; Rayman and Zaidel, 1991; Kim and Levine, 1994; Iacoboni and Zaidel, 1996). Olk and Hatje (2001) suggest that the bilateral presentation mode may produce greater visual field asymmetries by maximizing hemispheric independence not only of strategy, but also of resources, by means of simultaneously engaging both hemispheres in the automatic processing of the target in one visual field and of the distractor in the contralateral visual field (Rayman and Zaidel, 1991; Iacoboni and Zaidel, 1996).

Visual half-field tests have been using different paradigms, such as figural comparison paradigms (e.g., Rode et al 1995) and face discrimination

tasks (e.g., Heister et al. 1989). In the present study a lexical decision paradigm was employed, a paradigm well validated both in split-brain participants and controls (Zaidel et al., 1990, 1995; Iacoboni and Zaidel, 1996; Iacoboni et al., 1997). Such a paradigm involves the bilateral tachistoscopic presentation of words and non-words simultaneously to the right and left of a central fixation point of a monitor screen. Participants must decide at which side of the fixation point a word was presented, or indicate that no words were presented at either side.

Theories explaining the performance asymmetry of the two hemispheres in the VHLD task, similarly to the theories accounting for the DL situation, suggest both a direct transfer route as well as a callosal transfer route of the bilaterally presented verbal information. With regards specifically to the lexical decision situation, the visual field advantage is suggested to be due to the dominant hemisphere (usually the left) being the only one having access to dual routes of word recognition (Ellis and Young, 1988; Paap and Noel, 1991; Coltheart et al., 1993; Weems and Zaidel, 2004). The first route, termed the "lexical route", involves matching the word to its entry in the visual lexicon, activating the stored representation including the semantic system, and finally producing the response. This route is believed to exist in both hemispheres (Zaidel, 1998; Zaidel, 1999). The second, the "non-lexical route", available only to the dominant hemisphere, performs grapheme to phoneme conversion and therefore allows for "phonic reading" (Ellis and Young, 1988; Ellis et al., 1988). The two routes are influenced by different factors: the first by orthographic and semantic variables such as word length, frequency, and concreteness and the second by orthographic and phonological variables such as word length and regularity (Zaidel, 1999).

5.1.4 Limitations of previous studies and scope of the present study

Previous work investigating relationships between T concentrations and behavioural and brain lateralisation in healthy volunteers has provided interesting insights (for a review see chapter 1). Nonetheless, findings remain inconclusive, possibly due to a number of limitations in the research design of these studies. The present study was designed to overcome these limitations.

Firstly, previous work has measured handedness mostly as hand preference (e.g., Tan, 1991a; Moffat and Hampson, 2000). Only rarely have relative hand skill tests been employed (e.g., Tan, 1990c). Here, two measures of relative hand skill are employed (the Peg-Moving and the Tapping Speed tests) in addition to the measurement of hand preference by means of the EHI and the QHPT. Moreover, previous studies have only used a single measure of brain laterality, for example only the DL test (e.g., Moffat and Hampson, 1996, 2000; Gadea et al., 2003). The present study measures brain laterality with two different tests, which tap on two different modalities: the auditory CV-DL test and the VHLD test.

Furthermore, only a few studies have taken care to exclude female participants who were on oral contraceptives (Moffat and Hampson, 1996, 2000). This should be an explicit excluding criterion, since oral contraceptive use not only affects manual praxis (Szekely et al., 1998), but there are also data concerning suppressed T levels when using these drugs (Bancroft et al., 1980).

Menstrual cycle phase was not kept constant in almost all studies on T levels and language lateralisation, except for the study of Gadea (2003), where the sample included only female participants and where menstrual cycle phase was counterbalanced across participants. Controlling for menstrual cycle phase is important for two reasons: Firstly, T has a brief rise at ovulation (Valette et al., 1975; Vermeulen and Verdonck, 1976), although it has been suggested that this variability is small and the individual differences can overwhelm menstrual cycle

effects (Dabbs and De La Rue, 1991). Secondly, there are data supporting an influence of the menstrual cycle phase on DL performance (Altemus et al., 1989; Sanders and Wenmoth, 1998) as well as on performance in visual half-field tests (Hausmann et al., 2002). In the present study, all female participants were at menses during testing, as a greater cerebral asymmetry during menses compared to the mid-luteal phase has been observed (Hausmann and Güntürkün, 2000), even though findings are not conclusive (for a discussion see chapter 1). Still, menses is a clearly identifiable point in the cycle, making it convenient to control.

Circadian and circannual changes in T concentrations are well-known, with the daily peak occurring at approximately 8:00 a.m. and the nadir occurring around 8:00 p.m. (Lincoln et al., 1974; Neischlag, 1974; Dabbs, 1990b; Moffat and Hampson, 2000). Moreover, mean T concentrations are higher in autumn than in spring, at least in the Northern Hemisphere (Baron-Cohen et al., 2004). Circadian changes have been also described for C levels. The prime of the C peak is not dependent upon the absolute time and also it is not influenced by daylight. It is dependent on the wake-up time of each individual (Kudielka and Kirschbaum, 2003). Moreover, awakening C responses are influenced by health status but not by menstrual cycle phase. The much-cited series of papers by Tan (1990a, 1990b, 1990c, 1991a, 1991b, 1991c) has noticeably overlooked the issue of controlling for circannual and circadian changes in T levels. Moffat and Hampson, on the other hand, have done careful work in controlling these changes in T levels (Moffat and Hampson, 1996, 2000). In the study reported in their 1996 paper, all testing was carried out within a 3-month period at either 8.15 a.m. or 10.15 a.m. In the study reported in their 2000 paper all testing was similarly carried out in the morning and it lasted 26 months, counterbalancing males and females and left- and right-handed individuals within this period.

In the present study participants were tested in the afternoon rather than in the morning, following the suggestion by Sanders et al. (2002) that testing should be carried out preferably later in the afternoon when T levels are not changing rapidly. Moreover, since both C and T exhibit a morning peak, and this peak is highly dependent on sleeping habits but disappears rather quickly, testing in the afternoon seems a rather more rational choice. With regards to seasonal variations in T levels, carrying out all the testing in spring time[23] was preferred, as previous work has shown that men and women tested in the spring exhibit exaggerated patterns of asymmetry compared to participants tested in the fall (Wisniewski and Nelson, 2000), thus relationships with T may be easier to detect at this time of year. In addition to that, only young students were recruited, since its has been found that for males T concentration decreases with increasing age (in female saliva the concentration of T seems to be nearly independent of the age; Dabbs, 1990a).

Therefore, the purpose of the study described in this chapter was to further examine the relationships between free T concentrations and hand preference, hand skill, and patterns of linguistic lateralisation. It was hypothesised that these relationships will be specific to T and will not generalise to C.

Based on the results of chapter 4, the following predictions were made with regards to the relationship between T levels and praxic lateralisation:

(a) No relationships will be detected between T levels and hand preference.

(b) Relationships between T levels and hand skill as well as the QHPT test scores will be detected, in the direction of lower T levels being related to

[23] The testing period was actually the last term of the academic year (Trinity Term), so some testing was carried out in the summer (June). Testing could not have begun earlier, as students would not have been available to participate during the Easter Break.

better right hand skill (since it was found that females are more skilful with their right hand compared to their left hand and they moreover prefer the right rather than the left hand for reaching actions as opposed to males). It is expected that these relationships will be stronger for right-handers than left-handers and that they will be stronger for the Peg-Moving test compared to the Tapping-Speed test and the QHPT.

As far as the relationship between T levels and linguistic lateralisation is concerned, only other researchers' findings can be the basis of any predictions. Even though the literature does not provide a clear picture on the nature of the sex differences in linguistic lateralisation, there nevertheless seems to be support for the notion that males tend to exhibit more accentuated asymmetries compared to females (e.g., Wisniewski, 1998). It is therefore predicted that lower T concentrations will associated with less hemispheric asymmetry on language tasks.

5.2 Method

The study was reviewed by, and received ethics clearance through the CUREC of the University of Oxford. Maintenance of confidentiality of information is subject to normal legal requirements.

5.2.1 Participants

Sixty participants[24] (15 male right-handers, 15 female right-handers, 15 male left-handers, and 15 female left-handers) took part in the present study. Participants were undergraduate and graduate students enrolled in the University of Oxford (*mean age* = 22 years, *SD* = 3, *range* = 18-32). Participants

[24] These are the same participants as those that participated in the studies presented in chapters 3 and 4.

were reimbursed for their time with either course credit (RPS participants) or 10 pounds in cash (all the rest).

5.2.1.1 Inclusion/exclusion criteria

All participants underwent screening before being enrolled in the study. Exclusion criteria included having used any medication that affects the central nervous system as well as having taken oral contraceptives or hormonal replacements during the 6 months that proceeded the testing. All participants had to be free of neurological problems (e.g., epilepsy, meningitis, encephalitis, multiple sclerosis, stroke) and/or medical conditions interfering with hand function (e.g., arthritis), have normal or corrected visual acuity, normal hearing and to be native, monolingual English speakers. Screening was done by e-mail, using a short questionnaire, which was sent as an e-mail attachment (see Appendix 5.1). Participants completed the questionnaire in their own time and e-mailed it back to the researcher. Female participants were only included if they reported to have a normal menstrual cycle.

5.2.1.2 Recruitment

Participants were recruited in the following ways:

(i) Through the Department of Experimental Psychology's RPS.

(ii) Through posters that were put up throughout the University campus.

(iii) Through e-mails sent to different mailing lists of the University's Departments and Colleges.

(iv) Through advertisements placed on the web pages *www.dailyinfo.co.uk* and *www.facebook.com.*

When the potential participants contacted the researcher declaring their interest in participating in the research study, they were sent the information sheet for the study (see Appendix 5.2) and were screened for suitability to

participate via the e-mail questionnaire described above. The day and time of testing was then agreed upon.

5.2.2 Instruments

5.2.2.1 Behavioural laterality tests

Hand preference inventories: The participants filled in the hand preference inventories described in chapters 3 and 4 (i.e., AHPQ, EHI, WHQ, and HLBI). Given that the scores from the hand preference inventories are highly correlated (correlations varied from .88 to .98 and were all highly significant at the *a* = .001 level; see chapter 3) and that no preference questionnaire seems to differentiate from the others in terms of its sensitivity to sex differences (see chapter 4) the scores coming from the EHI were used, as this is the most popular means of measuring hand preference (see chapter 2). The 5-point response format was used (see chapter 4 for a discussion).

Hand skill tests: Participants were administered the hand skill tests described in chapter 4 (Peg-Moving, Dot-Filing, and Tapping Speed). Only the scores from the Peg-Moving and the Tapping Speed tests were used, as only these were shown to be sensitive to sex differences (see chapter 4).

QHPT: Participants were administered the Quantification of Hand Preference Test (see chapter 4).

5.2.2.2 Neuropsychological laterality tests

Consonant-Vowel Dichotic Listening test (CV-DL): The dichotic stimuli consisted of the six stop consonants (b, d, g, p, t, and k) paired with the vowel /a/ to form six consonant-vowel (CV) syllables (ba, da, ga, ka, pa, ta). The six syllables resulting from these combinations were paired with each other in all possible combinations to form 36 different syllable pairs. From these, the homonymic pairs (ba-ba, etc.) were included in the test as a perceptual control,

but they were not considered in the statistical analysis. Each syllable had a duration of roughly 35 ms, and there was an interval between the presentations of roughly 4 s. The 36 pairs of syllables were recorded three times (in three series), making the total number of trials 108. There was a longer pause between each series. The stimuli were presented to the participants using PXC 150 NoiseGard Headphones connected to an Acer Travelmate 290LCi personal computer.

The participants were informed that different syllables would be presented to each ear simultaneously and were asked to report only the syllable perceived most clearly (see Figure 5.1). Thus, one response for each trial was emphasised. However, some participants occasionally gave two responses, and then only the first one was used in the analysis, since the first response is highly correlated to the overall ear advantage (Boles, 1992). The instructions given were the following:

> You should listen to the six different sounds, which are given on this page. (Here the six syllables were shown on a page.) After each presentation, you should repeat whichever sound you hear. Say the sound loud and clear directly after it has been presented. Sometimes it will seem as if you hear two different sounds at the same time. Don't worry about this, but say the sound you seemed to hear best or most clearly. Don't spend time thinking but just repeat the sound as soon as it has been presented.[25]

[25] The usual means of administration of the CV-DL test is by using non-directed attention for the first set of 36 CV pairs, followed with directed attention to the right and the left ear for the two last sets of pairs. Directed attention is achieved by instructing the particpants to pay attention and to report only what was heard in the right or left ear according to the condition. In this study, only non-directed attention is used, as Foundas et al. (2006) found a signficant correlation between hand preference and dichotic listening scores only for the non-directed attention

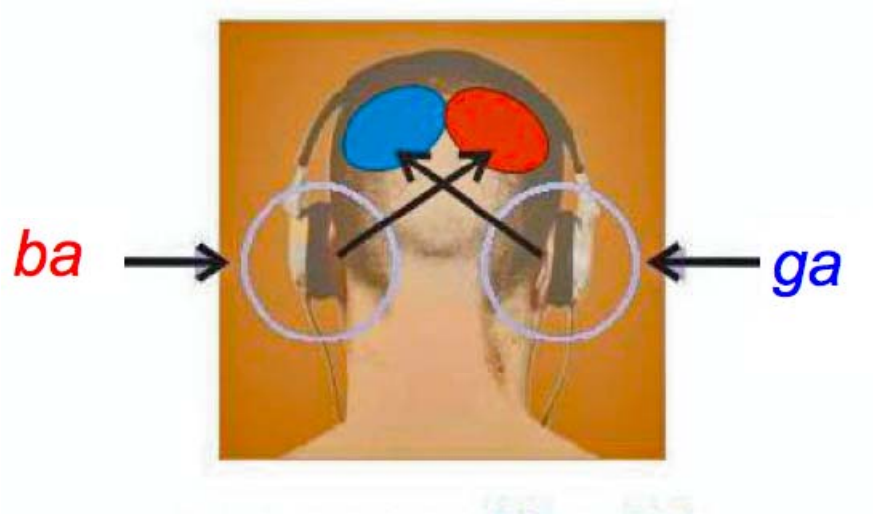

Figure 5.1. Set-up for the Dichotic Listening (DL) test. During the DL test, the participant listens to two different sounds simultaneously, one from each ear. Each sound is processed by the contralateral hemisphere.

Visual Half-Field Lexical Decision Test (VHLD): Twenty-four pairs of letter strings consisting of a pronounceable non-word and an English word, and 24 more pairs consisting of two pronounceable non-words were used as stimuli. Each word/non-word pair was presented twice with the order of the words counterbalanced. All stimuli consisted of either four (e.g., vieg/drug) or five (e.g., build/thirt) letters. (The complete list of stimuli is given in Appendix 5.3.) Displays in horizontal lowercase letter strings (Bold Courier New, font size 18) were presented on both sides of a central fixation cross on the 15" XGA TFT LCD screen of a personal computer (Acer TravelMate 290LCi), using E-Prime software 1.1.4.4 (Psychology Software Tools Inc.). The letters appeared black on a white background (see Figure 5.2). The innermost edge of the letter strings appeared 1 cm to the right or left of the fixation cross, to ensure that the eccentricity of each string was 3.0 degrees of visual angle horizontally. The order of the presentation of the pairs of stimuli was randomised, with each target

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condition. Moreover, test-retest relibility was found to be higher for the non-directed (r = 0.82) than the directed conditions (r = .77 and r = .76; Gadea et al., 2000).

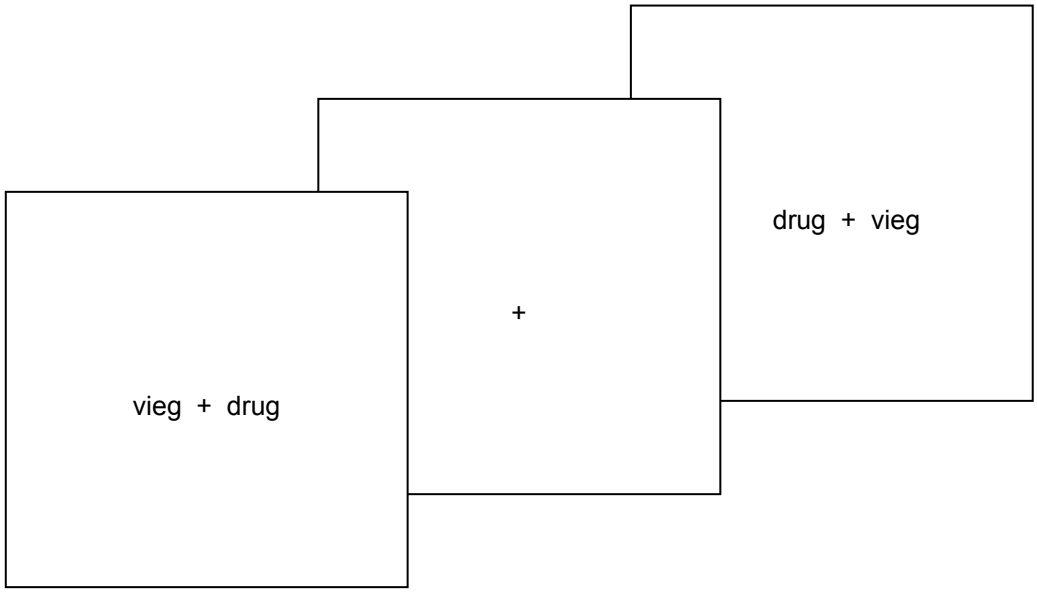

Figure 5.2. Set-up for the Visual Half-Field Lexical Decision (VHLD) task.

word appearing once in the left visual field (LVF) and once in the right visual field (RVF). A trial started with the presentation of a fixation cross for 500 ms followed by the presentation of the stimulus for 120 ms. This duration was chosen to minimise the possibility of scanning eye movements. The next trial began when a response was made or, in the case of non-responding, at the termination of the 5-s period. For a total of 72 trials, response accuracy and reaction times were recorded.

Participants were seated at a distance of 57 cm from the computer screen,[26] their eyes aligned to the fixation cross in the middle of the screen and with their index fingers placed on the “c” key (left hand) and “m” key (right hand). A chin rest was used to stabilise the head ensuring that the distance was kept constant throughout the testing session. Participants were instructed to indicate if a meaningful English word was presented by pressing a key ipsilateral to the

[26] At this distance, 1 cm on the screen is one degree of visual angle. This way stimuli were ensured to be projected in foveal to parafoveal vision.

word. When no meaningful word was detected on either side, they had to press the space bar. Participants were also asked to maintain fixation and respond as quickly and accurately as possible. Instructions were given on the computer screen before the testing started, but the crucial components were stressed again verbally. The instructions given were the following:

> During the task, you have to press the indicated button on the side where you thought an English word appeared, as fast and accurately as possible. Press “m” with your right index finger when you think you saw a word on the right and “c” with the left index when you think you saw a word on the left of the central fixation point. E.g.:
>
> hand + grut
>
> Press “c” in this case
>
> grut + hand
>
> Press “m” in this case
>
> Press the space bar with the thumbs of both hands if you think no English word was presented at all. E.g.:
>
> grut + psim
>
> Pay attention, there are never two English words presented at the same time. Keep your eyes fixed on the cross in the centre of the screen and respond as fast and accurately as possible.

A practice block of 16 trials preceded the experimental block, in order to familiarise participants with the paradigm. The word stimuli used in the practice block were different from those in the experimental block. Participants were given feedback during the practise block and should have achieved a 50%

accuracy to move on to the test block.

5.2.2.3 Hormonal assessments

Salivary hormones: Participants provided two 1-ml samples of saliva for T assay, as well as two 1-ml samples for C assay. The two samples for each hormonal assay were collected 15 minutes apart towards the end of the testing session. To minimise saliva impurities, participants are usually asked to refrain from eating, drinking, smoking, or brushing their teeth for 1 hour prior to testing. This was not necessary here, as participants had already spent the previous hour in the company of the experimenter. Parafilm was available to chew for saliva stimulation, but none of the participants needed to use it. Samples were directly collected from mouth to tube (Salicap) and were frozen at -80 ^{o}C until being sent off on dry ice for assay to the Biophysical Analysis Unit, Northumbria University.

5.2.3 Procedure

Participants were tested individually in a quiet room. The study was explained as soon as they arrived and they were encouraged to ask questions. They gave written consent before taking part in the study, but were explicitly told they remained free to leave at any time and without having to give any reason for doing so. The consent form was signed in two copies so that participants could keep one for their own records. Testing took place in the Department of Experimental Psychology, University of Oxford.

Participants performed the QHPT, completed one version of the hand preference questionnaire and performed the hand skill tests (Peg-Moving, Dot-Filling, and Tapping Speed), as described in chapter 4. Neuropsychological testing was then performed, using the CV-DL and the VHLD tests. Participants then gave their first two saliva samples (one for T and one for C assay). The

other version of the hand preference questionnaire was completed (with the order of administration of the two questionnaires counterbalanced) and finally the participants gave their last two saliva samples. All participants were debriefed after the completion of the study.

Testing was carried out over a period of 9 consecutive weeks during term-time (24.4.06 to 23.6.06) at either 3 p.m. or 4.30 p.m. in order to minimise the influence of circadian and circannual rhythms on T and C secretion.

Female participants were tested in the same phase of the menstrual cycle (menses). All participants were debriefed after the completion of the study.

5.2.4 Assays

Luminescence immunoassay (LIA) was used to measure the levels of T and C concentrations in the saliva samples. Each sample was assayed twice. The T and C luminescence kits were supplied by IBL-Harburg. Luminescence was measured using a Bio-Tek FL x 800 microplate reader used with kC4 Data Analysis Software (supplied by Labtech International Ltd.). Prior to determination, the frozen samples were thawed and centrifuged 10 minutes at 3000 g to remove particulate material. Hormonal determinations were performed by an experienced Bioassay technician (Biophysical Analysis Unit, Northumbria University), who was unaware of the hypothesis tested.[27]

5.2.5 Scoring

The EHI, the QHPT, the Peg-Moving, and the Tapping Speed tests were

[27] LIA is based on the competition principle. An unknown amount of antigen present in the sample and a fixed amount of enzyme labelled antigen compete for the binding sites of the antibodies coated onto the wells. After incubation the wells are washed to stop the competition reaction. After addition of the luminescence substrate solution the intensity of the luminescence measured is inversely proportional to the amount of the antigen in the sample. Results of samples are determined directly using the standard curve (Goncharov et al., 2006).

scored as described in chapter 3 (EHI) and chapter 4 (QHPT, Peg-Moving, and Tapping Speed).

CV-DL: The number of correctly reported items from the left and right ear was the variable of interest. A LI was calculated according to the formula:

$$LI = [(RE - LE)/(RE + LE)] \times 100$$

where: RE = number of correct right ear scores, and LE = number of correct left ear scores. A positive value indicates a right ear/left hemisphere advantage and a negative value a left ear/right hemisphere advantage.

VHLD: Trials with response times below 200 ms or above 1600 ms were discarded in order to ensure that the response was not too quick and therefore random, nor too late, again indicating a random response (Faust and Babkoff, 1997). Two LIs were calculated: (a) for lexical decision accuracy, whereby the index was the difference between the number of correct responses in the two visual fields divided by the sum of correct responses, according to the formula:

$$LI = (RVF - LVF)/(RVF + LVF)$$

where RVF = number of correct right visual field responses and LVF = number of correct left visual field responses, and (b) for reaction times (correct responses only), according to the formula:

$$LI = (RVF - LVF)/(RVF + LVF)$$

where RVF = mean response time for correct responses in the right visual field and LVF = mean response time for correct responses for the left visual field. For

both indices, a positive value indicates a right visual field/left hemisphere advantage and a negative value a left visual field/right hemisphere advantage.[28]

Salivary hormones: The mean hormonal levels of the T and C assays were used for each participant.

5.2.6 Statistical analysis

All analyses were performed using the SPSS v.14. To investigate the relationships between sex and of the different LIs on salivary T and C concentrations, univariate ANOVAs were performed, with hormonal concentrations as the dependent variables and sex and the direction of asymmetry according to the different indices as the fixed factors. The relationship between hormonal concentrations and praxic as well as linguistic lateralisation was further estimated using curve estimation regressions (linear and quadratic), where hormonal concentrations were the dependent variables and the lateralisation indices the fixed factors. All *p*-values were two-tailed and the *a*-level was set at .05.

5.3 Results

A female participant was excluded from T analysis and one female and two male participants were excluded from C analysis, as their hormonal levels were outliers.[29] For females, the mean T concentration was 83.83 pmol/l (*SD* = 60.89) and the mean C concentration was 6.23 nmol/l (*SD* = 2.16). For males, the mean T concentration was 346.36 pmol/l (*SD* = 133.86) and the mean C

[28] The LIs for the VHLD test were not multiplied by 100, following the convention used in the neuropsychological literature (e.g., Marshall et al., 1975; Mohr et al., 2005). The DL test index, on the other hand, is conventionally multiplied by 100 (e.g., Hugdahl et al., 2001).

[29] An outlier is defined as a case with a value between 1.5 and 3 times larger than the interquartile range.

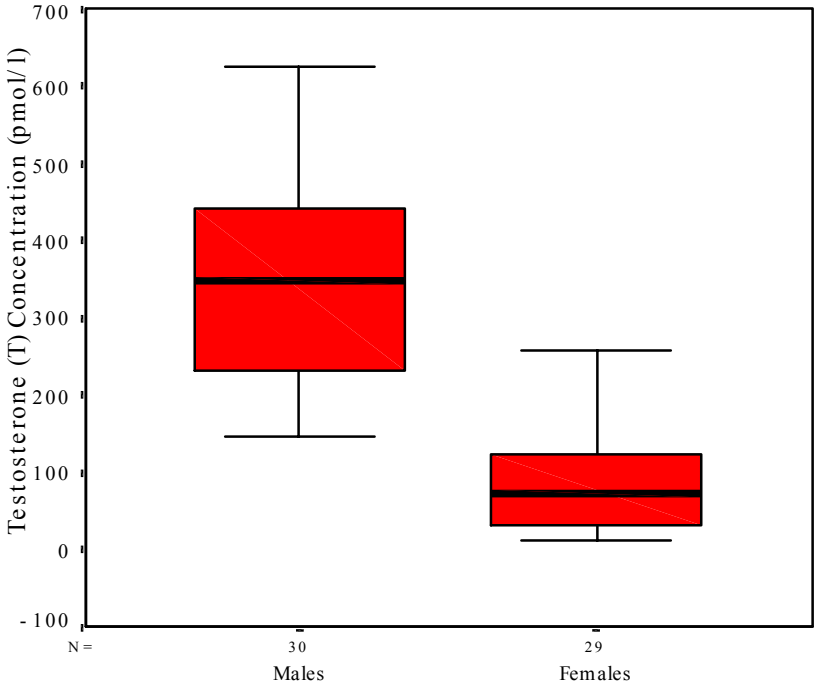

Figure 5.3. Box plots for Testosterone (T) concentrations for males and females. The box represents the interquartile range which contains 50% of values. The whiskers extend from the box to the highest and lowest values, excluding outliers. A line across the box indicates the median.

concentration was 7.19 nmol/l (*SD* = 2.80) (see Figures 5.3 and 5.4). These values are within the normal range of salivary T and C concentrations for both sexes (Vittek et al., 1985; Dabbs, 1991; Smyth et al., 1997). Male participants had significantly higher T levels than females (t = 9.52, df = 57, p < .001), but not C levels (t = 1.27, df = 55, p = .21), as expected.

5.3.1 Hormonal concentrations and hand preference

To investigate the relationship between direction of hand preference and hormonal levels, participants were divided into two groups according to direction of hand preference as measured by the EHI: right hand preference (n_r =

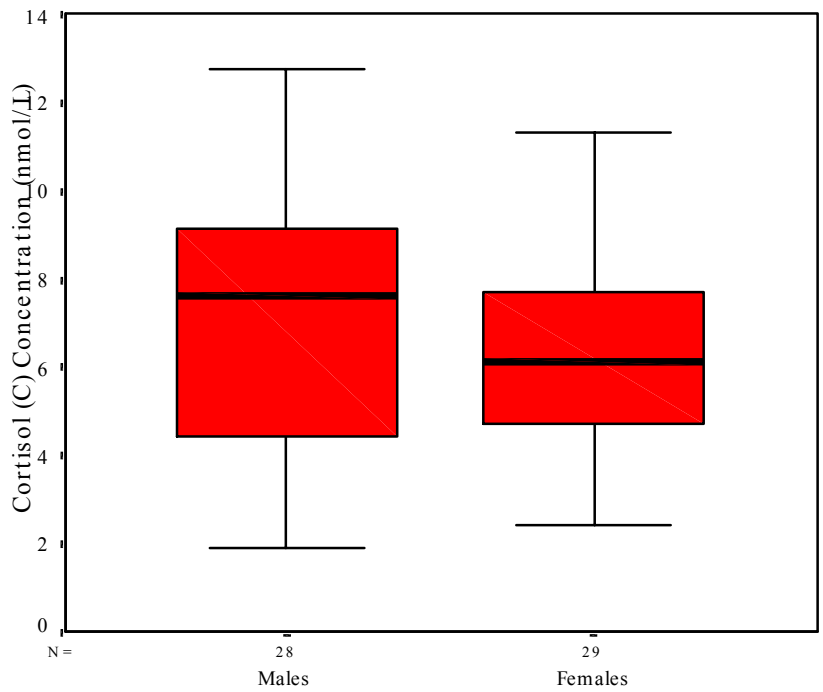

Figure 5.4. Box plots for Cortisol (C) concentrations for males and females. The box represents the interquartile range which contains 50% of values. The whiskers extend from the box to the highest and lowest values, excluding outliers. A line across the box indicates the median.

30) and left hand preference (n_l = 29). Univariate ANOVAs were run with T and C concentrations as the dependent variables and sex (male or female) and direction of hand preference according to the EHI scores (right or left) as the fixed factors. There was a significant main effect of sex for T concentration, F (3,55) = 92.82, $p < .001$, $\eta^2 = .63$, but no effect of handedness or an interaction between sex and direction of hand preference for T or C concentrations (all $p >$ .15).

Curve estimation regressions with T and C concentrations as the dependent variables and the EHI score as the fixed factor, showed that there was no linear or quadratic relationship between EHI scores and T or C concentrations (all $p > .31$). When the same regressions were run separately for males and females, no significant relationships emerged either (all $p > .15$).

5.3.2 Hormonal concentrations and hand skill

To investigate the relationship between direction of hand skill asymmetry and hormonal levels, participants were divided into two groups according to direction of hand skill as measured by the Peg-Moving test (right hand advantage [n_r = 28] and left hand advantage [n_l = 31]) and the Tapping Speed test (right hand advantage [n_r = 38] and left hand advantage [n_l = 21]). Two univariate ANOVAs were run with T and C concentrations as the dependent variables and sex (male or female) and direction of hand skill (right or left) as the fixed factors, separately for the two hand skill tests (Peg-Moving and Tapping Speed). There was a significant main effect of sex for T concentration for both the Peg-Moving test, F (3,55) = 90.43, $p < .001$, $\eta^2 = .62$, and the Tapping Speed test, F (3,55) = 94.70, $p < .001$, $\eta^2 = .63$, but no other main effects or interactions (all $p > .14$).

Curve estimation regressions with T and C concentrations as the dependent variables and the hand skill score as the fixed factor, were run separately for the two hand skill tests (Peg-Moving and Tapping Speed), which did not reveal any relationships between hand skill scores and T or C concentrations (all $p > .11$). The same regressions were then run separately for males and females. For the Peg-Moving test, there was a significant linear relationship between the test scores and T concentrations for males, F (1,28) = 4.72, $p = .038$ (see Figure 5.5), the best fitting relation being:

$$T = 312.742(\text{Peg-Moving score}) + 101.82$$

No other relationships were detected between the Peg-Moving test score and T or C concentrations for males or females (all $p > .12$). For the Tapping Speed test, there was a trend towards a linear relationship between Tapping

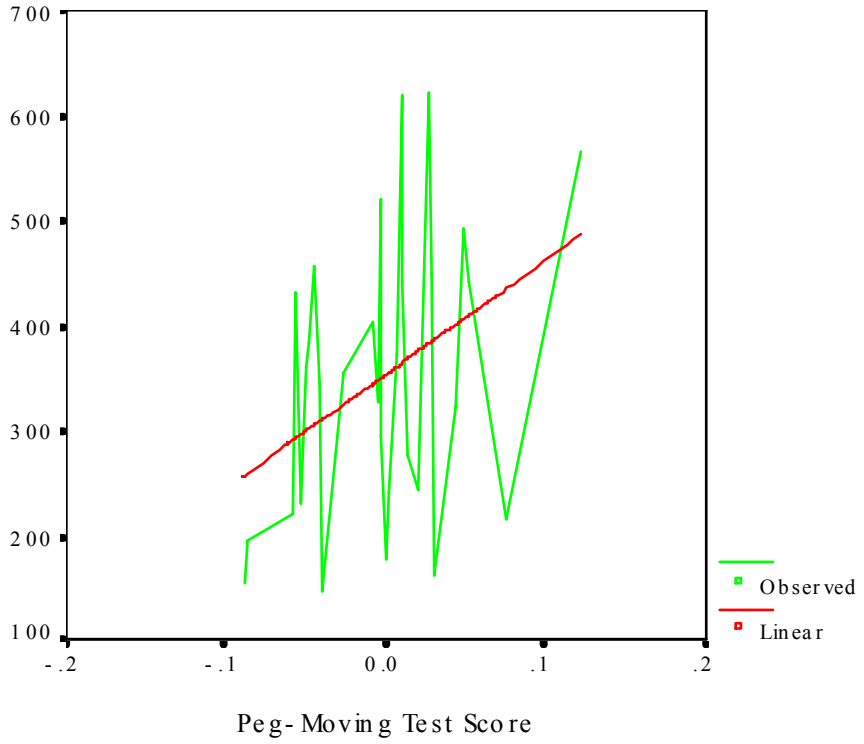

Figure 5.5. Regression line describing the relationship between Testosterone (T) concentrations and the Peg-Moving test score for males.

Speed test scores and T concentrations for males, $F(1,28) = 3.15$, $p = .087$ (see Figure 5.6), the best fitting relation being:

$$T = -255.69(\text{Tapping Speed score}) + 105.60$$

No other relationships were detected between hand skill scores and T or C concentrations for males or females (all $p > .20$).

5.3.3 Hormonal concentrations and the QHPT

To investigate the relationship between direction of hand preference using the QHPT and hormonal levels, participants were divided into two groups according to direction of hand preference as measured by the QHPT: right hand

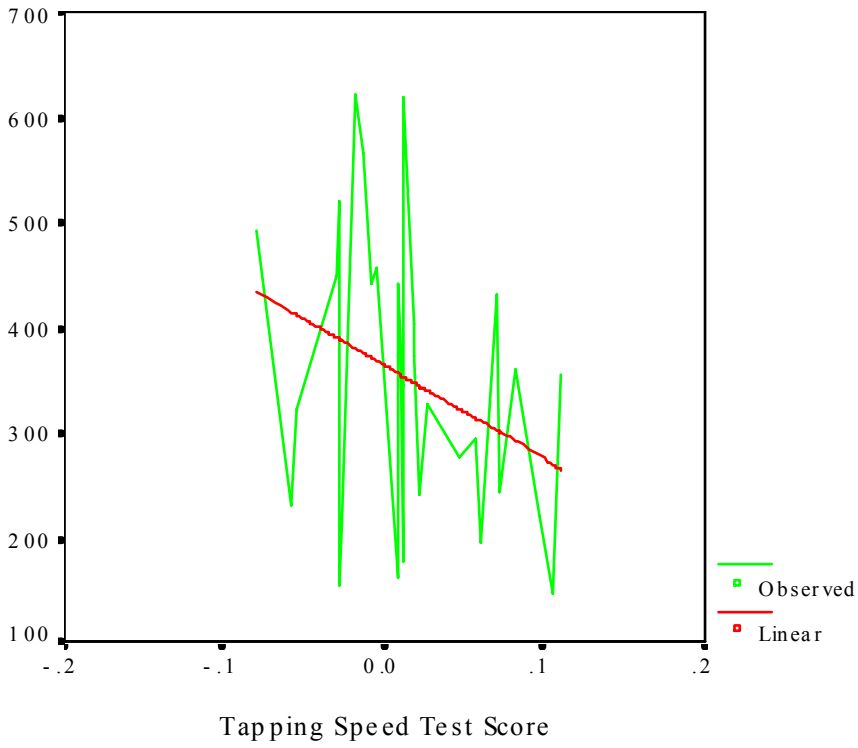

Figure 5.6. Regression line describing the relationship between Testosterone (T) concentrations and the Tapping Speed test score for males.

preference (n_r = 24) and left hand preference (n_l = 35). Univariate ANOVAs were run with T and C concentrations as the dependent variables, and sex (male or female) and direction of hand preference (right or left) as the fixed factors. There was a significant main effect of sex for T concentration, F (3,55) = 79.24, $p < .001$, $\eta^2 = .59$, but no other main effects of handedness or an interaction of sex and direction of hand preference for T or C concentrations (all $p > .25$).

Curve estimation regressions with T and C concentrations as the dependent variables and the QHPT score as the fixed factor, showed that there was no linear or quadratic relationship between QHPT scores and T or C concentrations (all $p > .19$). When the same regressions were run separately for males and females, no significant relationships emerged either ($p > .39$).

5.3.4 Hormonal concentrations and the CV-DL

To investigate the relationship between the direction of CV-DL asymmetry and hormonal levels, participants were divided into two groups according to direction of ear advantage: REA (n_r = 41) and LEA (n_l = 18). ANOVAs were run with T and C concentrations as the dependent variables and sex (male or female) and direction of asymmetry (right or left) as the fixed factors. Apart from the main effect of sex on T concentrations, F (3,55) = 69.42, $p < .001$, $\eta^2 = .56$, there were no other main effects or interactions (all $p > .08$).

Curve estimation regressions with T and C concentrations as the dependent variables and the CV-DL score as the fixed factor, showed that there was no linear or quadratic relationship between hand preference scores and T or C concentrations (all $p > .23$). When the same regressions were run separately for males and females, no significant relationships emerged either (all $p > .22$).

The proposition of Moffat and Hampson (1996, 2000) that there is an association between higher T levels and lateralisation of praxic and language functions in the same hemisphere was tested here as well. Differences in mean T concentrations were not found to be significant between neither left-handed participants with a LEA in the DL test compared to left-handed participants with a REA, nor for right-handed participants with a LEA compared to right-handed participants with a REA (both $p > .44$).

5.3.5 Hormonal concentrations and the VHLD

To investigate the relationship between the direction of VHLD asymmetry and hormonal levels, participants were divided into two groups according to direction of visual field advantage: RVFA (n_r = 18) and left visual field advantage (LVFA; n_l = 41), for lexical decision accuracy and RVFA (n_r = 36) and LVFA (n_l = 23), for lexical decision reaction times. ANOVAs were run with T and C concentrations as the dependent variables, and sex (male or female) and

direction of asymmetry (right or left) as the fixed factors, separately for the lexical decision accuracy index and for the lexical decision response times for correct responses index. For lexical decision accuracy, apart from the main effect of sex on T concentrations, F (3,55) = 74.33, $p < .001$, $\eta^2 = .58$, there were no other main effects or interactions (all $p > .25$). Similarly, for the lexical decision response times, there was a main effect of sex on T concentrations, F (3,55) = 82.16, $p < .001$, $\eta^2 = .60$, but no other main effects or interactions (all $p > .07$).

Curve estimation regressions were run with T and C concentrations as the dependent variables and the VHLD indices as the fixed factor, separately for the lexical decision accuracy index and for the lexical decision response times for correct responses index. A quadratic relationship between accuracy scores and T concentrations was detected, F (2,56) = 3.64, $p = .33$ (see Figure 5.7), the best fitting relation being:

$$T = 27.1056(\text{VHLD accuracy score}) + 299.340(\text{VHLD accuracy score})^2 + 52.69$$

No other relationships were detected between VHLD indices and T or C concentrations (all $p > .21$). When the same regressions were run separately for males and females, a trend towards a quadratic relationship was found for males for the accuracy index, F (2,27) = 2.65, $p = .089$ (see Figure 5.8), the best fitting relationship being:

$$T = 7.6170(\text{VHLD accuracy score}) + 226.03(\text{VHLD accuracy score})^2 + 90.07$$

No other relationships were detected between VHLD indices and T or C concentrations for males or females (all $p > .21$).

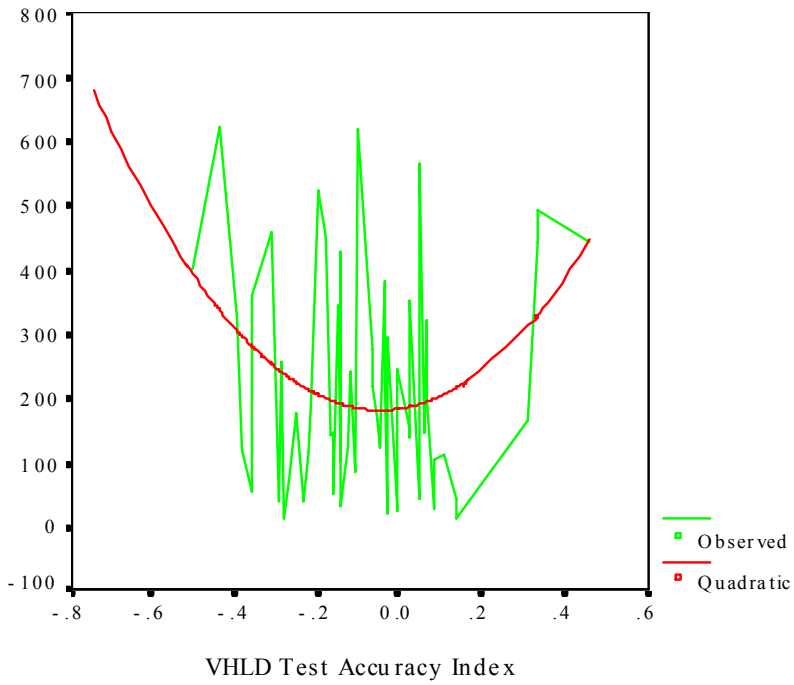

Figure 5.7. Regression line describing the relationship between Testosterone (T) concentrations and the accuracy index for the Visual Hemi-Field Lexical Decision (VHLD) test score.

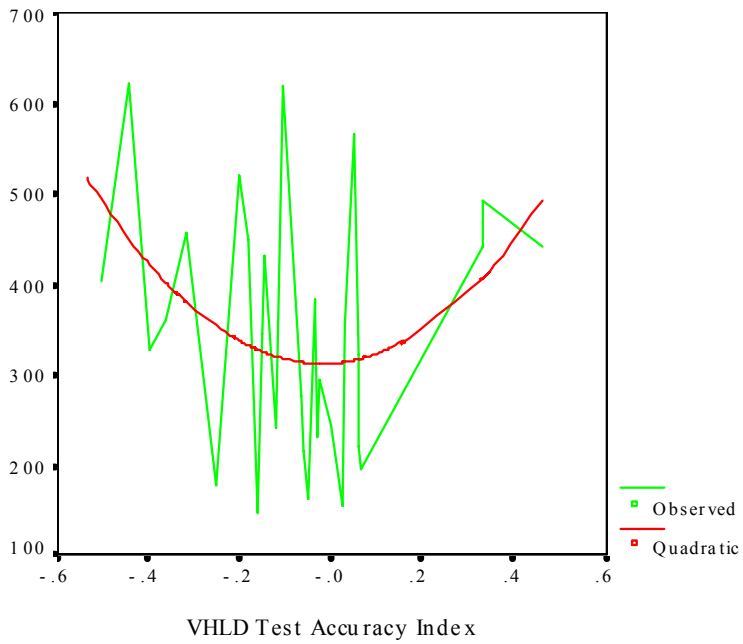

Figure 5.8. Regression line describing the relationship between Testosterone (T) concentrations and the accuracy index for the Visual Hemi-Field Lexical Decision (VHLD) test score for males.

5.4 Discussion

The aim of this study was to test the hypothesis that individual differences in T concentrations are associated with praxic lateralisation as reflected in hand preference and relative hand skill, and with linguistic lateralisation as measured by the CV-DL and the VHLD tests. A number of interesting relationships were detected.

A significant linear relationship was detected between the Peg-Moving test score and T concentrations for males as well as a trend towards a negative linear relationship between the Tapping Speed test and T concentrations, again for males. No relationships were detected between T concentrations and hand preference, as defined by either the EHI or the QHPT. These results are translated as follows: the male participants, who had higher T concentrations, took longer to move the pegs with the right hand compared to moving them with the left hand and they also produced less taps with the right compared to the left hand. In both cases, higher T concentrations were associated with the right hand being less skillful than the left hand. The prediction that these relationships would be stronger for right-handers than left-handers was not supported.

It could be suggested that these findings are in line with the findings of chapter 4's study, where it was shown than right-handed females are more skillful with their right hand compared to their left hand as opposed to right-handed males (relative hand skill was similarly measured by the Peg-Moving and the Tapping Speed tests in chapter 4's study). In other words, females, who overall as a sex have lower T concentrations than males, were found to be more skillful with their right hand (even though this finding accounts only for right-handers). This same effect was found here within males, rather than between sexes: those male participants who had low T concentrations were more skilful with their right hand. Moreover, the sex effect found in chapter 4 was slightly greater for the Peg-Moving test compared to the Tapping Speed test. Similarly,

here the relationship between T concentrations and the Peg-Moving test score was significant, whereas the same relationship failed to reach significance for the Tapping Speed test. Furthermore, in parallel with chapter's 4 findings of no differential sensitivity in capturing a sex difference among the hand preference tests, no relationships were detected between hand preference and sex hormones in the present study.

As far as linguistic lateralisation is concerned, a quadratic relationship between the VHLD test accuracy scores and T concentrations was detected over the whole sample. When analyzing data separately for the two sexes, a trend towards a quadratic relationship was detectable only for males. In both cases, more brain asymmetry, or greater degree of linguistic lateralisation, was associated with higher T levels. No relationships of T concentrations were found with either the CV-DL test or the reaction time index of the VHLD test.

For both praxis and language, associations with lateralisation were observed only for T concentrations and did not generalise to C, a steroid hormone that shows a similar circadian rhythm to T, but for which no hormone-behaviour relationships were hypothesised. Therefore, hormonal relationships were specific to T.

Overall, results are in line with Gadea et al. (2003) who found that higher concentrations of T are associated with a lesser degree of interhemipsehric share of linguistic information, as measured by the CV-DL test. The proposition of Mofatt and Hampson (1996, 2000) of an association between a higher T levels and lateralisation of praxic and language functions in the same hemisphere was not replicated here (and was not demonstrated by Gadea et al., 2003, either). On the other hand, as far as praxic lateralisation is concerned, the present findings do not support those of Moffat and Hampson (1996) or Gadea et al. (2003), who found that higher T levels are associated with right-handedness, even though both of these studies measured handedness in terms

of hand preference and Gadea et al. (2003) used only female participants in their study. Moffat and Hampson (2000) did not find any association of T with handedness as measured by a handedness inventory, in line with the present findings.

Different kinds of relationships with T concentrations were detected for praxic and linguistic lateralisation, more specifically linear relationships for relative hand skill and quadratic for the VHLD accuracy scores. The claim by Gadea et al. (2003) that an integrated theory about lateralisation and T should take into account two points is therefore supported: First, asymmetry for praxic function could be relatively independent of asymmetry for linguistic function; second, the relationship of T with asymmetry for praxis and language could be different if one considers the direction or the degree of that asymmetry. It might be the case that T has independent effects on praxic and linguistic lateralisation, in such a way that when it comes to praxic lateralisation, direction of lateralisation is what is affected, whereas when it comes to linguistic lateralisation, degree is affected. The present data suggest that higher concentrations of T are associated with a praxic intrahemispheric organisation located at the right hemisphere and, on the other hand, with a more asymmetrical linguistic organisation, indicating greater interhemispheric share of information. Both organisations are to be more often encountered in males compared to females.

The theoretical perspectives proposed for the association between T levels and functional asymmetries by the sexual differentiation hypothesis seem to fit the present data. With respect to manual preference, both the sexual differentiation and the Geschwind and Galaburda hypothesis suggested that high levels of T would be associated with left-handedness or ambidexterity, while the callosal hypothesis proposed that high levels of T would be related to right-handedness. Thus, the first two hypotheses were supported by the present

findings, as higher T levels were associated with superior left hand skill, as least in males. With respect to linguistic lateralisation, the sexual differentiation and the callosal hypothesis would predict a higher lateralisation index related to higher T levels, while Geschwind and Galburda hypothesised an opposite pattern. Here, the predictions of the sexual differentiation and the callosal hypothesis were supported since the higher levels of T are associated with a higher degree of interhemispheric share of linguistic information. Thus, the sexual differentiation hypothesis receives support from the present findings for both praxic and linguistic lateralisation.

The present findings, combined with the findings of chapter 4, further support the notion that hand preference and relative hand skill have different properties (for a discussion see chapter 2), at least as far as sex differences are concerned. Relative hand skill was not only found to be more sensitive in capturing a sex difference in chapter 4, but it was further shown in this chapter that it is associated with T concentrations. The QHPT, which is a behavioural test of hand preference, seems to be a borderline case between preference and skill; no associations with T concentrations were detected, but it was found to be sensitive in detecting sex differences (see chapter 4). The failure to detect significant relationships between the QHPT score and T concentrations may be also due to the fact that this test was shown to be the least powerful in detecting sex differences in the first place, compared to the relative hand skill tests.

The Peg-Moving and the Tapping Speed tests were found to have differential power to (a) detect sex differences and (b) show significant associations with T concentrations, with the Peg-Moving test being the more powerful of the two. Whereas the Peg-Moving test requires participants to move pegs from one row to another, the Tapping Speed test asks them to tap on a tally counter. One major difference is the demands on visual guidance in order for the tests to be executed. Visual guidance is essential for the Peg-Moving

test, but unnecessary for the Tapping Speed test. The way these different demands on visual guidance may affect sex differences is unclear.

Another differentiating factor between these two tests is the movement type they require. The Taping Speed test is in essence a repetitive movement of the thumb, while the rest of the palm is immobilising the tally counter in what is termed a power grip (Elliott and Connolly, 1984). The Peg-Moving test requires more complex moving patterns: grasping the peg from one row, moving it to the next row and placing it in the appropriate hole, before the same process starts again for the next peg. Thus, apart from the fine manipulations of the pegs, the whole upper limb (and for some participants even the trunk) is involved. Thus, following the distinction made by Elliot (1979), the Tapping Speed test requires only intrinsic movements, whereas the Peg-Moving test is a combination of intrinsic and extrinsic movements. Intrinsic movements are defined as coordinated movements of the digits to manipulate an object within the hand. Extrinsic movements are defined as movements of a prehended object by displacement of the hand as a whole, using the upper limb. The Peg-Moving test further requires precision and delicacy, both when grasping the peg, but most importantly when placing it in the appropriate hole.

Moreover, the nature of the intrinsic movements involved in the two tests differs. According to Elliot and Connolly (1984), intrinsic movements are distinguished into simple (which is the case for the Peg-Moving test) and reciprocal (which is the case for the Tapping Speed test) synergies. Simple synergies are defined as those in which all movements of the participating digits, including the thumb, are convergent flexor synergies, in other words, the movements of all the digits are the same. Reciprocal synergies, by contrast, involve combinations of movements in which the thumb and the other participating digits show dissimilar or reciprocating movements, such as flexion of the fingers with adduction or extension of the thumb. Thus, only in the case of

reciprocal synergies is the thumb's capacity for movement independent of the fingers used in the manipulation of objects. Again, the way these differences in the movements required may affect sex differences needs to be further elucidated.

A point of interest of the present findings is that an association with T concentrations was found only for the VHLD test and not the CV-DL test. These two neuropsychological tests differ in terms of the modality they engage to study lateralisation as well as in terms of the task they employ. Whereas the VHLD is a visual test, the CV-DL is an auditory test. (Here a parallel with the Peg-Moving test, employing vision and being more powerful than the Tapping-Speed test which does not employ vision, could be drawn, even though such a parallel is a weak one). Moreover, the two neuropsychological tests differ in terms of the paradigms used to study language. The VHLD uses word stimuli, whereas the CV-DL uses consonant-vowel syllables. This latter kind of stimuli has been criticised in terms of ecological validity, as it has been argued that the CV-DL syllables constitute a light linguistic load and thus do not require higher-level mechanisms for processing, with nearly equal representation in both hemispheres (Keith et al., 1985).

The failure to detect any hormonal relationships with the DL test, may be further due to the DL procedure tending to underestimate the proportion of the right-handed population that is left-hemisphere dominant for language perception (Segalowitz and Bryden, 1983), estimating a 85-89% of the right-handed population to be left-hemisphere dominant whereas clinical studies give an estimation of 95.5% (Welsh and Elliott, 2001). This discrepancy has been attributed to the fact that dichotic tasks are generally well performed, making differences between the two ears small (Bryden, 1988a).

It might be of interest to note that results were stronger for the male participants. This finding is in line with the findings of Moffat and Hamspon

(2000) who reported effects on a smaller scale for females compared to males as well with the findings of Witelson (1985; 1991) who found an association of prenatal T with left-handendess and atypical dominane only in males. A number of explanations could be proposed for this sex difference. With regards to the assessment of salivary T concentrations, this has been found to be less accurate in females than in males (Shirtcliff et al., 2002; Taieb et al., 2003). There is a sex difference in the association between salivary and serum T measurements, and this sex difference could affect the detection of T-behaviour association more for females than for males (Shirtcliff et al., 2002). Moreover, sex is associated with differential stability in salivary T measures over time is such a way that concentrations are considerably more stable over time for males than females (Granger et al., 2004). This similarly suggests that the probability of detecting significant T–behaviour relationships may be lower in females than in males (ibid.). In addittion, T concentrations in males show a bigger range, making the detection of relationships easier. Another possibility is that the difference in the ability to detect results for the female participants may reflect sex differences in the cortical organisation of hand movements. Indeed, as discussed in chapter 1, anatomical asymmetry has been found to be associated with handedness only in males, but not in females (Amunts et al., 2000).

The study presented in this chapter has a number of limitations. Recent brain imaging studies have shown that language is composed of specialised subcomponents that are lateralised. Phonological, production, syntactical, and semantic aspects of language are represented in different specialised brain structures, so that different facets of language are served by different loci in the brain (Posner et al., 1988; Posner and Raiche, 1994). Thus, the use of just the CV-DL and the VHLD tests means that only two of multiple subcomponents of language were investigated, namely phonology and semantics. Other language subcomponents could have a different relationship with T concentrations.

Additionally, language comprises of receptive and expressive aspects. The CV-DL and the VHLD tests tap only the receptive aspect of language. Moreover, there is a debate whether language can be treated as a separate mental faculty or should be approached as part of a more general cognitive system (Fodor, 1983), intertwined with prosody, memory, and attention (Knecht et al., 1996; Binder et al., 1997). For all the above reasons, the assessment of linguistic lateralisation based on the CV-DL and VHLD tests serves only as a first step in elucidating the factors underlying the diversity in large-scale neural language organisation.

Furthermore, a basic critique of visual field studies as a means to detect hemispheric language dominance is that the left-to-right reading habit (which is in itself independent from cerebral language dominance) or the favourable foveal viewing position of the initial letters of a word in the left visual field may enhance or even produce the RVFA for the processing of verbal stimuli (Schwartz and Kirsner, 1986). Although it has been demonstrated that a RVFA can persist in participants with a leftward reading habit (Shanon, 1982; Babkoff and Ben-Uriah, 1983; Vaid, 1988; Faust et al., 1993; Eviatar, 1997; Lavidor et al., 2002), one does not know to what degree the reading habit contributes to it (Voyer, 2003). If this contribution is substantial it might well have exaggerated the classification of hemispheric language dominance as left-lateralised (Krach et al., 2006). Still, having instructed participants to use central fixation should have minimised such effects.

Using neuropsychological tests to assess brain laterality is a limitation of the study in itself. Neuropsychological tests rely on performance differences between the two hemispheres, thus assessing laterality only indirectly. Thus, the effects on perceptual asymmetry found by neuropsychological tests may be the result of differences in performance as such rather than true differences in cerebral dominance (Sommer et al., 2004). Alternatively, as proposed by Kimura

and Harshman (1984), the two sexes might differ in their approach to a given task, such that if females used a more verbal method of encoding and recalling tachistoscopically presented stimuli, they would show reduced left-field superiorities. Even though these behavioural differences might still reflect a sex difference in brain organisation, the interpretation of differences in perceptual asymmetry as reflecting differences in brain asymmetry is not the only possible one.

Another potential limitation of the study is that females were tested at menses and not at the mid-luteal phase. Hormonal fluctuations within the menstrual cycle have an important impact on functional cerebral asymmetries (for a discussion see chapter 1). Yet, different studies provide a remarkably controversial picture as to when in the menstrual cycle asymmetry is greater (for review see Sanders and Wenmoth, 1998). Since the field of effects of menstrual cycle on laterality is still unclear, testing females at menses might have provided the advantage of assuring homogeneity in the phase of the menstrual cycle for all participants without having to specifically measure progesterone levels, but at the same time it might have hindered the power of the study to detect relationships of T levels with praxic and linguistic laterality for the female participants. Still, menses is an easily identifiable point in the cycle, which was kept constant for all female participants.

Some practical issues regarding the collection of the saliva samples may have further threatened the validity of the findings of the study. T concentrations can be influenced by the presence of blood and its components even when samples are not visibly contaminated with blood. The bias at visibility limit of blood contamination is 8% for T and 2% for C (IBL Laboratories, 2004). In the present study, samples were systematically inspected at the point of collection and if visibly contaminated with blood they were excluded from analyses for T. Unfortunately, it was not possible to check whether any blood contamination

existed below visibility levels. Moreover, samples were not collected at the same evening time for all participants, but half of the participants gave the samples at about 4.15 p.m., whereas the other half at 5.45 p.m.

Measuring T concentration in adults limits what researchers may infer regarding the prenatal environment. Although adult T concentrations are considered an indication of the prenatal environment (Jamison et al., 1993), and they moreover present the advantage of enabling the specific recruitment and testing of left-handed individuals (something that is not feasible when prenatal hormonal levels are measured), they are nevertheless an indirect measurement. Moreover, T has been found to have both organisational and activational effects on functional lateralities (e.g., Wisniewski, 1998). Thus, even though diurnal and circannual T rhythms were carefully controlled, the exclusive use of adult T concentrations does not allow for the disentangling of the organisational and activational effects of T.

Therefore, in addition to measuring adult T concentrations, future studies should also measure prenatal levels of T. This can be done indirectly by means of the putative somatic marker for prenatal T that was recently proposed: the 2nd to 4th (2D:4D) digit length ratio (Manning et al., 1998; Sanders et al., 2002). Manning et al. (2000b) have indeed used the 2D:4D length ratio to shown that low ratios are associated with faster left-hand speed relative to right-hand speed in a Peg-Moving test, in line with the present findings. Fink et al. (2004) further found that 2D:4D length ratio is related to the degree of hand skill, such that low 2D:4D length ratio is correlated with enhanced left-hand performance. The 2D:4D length ratio has not been used in a linguistic lateralisation study to date.

Future studies need to consider possible differences in brain lateralisation related to menstrual cycle. It might be more fruitful to test women in the mid-luteal phase of their cycle, rather than during menses, as was done here, or to have a repeated measures design, whereby laterality will be assessed at both

points of the menstrual cycle. Moreover, the assessment of linguistic laterality could include a larger number of tests that cover a wider range of language sub-components. Replacing neuropsychological testing, which measures laterality based on performance differences, with brain imaging techniques, which assess physiological changes in the brain while language tasks are carried out, would also be a substantial methodological improvement. A few improvements on the saliva collection procedure are also feasible, such as collection of the samples at the same time for all participants and limiting the time window of the collection of the data for the study to less than three months, which was the time window used in the present study.

Overall, the present study revealed interesting relationships of adult T concentrations with the direction of praxic laterality as well as with the degree of linguistic laterality. More specifically, the data suggest that the higher levels of T are associated with a praxic intrahemispheric organisation located at the right-hemisphere and with a higher degree of interhemispheric share of linguistic information. These relationships were stronger for the male participants. The present findings provide support for the sexual differentiation hypothesis in terms of both praxic and linguistic lateralisation.

Chapter 6

Relationships of prenatal T and adult T and C concentrations with praxic and linguistic lateralisation: a brain imaging study

6.1 Introduction

Among the most influential line of theories on the sex differences in praxic and linguistic lateralisation are the theories associating lateralisation with prenatal T levels (Hines and Shipley, 1984; Geschwind and Galaburda, 1987; Witelson and Nowakowski, 1991). The study presented in chapter 5 investigated these theories further, by means of assessing adult T and C levels through saliva samples. Findings supported the notion that higher levels of T are associated with a praxic intrahemispheric organisation located at the right-hemisphere and a higher degree of interhemispheric share of linguistic information.

One important limitation of the study presented in chapter 5 was the method used to assess linguistic lateralisation. More specifically, the assessment was done though neuropsychological testing, using the CV-DL and the VHLD tests. Neuropsychological tests infer lateralisation through performance differences between the two hemispheres. Thus, they measure lateralisation only indirectly and even though they are adequately reliable to estimate laterality effects for group studies, they are not considered ideal for

individual assessment of linguistic laterality (Krach et al., 2006). Moreover, chapter 5's study measured only adult T concentrations. The purpose of the present study was to extend the results obtained in chapter 5, using a new technique for the measurement of brain laterality, fTCD, and to compliment the measurement of adult T levels with the indirect measurement of prenatal T levels, via the recently proposed somatic marker 2D:4D length ratio.

6.1.1 Linguistic lateralisation assessment

The gold standard method used to demonstrate brain laterality for cognitive functions is the Wada technique, in which the function of one cerebral hemisphere is transiently disrupted by administration of sodium amytal via the carotid artery (Wada, 1949; Wada and Rasmussen, 1960). This method has several limitations, most importantly its invasiveness which is associated with a number of possible medical complications (Woods et al., 1988; Loring et al., 1992), making it suitable only for the presurgical assessment of candidates for brain surgery. Functional MRI is starting to replace the Wada technique in clinical assessment, but it is too expensive for routine use in research studies (Pelletier et al., 2007).

Functional TCD has been shown to be a reliable alternative for the study of brain laterality. It is non-invasive, inexpensive, relatively easy to administer, and it appears to be completely safe (Deppe et al., 2004). This method involves putting probes on either side of the head and using ultrasound to measure blood flow in the middle cerebral arteries (MCAs). It has been described as a "stethoscope for the brain" (Gomez, C. cited in Barber, 2000). It is insensitive to movement artifacts and can be easily repeated for follow-up. Functional TCD's spatial resolution is rather poor, restricted to the basal artery territories, but it has excellent temporal resolution and provides continuous measurement of blood flow changes which are associated with functional cortical activation (Deppe et

al., 2000a). Its only limitation is that some individuals lack an acoustic temporal bone window for insonation of the MCAs.

Although Doppler ultrasound was first applied to patients in the 1960s (Satomura and Kaneko, 1960), it was not appreciated for many years that sufficient ultrasound could pass through the skull to allow recording from intracerebral vessels. It was only in the 1980s that successful insonation of the MCAs was described by Aaslid et al. (1982). A breakthrough in the use of fTCD came from the work of Deppe and colleagues, who devised analytic methods that took into account both the activity from the heart rate cycle, and any differences in overall blood flow between left and right sides, using an analysis package called “Average” (Deppe et al., 1997b). Thus, analysis of cerebral functional lateralisation by fTCD now constitutes a fully automated, objective procedure. Prior to this, measurements of blood flow in left and right MCAs tended to be too noisy to give reliable results. However, with these more sophisticated techniques, it was possible to show reliable left hemisphere activation for language tasks in typical adults, as well as the expected higher rate of right hemisphere language dominance in left-handers (Knecht et al., 2000). Functional TCD was moreover shown to give highly congruent results for the assessment of hemispheric lateralisation with fMRI (Deppe et al., 1999; 2000b). It has also been validated in determining the hemispheric dominance for language by direct comparison with the Wada test (Knecht et al., 1998a).

The cerebral blood flow velocity (CBFV) changes in the MCAs are taken to indicate the downstream increase of regional metabolic activity during a task. Functional TCD thus adds to the perfusion-sensitive techniques of functional imaging (fMRI, PET, etc). These techniques are based on the fact that cerebral perfusion is closely coupled to cerebral metabolism and neural activation. In particular, changes in cerebral perfusion during cognitive tasks result in a more rapid CBFV in the feeding basal intracranial arteries compared with rest periods

(Aasslid, 1987; Droste et al., 1989a, 1989b; Hartje et al., 1994; Silvestrini et al., 1994, 1995; Rihs et al., 1995; Knecht et al., 1998a). Evidence has also accumulated that the diameter of the large cerebral arteries does not change significantly under a variety of physiological stimuli (Huber and Handa, 1967; Harder, 1984). Assuming that the diameter of the basal cerebral arteries remains unchanged over time, CBFV changes during cognitive tasks are necessarily related to volume flow changes. Hence, changes in CBFV reflect changes in cerebral metabolism due to cerebral activation.

In fMRI and PET studies, lateralisation is usually determined by calculating the difference between the activated brain regions in the left and the right hemisphere relative to the sum of all activated regions in both hemispheres. Functional TCD provides identical information in a much more efficient way, by directly comparing the relative blood flow velocity changes in the two MCAs. The quantitative measures obtained by fTCD are moreover not biased by defining variable statistical thresholds, as is often the case in the analysis of fMRI data. The typical sensitivity in these studies for detecting perfusion asymmetries between two basal arteries is of the order of 1% (Deppe et al., 1997a; Knecht et al., 1997, 1998a).

The paradigm that is principally used with fTCD to demonstrate cerebral lateralisation for language is the Word Generation task. For this task, the participant is shown a letter and asked to silently generate as many words as possible beginning with that letter. After an interval of silent word generation, the participant is asked to report the words he thought of, before having a rest period to allow task-related activation to return to baseline. A LI is computed by averaging blood flow difference for event-related changes for 20 or more trials of this kind, for a 4 s period centred on the maximal difference during the word generation interval (see Figure 6.1). The Word Generation task is also

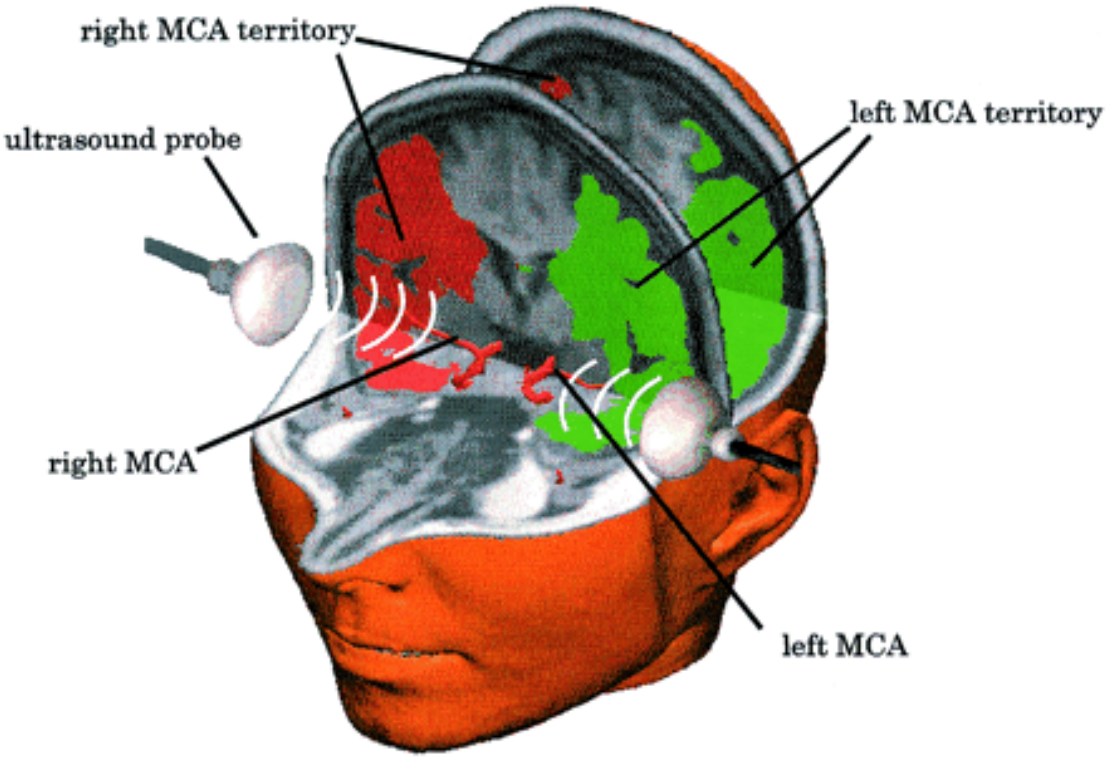

Figure 6.1. Schematic diagram of the way linguistic lateralisation is determined. Perfusion increases, and therefore neuronal activation during word generation, are assessed in the vascular territories of the left (marked in red) and right (marked in green) middle cerebral arteries (MCAs).[30]

particularly effective in demonstrating lateralisation in fMRI studies (Benson et al., 1999).

6.1.2 Assessment of behavioural LIs

Further to the fTCD, a number of behavioural tests were administered within this study. These tests (i.e., the Line Bisection, Drawing "H", Drawing a Head in Profile, Verbal Recall of Coin Head Orientation, and the Ambiguous

[30] Figure taken from Knecht et al. (2000).

Figures tests) represent well-established differences between left- and right-handers (Martin and Jones, 1999b; Jewell and McCourt, 2000; Viggiano and Vannucci, 2002). It was therefore considered interesting to investigate if they convey any relationships with T levels. Moreover, three postural lateral preferences were recorded (i.e., Arm-Folding, Leg-Crossing, Finger-Clasping) and their relationship with T levels was investigated as well.

For the purposes of the Line Bisection task, participants are asked to manually bisect a horizontal line by putting a short vertical line across it. This task is the most frequently employed of the many tasks used to study hemineglect[31] (Jewell and McCourt, 2000). Left neglect patients typically bisect horizontal lines significantly to the right of veridical centre (e.g., as if they either ignore the majority of the left-hand side of the stimulus or are, alternatively, hyperattentive to the right-hand side). Neurologically normal individuals also systematically misbisect horizontal lines or similar tasks (even though the magnitude of the errors is much smaller than in neglect patients), generally erring to the left of the centre (Bowers and Heilman, 1980; Bradshaw et al., 1985, 1987; Halligan and Marshall, 1989), a phenomenon Bowers and Heilman (1980) first referred to as “pseudoneglect”. Both right- and left-handers err leftward of veridical centre, although right-handers err farther to the left than left-handers (Luh, 1995). Jewell and McCourt (2000) in their meta-analysis on 73 studies (or sub-studies) using the Line Bisection task, concluded that handedness has a small effect on bisection errors, with right-handers erring slightly further to the left than left-handers. With regards to sex differences, it is the case that very few studies have examined sex as a factor in line bisection

[31] The visuospatial (or hemispatial) neglect syndrome entails difficulty in reporting, responding or orienting toward stimuli located within contralesional hemispace, as defined in terms of retinotropic, egocentric (body-referenced) or allocentric (object-reference) coordinate systems where such impairment is not due to either motor or sensory defects (Heilman et al., 1993).

performance. Most studies have used mixed sex participant groups (e.g., Chokron and Imbert, 1995) or failed to report the sex of the particpants (e.g., Berti et al., 1995). The majority of the studies examining the influence of sex report non-significant effects (e.g., Bradshaw et al., 1985). However, Roig and Cicero (1994) found that males err more to the left of centre than females. Wolfe (1923), on the other hand, report that male participants misbisect horizontal lines further to the right than do females. Jewell and McCourt (2000) concluded in their meta-analysis that males make slightly larger leftward errors than females.

The Drawing a Head in Profile test asks participants to sketch a quick profile of their mother. The direction the head is facing towards is the variable of interest. No sex effects have been reported to date, but it has been shown that right- and left-handed individuals tend to draw heads facing to the left and to the right, respectively (Shanon, 1979; van Sommers, 1984; Martin and Jones, 1998). This tendency has been attributed to the constraints of bodily posture (see Meulenbroek and Thomassen, 1992; Rosenbaum et al., 1995).

One further possibility is that the right hemisphere is more involved in facial processing, so that information to the observer's left is accessed directly. Since right-handers are assumed to be more strongly lateralised than left-handers, they may be more likely to display the leftward bias. Gilbert and Bakan (1973) indeed found a left-looking preference in matching facial composites to whole faces for right- but not left-handers, who showed no consistent preference. Rhodes (1985) did not replicate this difference, but found that both groups demonstrated a left-looking bias.

Another theory that has been proposed to explain this phenomenon is the Motor Imagery Theory (Jeannerod, 1997; Martin and Jones, 1999b; Viggiano and Vannucci, 2002). According to this theory, the brain processes that are involved when specific movements are performed are also activated in the absence of the physical movements themselves. Thus, there is an isomorphism

between the structure of the movement and the structure of the image or mental representation because of the same underlying neural mechanisms. There is now considerable evidence, particularly from PET studies, that patterns of cerebral motor activation in the absence of movement are both widespread and highly specific, varying as a function of factors such as the meaningfulness of the imagined movement, its reference to the person, and the person's mnemonic strategy (e.g., Decety et al., 1994, 1997). Moreover, there is behavioural evidence for the involvement of motor processes in the maintenance of visuospatial information in memory (e.g., Logie, 1995). For example, if the left hand is used to grip or draw an object, the relevant components of the object itself (the handle of the cup, the profile of a face, etc.) should be stored in memory with the same spatial position and direction they have when they are manipulated by the same left hand (the cup is being gripped, the face is being drawn, etc.). Indeed, Martin and Jones (1999b) found a handedness effect on drawing the faces (left facing or right facing) while no difference emerged in drawing a bicycle.

As far as the Drawing "H" task is concerned, right-handers have been found to draw the horizontal line of a capital "H" from left to right, whereas left-handers have been found to draw the line from right to left (Rice, 1930; Gesell and Ames, 1946; Reed and Smith, 1961).

These directionality[32] trends have been suggested, similarly to profile drawing, to reflect some aspect of lateralisation of cerebral function with the right-handed population including more individuals of pronounced lateral dominance thus showing stronger directionality trends than the left-handed population. A second hypothesis on the directionality of line drawing is that tensor movements outward from the body are smoother, more rapid, more

[32] Directionality is defined as the tendency of a movement to pursue a characteristic course under given conditions (Dreman, 1974).

accurate, and less fatiguing than flexor inward movements (Brown et al., 1948; Bartlett, 1957). Shanon (1979), on the other hand, compared right- and left-handed participants with different reading habits (left-to-right or right-to-left) using graphological and drawing directionality tasks. He found that right-handers with either reading habits did not differ in their directionality preferences, but the left-handers did. He therefore suggested that directionality of right-handers is determined by biological factors, whereas left-handers are more influence by environmental factors. Alter (1989) proposed that the presence of a directional bias is further influenced by sex, as male right-handers exhibit a significantly stronger leftward directionality in their drawings, than right-handed females.

The Verbal Recall of Coin Head Orientation test entails participants recalling the direction the head of the Queen faces towards on British coins. Interestingly, people's recall of the direction is below the chance level of performance (Martin and Jones, 2006), with the majority of people remembering the Queen's head to be facing left, when in fact it is facing right. This effect has been attributed, among others factors (for a review see Jones and Martin, 2004; Martin and Jones, 2006), to handedness. Indeed, McKelvie and Aikins (1993) found that right-handed people are more likely than left-handed people to incorrectly recall the Queen's head as facing left. Generally, right- and left-handed people tend to be associated with remembering stimuli as left- and right-facing, respectively (Martin and Jones, 1999a; Viggiano and Vannucci, 2002). Because most people are right-handed, the contralateral handedness effect may contribute to the coin-head memory illusion for coins on which the head faces right.

Handedness being a factor in misremembering head orientation can be explained by the same theories proposed to explain the directionality in head profile drawing, that is the Motor Imagery Theory and the exaggerated hemispheric lateralisation for right-handers (Logie, 1995; Martin and Jones,

1999a). Another reason why misremembering of head orientation may be a function of handedness is that participants may answer the question by imagining a coin in their preferred hand (McKelvie and Aikins, 1993). If one assumes that it is more “natural” to see the head facing in the direction of the fingers and that a right-hander will imagine the hand with fingers pointing more to the left than to the right, and that a left-hander will imagine the hand pointing more to the right, then it follows that right-handers will score below chance and left-handers will score above chance.

For the Ambiguous Figures test, participants are shown a series of figures and they are asked to name the object they see. These figures are multistable visual stimuli that can be perceived in any one of two perceptual configurations. Ambiguous figures can spontaneously shift from one configuration to another and these changes can occur without any detectable change in context, expectation, or intention of the perceiver (Tsai and Kolbet, 2008). Again, directionality of the perceived configuration is the variable of interest.

Arm-Folding, Finger-Clasping, and Leg-Crossing are three postural asymmetries that are believed to be under genetic control, compatible with the type which has been used to explain the inheritance of handedness (Reiss, 1994). For the Arm-Folding task, participants are asked to fold their arms. The forearm that crosses over the other is recorded. With regards to a sex difference in Arm-Folding, Wiener (1932), Ferronato et al. (1974), Pelecanos (1969), Beckman and Elston (1962), and Dittman (2002) all found no association. McManus and Macscie-Taylor (1979) reviewed data on 17 populations for whom data were given on sex differences and they found no evidence of overall differences between the two sexes being significant. Karev (1993), on the other hand, found an excess of the left type being more pronounced in females. Moreover, no association with handedness has been found (Bryden, 1989).

For the Finger-Clasping task, participants are asked to clasp their hands with their fingers interlocking. The thumb that is on top is recorded. As far as sex differences are concerned, McManus and Mascie-Taylor (1979) reviewed data on 36 populations and concluded that overall the excess of the left type is more pronounced in females but this sexual dimorphism is not significant. Zheng et al. (1999) and Dittman (2002) also found no sex differences in Finger- Clasping. With regards to handedness, Wiener (1932), Ferronato et al. (1974), and Beckman and Elston (1962) found no correlation between handedness and Finger-Clasping. The study of Pelecanos (1969), on the other hand, claimed to have found a highly significant positive correlation, but that study involved a very low incidence of left Finger-Clasping. McManus and Mascie-Taylor (1979) in their review concluded that there is no evidence for a correlation between handedness and finger clasping. Reiss (1997), Bryden (1989), and Karev (1993) found no association with handedness either.

For the Leg-Crossing task, participants are asked to cross their legs. The leg on top is recorded. Bryden (1989) and Reiss (1995) found an association with handedness, and Dittmar (2002) further found a sex difference for this task, with more males being left-footed.

6.1.3 Hormonal assessment

In addition to the measurement of adult hormonal levels in saliva samples, prenatal hormonal levels were assessed using the 2D:4D length ratio. The 2D:4D length ratio has been long known to be sexually dimorphic (Baker, 1888; George, 1930) with males on average having lower ratios than females (Phelps, 1952). The 2D:4D length ratio is further thought to be correlated with prenatal T because relative finger length is set before birth, probably by week 14 of pregnancy (Garn et al., 1975), and because in adults, the 2D:4D length ratio

is correlated negatively with T in males and positively with estrogen in both sexes (Manning et al., 1998).

The 2D:4D length ratio is under the control of the Homebox or Hox genes which also control the differentiation of the testes and ovaries (Herault et al., 1997; Peichel et al., 1997). The common control of the differentiation of the gonads and digits means that the functioning of the former may be reflected in the formation of the latter (Manning et al., 1998). Patterns of 2D:4D length ratios may therefore reflect aspects of gonadal function such as production of T and E in utero (Manning et al., 1998, 2000a).

Manning and colleagues have collected ample evidence for the relationship of the 2D:4D length ratio with sex hormones. They have shown that some sexually dimorphic traits with an excess of males, are associated with a low 2D:4D length ratios (autism and Aspergers syndrome; Manning et al., 2001, fast running speed; Manning and Taylor, 2001). Other dimorphic traits with an excess of females are associated with high 2D:4D length ratios (good verbal fluency and breast cancer; Manning, 2002). Moreover, it has been found that mothers with a high waist-hip-ratio, (associated with high T and low E), tend to have children with low 2D:4D length ratios (Manning et al., 1999), that children with CAH have lower 2D:4D length ratios than controls (Brown et al., 2002; Okten et al., 2002), that high sensitivity to T, as measured by the structure of the T receptor, is associated with low 2D:4D (Manning et al., 2003) and that mothers with low 2D:4D length ratios tend to have children with low 2D:4D length ratios and high concentrations of T relative to E in their amniotic fluid (Manning, 2002; Lutchmaya et al., 2004). With regards to laterality, Manning et al. (2000b) have shown that low 2D:4D length ratios are associated with faster left-hand speed relative to right-hand speed and Fink et al. (2004) further found that a low 2D:4D length ratio is correlated with enhanced left-hand performance.

6.1.4 Limitations of the previous study and scope of the present study

The present study has been designed to investigate whether the results presented in chapter 5 on the relationship between T levels and praxic and linguistic lateralisation can be replicated using the fTCD for the assessment of linguistic lateralisation, a technique that is more reliable than neuropsychological testing.

A point of interest is that chapter 5's study was able to describe significant relationships almost exclusively for the male participants. A number of reasons can be proposed to explain this asymmetry in findings, mainly the fact that the measurement of T is less accurate in females than in males (Shirtcliff et al., 2002; Taieb et al., 2003) and that T concentrations in males show a bigger range, making the detection of relationships easier. On these grounds, for the purposes of the present study only male participants were recruited, in an attempt to increase the power of the study, given time and resources limitations.

Including only male participants does not, however, imply that this study is not about sex differences in lateralisation. On the contrary, the study of within-sex differences can illuminate the development of sex differences (Gladue and Bailey, 1995). Differences in early T exposure contribute to within-sex variation as well as between-sex variations. Traits that are masculinised during early developmental periods are more exaggerated in people who experienced higher T levels in utero. On a different line of thinking, Hausman and Güntürkün (1999) further claimed, based on the coherence between sexual dimorphism in brain asymmetry tasks and the influence of menstrual cycle, that not sex per se, but rather the different underlying gonadal steroid hormone levels are the important factor in sex–specific tasks (Heister et al., 1989). Again, studying sex differences using only male participants is justified.

For the purposes of the present study, the male participants that took part in the study presented in chapter 5 were followed up. This way a wealth of

information on hand, foot, and eye preferences, relative hand skill as well as linguistic lateralisation as assessed by neuropsychological testing could be available. Since the present study was a follow-up a year later than the first study, salivary T was measured anew.

Moreover, the present study was an improvement compared to chapter 5's study as far as the control for circannual and circadian variations of T concentrations is concerned, in the two following ways: all testing was carried out within one month (June 2007) and all participants gave saliva samples on the same times in the evening: 5 p.m. and 5.15 p.m. Participants did so unsupervised when they returned home after testing, but explicit instructions were given beforehand. Anyhow, most of the participants already had experience in saliva collection through their participation in chapter 5's study.

Finally, in addition to measuring adult T concentrations, for the purposes of the present study prenatal T levels were also measured indirectly by means of the 2D:4D length ratio.

6.2 Method

The study was reviewed by, and received ethics clearance through the CUREC of the University of Oxford. Maintenance of confidentiality of information is subject to normal legal requirements.

6.2.1 Participants

Thirty-five male participants took part in the present study, 12 right-handers and 23 left-handers for writing hand. They were all undergraduate and graduate students enrolled in the University of Oxford (*mean age* = 23 years, *SD* = 3, *range* = 19-33), who had taken part in the study described in chapter 5. Participants were reimbursed for their time with cash (15 pounds).

6.2.1.1 Inclusion/Exclusion criteria

Participants had already undergone screening when they were originally recruited. They were thus native, monolingual English speakers with normal or corrected visual acuity and normal hearing. Before being enrolled in the follow-up it was checked that they were not on any medication that affects the central nervous system during the 6 months that proceeded the testing and that they were still neurologically intact and/or did not have any medical conditions interfering with hand function. This second screening was done by e-mail, using a short questionnaire, which was sent as an e-mail attachment (see Appendix 6.1). Participants completed the questionnaire in their own time and e-mailed it back to the researcher.

6.2.1.2 Recruitment

Participants were called back for the follow-up by e-mail. When the participants declared their interest in taking part, they were sent the information sheet for the follow-up (see Appendix 6.2) and were screened for suitability to participate via the e-mail questionnaire described above. The day and time of testing was then agreed upon.

6.2.2 Instruments

6.2.2.1 Assessment of linguistic lateralisation

Word Generation task: The Word Generation task was administered as described by Knecht et al. (1998a). Participants were seated in front of a computer screen and two probes were attached to their heads using an elastic headband (see Figure 6.2). Five seconds after a cueing tone the participants were presented with a letter on the screen for 2.5 s. The cuing tone was used to help focus attention on the upcoming task and to activate the attention of the dominant hemisphere. The language task consisted of silently finding as many

words as possible starting with the displayed letter. After a secondary auditory signal following 15 s after the presentation of the letter, the participants had to report the words they had found. This way, cooperation to the task was controlled (i.e., that participants were indeed using the 15-s period to generate pertinent words). All words (or as many as possible) had to be reported within a 5-s time period. The next letter was presented in the same way after a relaxation period of 30 s. The letters were presented in a random order and no letter was displayed more than once. The instructions given were the following:

> When you hear the first tone, let your mind go blank. When you see a letter on the screen try to think of as many words as you can that begin with that letter. Do this silently and then say the words when you hear the next beep. We will be recording these using a tape recorder. Stop generating words and let your mind go blank again at the next beep. Don't worry if there is not enough time to say all the words you thought of. It is important that you do not talk during the rest period.

6.2.2.2 Hormonal assessment

Salivary hormones: Participants provided two 1-ml samples of saliva for T assay, as well as two 1-ml samples for C assay. C was used as a control hormone. The participants gave two saliva samples at 5 p.m. and two more at 5.15 p.m. on the same day of the testing. Since participants had to provide the samples on their own after the testing had finished, they were given a saliva kit consisting of four test tubes (Salicaps), parafilm (to chew if necessary for saliva stimulation), a stirring stick, an instructions sheet (see Appendix 6.3), a bag to put the test tubes in, and an envelope to place the bag inside. They were asked to store the samples in their refrigerators overnight and return them to the researcher the following morning. The samples were frozen upon collection at

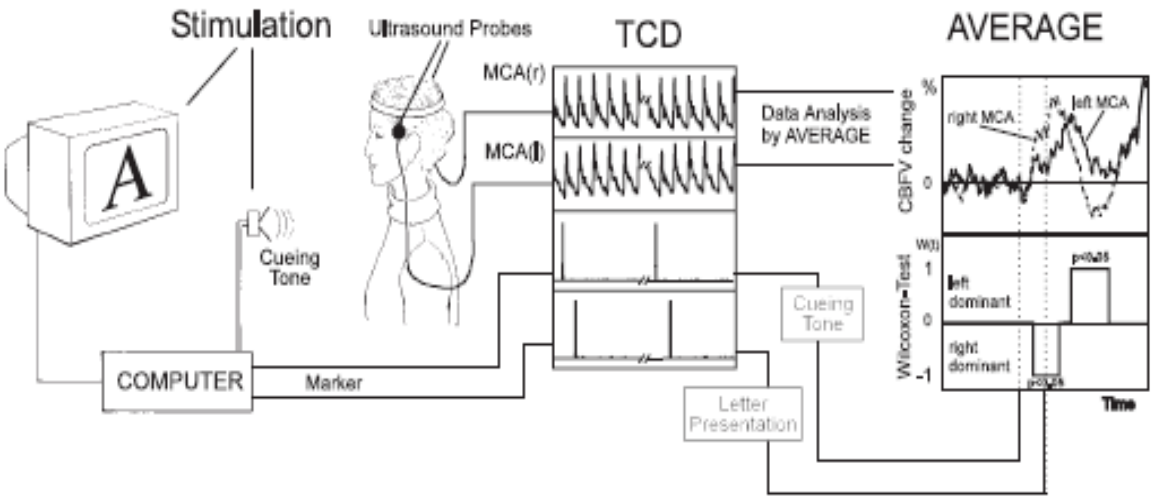

Figure 6.2. Setup for the determination of hemispheric language dominance, using functional transcranial Doppler ultrasound (fTCD).[33]

-80 °C until being sent off on dry ice for assay to the Biophysical Analysis Unit, Northumbria University.[34]

2D:4D length ratio: The length of the second and fourth digit of both the left and the right hand was measured in the ventral surface of the hand from the tip to the basal crease using a vernier caliper which measured to the nearest .01 mm (see Figure 6.3).

6.2.2.3 Behavioural testing

The behavioural tests that were administered and the lateral preferences that were recorded were the followng (in the order followed durng testing):

Line Bisection. Participants were asked to manually bisect a horizontal line presented to them on a test sheet (without measuring it), by putting a short vertical line across it using a pen. The distance of the vertical line from

[33] Figure taken from Deppe et al. (1997b).

[34] Saliva samples for steroid measurement may be stored 7 days at room temperature, four weeks at 2-8 °C and for longer periods at < -20 °C (Gröschl et al., 2001; IBL Laboratories, 2004).

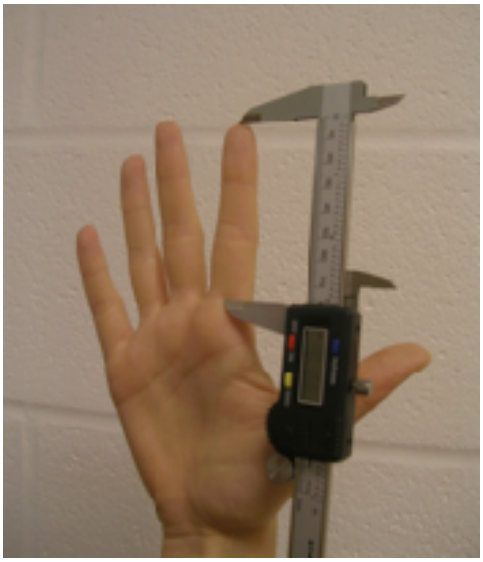

Figure 6.3. The vernier caliper used to measure finger length.

the beginning of the line was the participants' score.

Drawing a Quick Profile of One's Mother. Participants were asked to draw a quick sketch of their mother's head in profile in a box provided on the test sheet. They were asked to do so without spending more than a minute or two. The orientation of the head was recorded (rightward or leftward).

Arm-Folding. Participants were asked to fold their arms (see Figure 6.4). The arm on top (right or left) was recorded. In addition, participants were asked to indicate how comfortable this position felt ("How comfortable is this?") on a 10-point scale ranging from 1 (*not at all comfortable*) to 10 (*extremely comfortable*). They were then asked to fold their arms so that the non-preferred arm was on top and to indicate how comfortable this position felt on the same 10-point scale.

Drawing "H". Participants were asked to draw an upper case printed *H*. The direction in which the horizontal bar was drawn (rightward or leftward) was recorded.

Finger-Clasping. Participants were asked to clasp their fingers (see Figure 6.4). The thumb on top (right or left) was recorded. In addition,

participants were asked to indicate how comfortable this felt ("How comfortable is this?") on a 10-point scale ranging from 1 (*not at all comfortable*) to 10 (*extremely comfortable*). They were then asked to clasp their fingers so that the non-preferred thumb was on top and to indicate how comfortable this position felt on the same 10-point scale.

Verbal Recall of Coin Head Orientation. Participants received a Queen cue: "British coins have the head of the Queen on them. Does the Queen's head face to your left or to your right?" Participant's response was to circle *left* or *right*. They were asked to guess, if necessary. In addition, participants responded with a confidence question ("How confident are you that your choice is correct?") on a 10-point scale ranging from 1 (*not at all confident*) to 10 (*extremely confident*).[35]

Leg-Crossing. Participants were asked to cross their legs (see Figure 6.4). The leg on top (right or left) was recorded. In addition, participants were asked to indicate how comfortable this position felt ("How comfortable is this?") on a 10-point scale ranging from 1 (*not at all comfortable*) to 10 (*extremely comfortable*). They were then asked to cross their legs so that the non-preferred leg was on top and to indicate how comfortable this position felt on the same 10-point scale.

Ambiguous Figures.[36] Participants were presented with six cards, each one with an ambiguous figure printed on it. Each figure had one component facing left and the other facing right. The figures were presented briefly until the participant named one of the components correctly. The figures presented depicted a swan or a cat, a whale or a snail, a face or a body, a rabbit or a

[35] The nationality of the participants was not controlled for, which might have compromised the results of the test. Nevertheless, all participants were UK residents studying at Oxford and were expected to be familiar with British coins.

[36] The Ambiguous Figures test was not administered to the five first participants, therefore the sample size for this test was n = 30.

Figure 6.4. Arm-Folding, Figner-Clasping, and Leg-Crossing (right arm, thumb, and leg on top respectively).

duck, a goose or a hawk, and a lorry or a van (see Figure 6.5). They were presented with this order to all participants.[37] The orientation in which the figure was recognised was recorded, for example, for the first figure "cat" was recorded as "right" and "swan" as "left".

6.2.3 Procedure

Participants were tested individually in a quiet room. The study was explained as soon as they arrived and they were encouraged to ask questions. They gave written consent before taking part in the study, but were explicitly told they remained free to leave at any time and without having to give any reason for doing so. The consent form was signed in two copies so that participants could keep one for their own records. Testing took place in the Department of Experimental Psychology, University of Oxford.

Participants were asked to sit in the chair provided and were given the choice to watch the first few minutes of a movie on a portable DVD player, while

[37] The order was different for the first two participants that took the test, the order for those being lorry/van, face/body, swan/cat, whale/snail, goose/hawk and rabbit/duck.

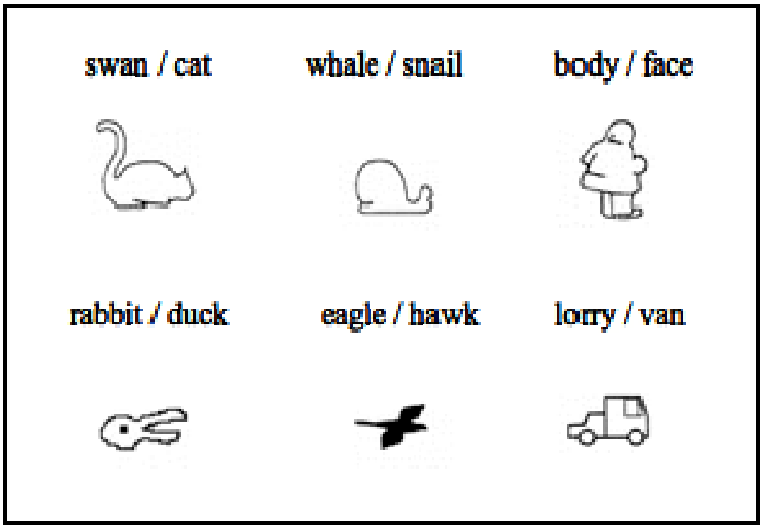

Figure 6.5. The pictures used in the Ambiguous Figures test.[38]

the probes were being placed in position. The fTCD data were collected for the Word Generation task and after the imaging session was completed, participants performed the behavioural and lateral preference tasks. Finally, they were given the saliva kit and were instructed on how to provide the samples.

Testing was carried out over a period of one month (01.6.07 to 29.6.07) at either 10 a.m., 12 p.m., or 2 p.m., but all the saliva samples were given at 5 p.m. and 5.15 p.m in order to minimise the influence of circadian and circannual rhythms on T and C secretion. All participants were debriefed after the completion of the study.

6.2.4 Assays

LIA was used to measure the levels of T and C in the saliva samples. Each sample was assayed twice. The T and C luminescence kits were supplied by IBL-Harburg. Luminescence was measured using a Bio-Tek FLx800

[38] Figures taken from Bernstein and Cooper (1997).

microplate reader used with kC4 Data Analysis Software (supplied by Labtech International Ltd.). Prior to determination, the frozen samples were thawed and centrifuged for 10 minutes at 3000 g to remove particulate material. Hormonal determinations were performed by an experienced Bioassay technician (Biophysical Analysis Unit, Northumbria University), who was unaware of the hypothesis tested.

6.2.5 Imaging data collection and analysis

To measure CBFV changes in the basal arteries as an indicator of downstream increase of regional metabolic activity during the Word Generation test, a commercially available dual ultrasonographic Doppler device was used (DWL Multidop T2: manufacturer, DWL Elektronische Systeme, Singen). The right and left MCAs were insonated at the optimal depth for each participant (45-56 mm) with two transducer probes (2 Mhz) attached to a flexible headband and placed at the temporal skull windows bilaterally. The angles of insonation were adjusted to obtain the maximal signal intensity.[39] Visual stimuli (letters) were presented on a PC controlled by Presentation software (Neurobehavioural systems), which sent marker pulses to the Multidop system to mark the start of each epoch. The spectral envelope curves of the Doppler signal were recorded with a rate of 28 sample points per second and stored for off-line processing.

[39] The fTCD measurement of the CBFV is dependent on the angle of insonation (Bartels and Flugel, 1994). Changes if this angle from 0° to 30° can result in differences in the calculated, absolute CBFV in the magnitude of 15% between examinations or sides. Also, in a narrowed arterial segment incidentally insonated during the test, the absolute velocity increase in blood flow due to cerebral activation would be greater than in a regular segment. This is why flow velocities used for statistical analyses were normalised. Flow velocities at rest were set as zero baseline and CBFV changes during the activated state were expressed as values in percentages relative to this baseline. The use of relative CBFV values eliminated the variability associated with changes in insonation angle or vesel diameter.

Data were analysed using Average software, with the data being processed using the Autoedit function of Average 1.85, which downsamples the blood flow envelope from each probe to 25 Hz, adds a channel corresponding to the heart beat, normalises the left and right cerebral blood flow velocity curve to a mean of 100%, and removes heart beat activity using the heart cycle integration described by Deppe et al. (1997b). Artefacts like those elicited by probe displacement were automatically detected by comparison of the number of pulses per time unit of the entire recording session with the frequency of peaks in a given segment. Frames of recording were rejected when these frequencies differed by more than one third. Additionally, epochs containing CBFV values outside the range of 30% to 200% of the mean velocity were rejected. The remaining data were segmented into epochs that related to cueing tone, and were then averaged (see Figure 2). The epochs were set to begin 18 s before and to end 36 s after the cueing tone. The mean velocity in the 18-s precueing interval ($V_{pre.mean}$) was taken as the baseline value. The relative CBFV changes (dV) during cerebral activation were calculated by the formula:

$$dV = (V(t) - V_{pre.mean}) \times 100/V_{pre.mean},$$

where V(t) is the CBFV over time. Relative CBFV changes from repeated presentations of letters (on a total of 23 trials) were time-linked to the cueing tone. Differences in the velocity changes in the two MCAs in every patient were statistically evaluated by the Wilcoxon test for each time point. This nonparametric test is less sensitive to outliers when only a limited number of epochs can be averaged.

An fTCD Laterality Index (LI) was then calculated by the following formula:

$$LI = \frac{1}{t_{int}} \int_{t_{max}-0.5t_{int}}^{t_{max}+0.5t_{int}} \Delta V(t)\,dt$$

where $\Delta V(t) = dV(t)_{left} - dV(t)_{right}$ is the difference between the relative velocity changes of the left and right MCAs. The term t_{max} represents the latency of the absolute maximum of $\Delta V(t)$ during an interval of 10-18 s after cueing, that is during verbal processing. For integration, a time period of t_{int} = 2 s was chosen (see Figure 6.6).

6.2.6 Statistical analysis

Functional data were analysed using the Average software for Windows, which has been developed for the analysis of fTCD data (Deppe et al., 1997b). Further analyses were performed using the Statistical Package for the Social Sciences (SPSS) v.14. Non-parametric tests were used, as the sample size was not adequate for parametric testing. The Kolmogorov-Smirnov *Z* test was used to assess the hypothesis that LIs in right- and left-handers were drawn from different populations, as well as the hypothesis that hormonal levels of right- and left-hemisphere language dominant participants were drawn from different populations. Unlike the parametric *t*-test for independent samples or the Mann-Whitney *U* test, which test for differences in the location of two samples (differences in means and differences in average ranks, respectively), the Kolmogorov-Smirnov *Z* test is sensitive to differences in the general shape of the distributions in the two samples, that is differences in dispersion and skewness (Spence et al., 1990).

The relationship between hormonal levels and degree of linguistic lateralisation was estimated using curve estimation regressions. Hormonal measurements (i.e., 2D:4D length ratios and salivary T and C

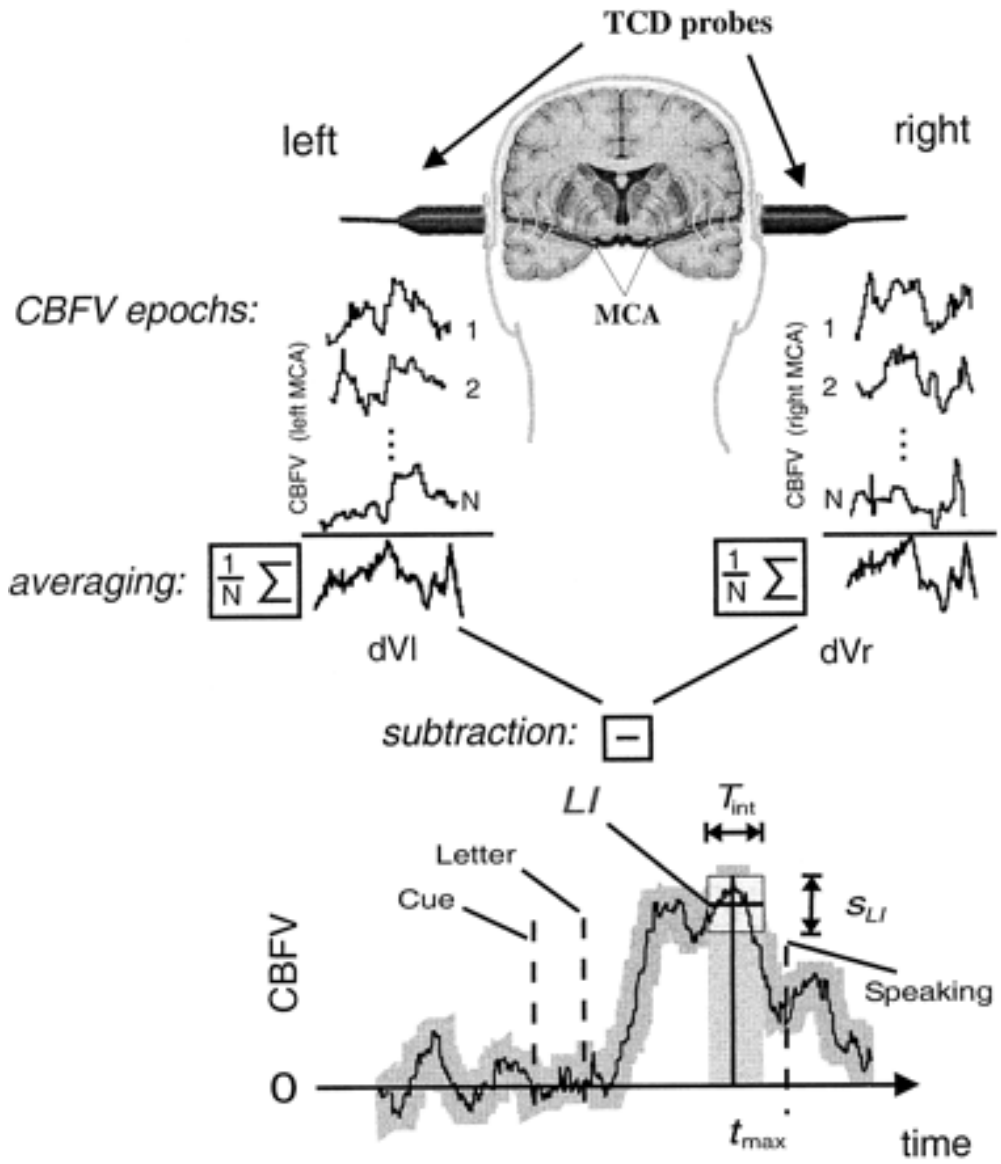

Figure 6.6. Schematic of the averaging procedure. The top panel shows the way in which relative event-related cerebral blood flow velocity (CBFV) changes in both middle cerebral arteries (MCA) during individual repetitions of the task (1 through N) are collected and averaged. The bottom panel depicts the subtraction of averaged CBFV changes in the right from the left MCA, providing a measure of the mean interhemispheric CBFV difference (dVl-dVr) over the course of the task, with the corresponding standard deviations at each point in time (gray shading).[40]

[40] Figure taken from Knecht et al. (1998b).

concentrations) were the dependent variables and the degree of linguistic lateralisation the independent one. The Kolmogorov-Smirnov *Z* test was also used to assess the hypothesis that hormonal levels in participants with different directional preferences in the behavioural tests (Drawing "H", Drawing a Quick Profile of One's Mother, Verbal Recall of Coin Head Orientation, Ambiguous Figures) and the postural lateral preferences (Arm-Folding, Finger-Clasping, Leg-Crossing) were drawn from different populations. The relationship between hormonal levels and Line Bisection scores was estimated using curve estimation regressions. Hormonal levels (i.e., 2D:4D length ratios, salivary T and salivary C concentrations) were the dependent variables and the Line Bisection score the independent one.

All *p*-values were two-tailed and the *a*-level was set at .05.

6.3 Results

6.3.1 Functional TCD and hormonal concentrations

One participant (left-handed) was excluded, because sonography was not possible due to the lack of a temporal bone window (inadequate ultrasonographic penetration of the skull by the ultrasound beam). In the remaining 34 participants (12 right-handers, 22 left-handers) the overall distribution of linguistic lateralisation was bimodal with five participants (14.7%; 1 right-hander and 4 left-handers) being right -hemisphere language dominant and 29 participants (85.3%; 11 right-handers and 18 left-handers) being left-hemisphere language dominant (see Figure 6.7).

In the present sample, the distribution of linguistic lateralisation was equivalent in right- and left-handers (Z = .94, p = .34). The mean index of language dominance was 2.38 (*range* = -4.90, 6.86, *SD* = 2.84) for right-handers and 2.67 (*range* = -3.03, 6.24, *SD* = 2.56) for left-handers.

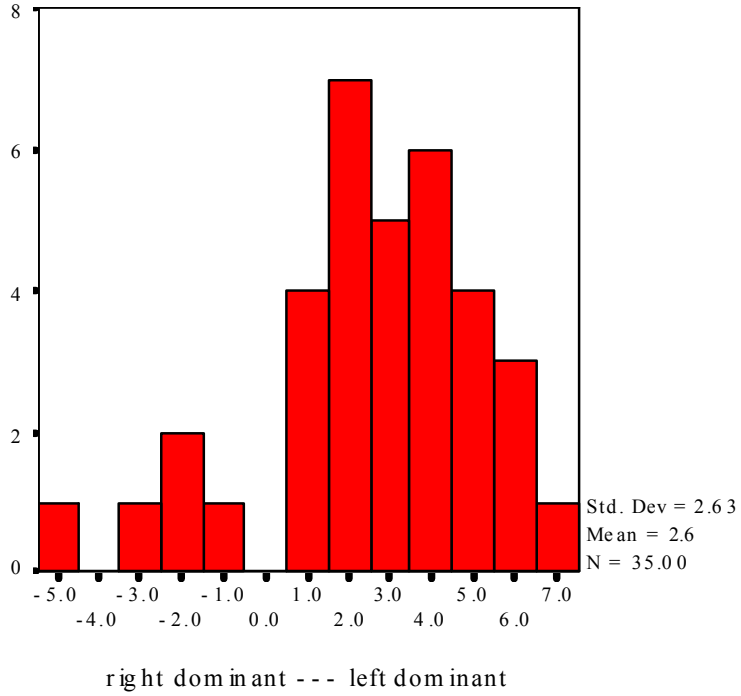

Figure 6.7. Frequency histogram of the bimodal distribution of hemispheric language lateralisation in 34 male participants as assessed by functional transcranial Doppler untrasound (fTCD).

6.3.1.1 Salivary hormones

One participant (left-handed) was excluded from the analysis, as there was no sample in the test tubes for both the T samples and the single sample provided for the C analysis was contaminated with blood thus it was unsuitable for analysis. One more participant (left-handed) was excluded from C analysis, as his C concentration was an outlier.[41] Mean T concentration was 261.39 pmol/l, (*range* = 64.58 - 576.50, *SD* = 115.75) and mean C concentration was 5.14 nmol/l (*range* = .54 - 5.45, *SD* = 3.39).

Only five participants were left hemisphere dominant, therefore parametric tests were not appropriate to test the hypothesis that hormonal levels in right and left hemisphere dominant participants are significantly different. The

[41] An outlier is defined as a case with a value between 1.5 and 3 times larger than the interquartile range.

Kolmogorov-Smirnov test was run separately with T and C concentrations as the dependent variables and with direction of linguistic lateralisation (right or left) as the fixed factor, but no significant relationships were detected for either T or C concentrations (both $p > .17$).

To test the hypothesis that the relationship between degree of linguistic lateralisation and hormonal levels is quadratic, curve estimation regressions were run separately with T and C concentrations as the dependent variables and with the index for linguistic lateralisation as the fixed factor. A quadratic relationship was indeed detected, F (31) = 4.98, p = .013 (see Figure 6.6), the best-fitting relation being:

$$T = 6.09(\text{LI linguistic lateralisation}) + 3.41(\text{LI linguistic lateralisation})^2 + 199.94.$$

No relationships were detected between language lateralisation and C concentrations (all $p > .24$).

6.3.1.2 2D:4D length ratio

In the present sample, the mean 2D:4D length ratio for the right hand was .97 (*range* = .91 – 1.05, *SD* = .03) and for the left hand .97 (*range* = .88 – 1.03, *SD* = .03). These values are within the normal range (Manning et al., 2000). The 2D:4D length ratio was not correlated with T concentrations for either hand (both $p > .34$), contrary to what was expected.

To test the hypothesis that the relationship between degree of linguistic lateralisation and hormonal levels is quadratic, curve estimation regressions were run separately with the right and left hand 2D:4D length ratios as the dependent variables and with the index for linguistic lateralisation as the fixed factor, but no significant relationships were detected for either hand (all $p > .33$).

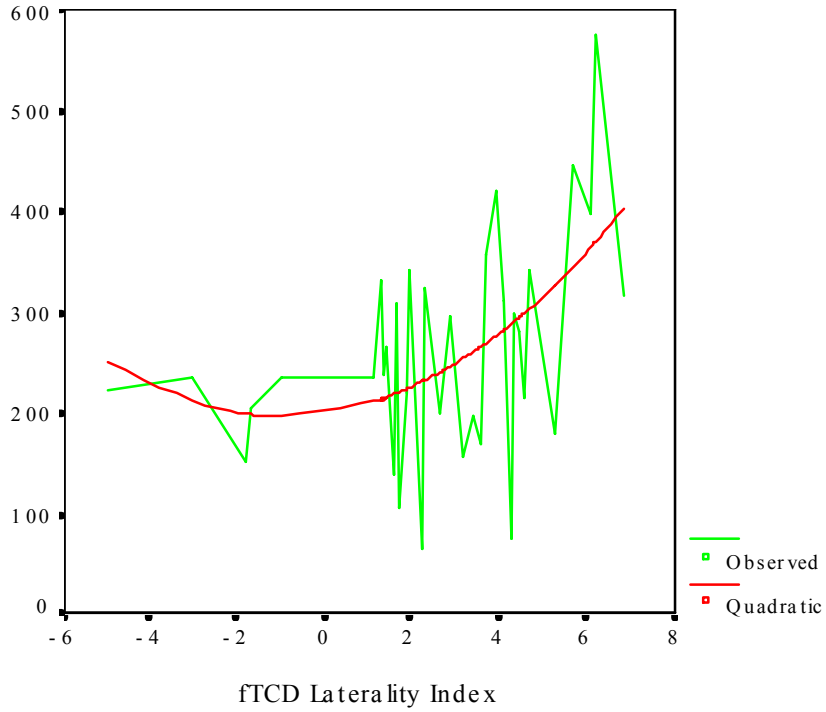

Figure 6.8 Curve estimation of the relationship between T concentrations and linguistic lateralisation as assessed by functional transcranial Doppler ultrasound (fTCD).

6.3.2 Behavioural tests and hormonal concentrations

Results for the behavioural tasks are given in Table 6.1, separately for right- and left-handers.

6.3.2.1 Salivary hormones

Line Bisection. The relationship between salivary hormonal levels and Line Bisection scores was estimated using curve estimation regressions, separately for T and C concentrations as the dependent variables and with the Line Bisection score as the independent one, but no significant relationships were detected for either T or C concentrations (all $p > .29$).

Table 6.1. Descriptive statistics for the behavioural tests.

Test	Right-handers (n_r = 12)	Left-handers (n_l = 22)
Line Bisection		
Mean (mm)	57.46	58.18
Range	51-63	53-62
SD	3.20	2.50
Head in profile Facing rightwards (%)	46.2	54.5
Drawing "H" Rightward direction (%)	76.9	45.5
Coin head orientation		
Accuracy (% correct)	76.9	40.9
Confidence		
Mean	7.46	5.83
Range	3-10	1-10
SD	2.44	2.38
Ambiguous figures		
Swan/Cat		
Rightward direction (% cat)	20	10
Whale/Snail		
Rightward direction (% snail)	20	15
Face/Body		
Rightward direction (% body)	90	75
Rabbit/Duck		
Rightward direction (% duck)	30	65
Goose/Hawk		
Rightward direction (% hawk)	60	85
Lorry/Van		
Rightward direction (% van)	0	15

Table 6.1. (continued)

Test	Right-handers (n_r = 12)	Left-handers (n_l = 22)
Arm-folding		
Right arm on top (%)	23.1	54.5
Comfort in preferred position		
Mean	7.85	7.36
Range	5-10	3-10
SD	1.41	1.89
Comfort in the non-preferred position		
Mean	4.85	3.82
Range	1-9	2-8
SD	1.86	1.50
Finger-clasping		
Right thumb on top (%)	23.1	31.8
Comfort in preferred position		
Mean	8.62	8.00
Range	6-10	4-9
SD	1.26	1.27
Comfort in the non-preferred position		
Mean	4.85	4.36
Range	3-8	2-7
SD	1.52	1.26
Leg-crossing		
Right leg on top (%)	76.9	22.7
Comfort in preferred position		
Mean	7.62	6.77
Range	3-10	1-9
SD	1.80	2.09
Comfort in the non-preferred position		
Mean	6.08	5.18
Range	2-8	1-8
SD	1.66	1.79

Drawing a Head in Profile. The Kolmogorov-Smirnov *Z* test was run separately for T and C concentrations as the dependent variables and the direction the profile of the head was facing to (rightward or leftward) as the grouping factor. No significant relationships were detected for either T or C concentrations (all $p > .70$).

Drawing "H". The Kolmogorov-Smirnov *Z* test was run separately for T and C concentrations as the dependent variables and with the direction in which the horizontal bar was drawn (rightward or leftward) as the grouping factor. No significant relationships were detected for either T or C concentrations (all $p > .44$).

Verbal Recall of Coin Head Orientation. The Kolmogorov-Smirnov *Z* test was run separately for T and C concentrations as the dependent variable and with the direction the head of Queen was recalled to be facing to (right or left) as the grouping factor. No significant relationships were detected for C concentrations (all $p > .69$), but a significant relationship was detected with T concentrations, $Z = 1.44$, $p = .033$, with participants recalling the Queen's head facing right having higher mean T concentrations (303.18 pmol/l, $SE = 33.04$) than participants recalling the Queen's head as facing left (231.77 pmol/l, $SE = 16.44$). There was no difference in confidence levels between correct and incorrect responses, $Z = .58$, $p = .89$.

Ambiguous Figures. The Kolmogorov-Smirnov *Z* test was run separately for T and C concentrations as the dependent variables and the orientation in which each figure was recognised (right or left) as the grouping factor. No significant relationships were detected for either T or C concentrations for any of the figures (all $p > .24$).

Arm-Folding. The Kolmogorov-Smirnov *Z* test was run separately for T and C concentrations as the dependent variables and with the forearm placed on top as the grouping factor (right or left). No significant relationships were

detected for either T or C concentrations (all $p > .66$). Moreover, there was no difference in the comfortability rating for participants having placed the right or left forearm on top for either the preferred ($p > .42$) or the non-preferred arm ($p > .97$).

Finger-Clasping. The Kolmogorov-Smirnov Z test was run separately for T and C concentrations as the dependent variables and with the thumb placed on top as the grouping factor (right or left). No significant relationships were detected for either T or C concentrations (all $p > .66$). Moreover, there was no difference in the comfortability rating for participants having placed the right or left hand on top for either the preferred ($p > .94$) or the non-preferred thumb ($p > .93$).

Leg-Crossing. The Kolmogorov-Smirnov Z test was run separately for T or C concentrations as the dependent variable and with the leg placed on top as the grouping factor (right or left). No significant relationships were detected for either T or C concentrations (all $p > .87$). Moreover, there was no difference in the comfortability rating for participants having placed the right or left leg on top for either the preferred ($p > .99$) or the non-preferred leg ($p > .29$).

6.3.2.2 2D:4D length ratio

Line Bisection. The relationship between 2D:4D length ratios and line bisection scores was estimated using curve estimation regressions, separately for the right and left hands, with 2D:4D length ratios as the dependent variables and with the Line Bisection score as the independent one, but no significant relationships were detected for either hand (all $p > .14$).

Drawing a Head in Profile. The Kolmogorov-Smirnov Z test was run separately for the right or left hands, with the 2D:4D length ratios as the dependent variable and the direction the profile of the head was facing to (right

or left) as the grouping factor. No significant relationships were detected for either hand (all $p > .54$).

Drawing "H". The Kolmogorov-Smirnov Z test was run separately for the right or left hands, with the 2D:4D length ratios as the dependent variable and with the direction in which the horizontal bar was drawn (rightward or leftward) as the grouping factor. No significant relationships were detected for either hand (all $p > .74$).

Verbal Recall of Coin Head Orientation. The Kolmogorov-Smirnov Z test was run separately for the right or left hands with the 2D:4D length ratios as the dependent variable and with the direction the head of Queen was recalled to be facing to (right or left) as the grouping factor. No significant relationships were detected for either hand (all $p > .46$).

Ambiguous Figures. The Kolmogorov-Smirnov Z test was run separately for the right or left hand, with the 2D:4D length ratios as the dependent variable and the orientation in which each figure was recognised (right or left) as the grouping factor. No significant relationships were detected for either hand for any of the figures (all $p > .29$). The only significant relationship was detected for the rabbit/duck ambiguous figure and the 2D:4D length ratio of the right hand, $Z = 1.48$, $p = .024$. Participants recognising the figure as a duck (i.e., facing right) had higher mean 2D:4D length ratios (.98, $SE = .01$) compared to those recognising the figure as a rabbit (i.e., facing left) (.96, SE = ,01).

Arm-Folding. The Kolmogorov-Smirnov Z test was run separately for the right or left hand, with the 2D:4D length ratios as the dependent variable and with the forearm placed on top as the grouping factor (right or left). No significant relationships were detected for either hand (all $p > .16$).

Finger-Clasping. The Kolmogorov-Smirnov Z test was run separately for the right or left hand, with the 2D:4D length ratios as the dependent variable and

with the thumb placed on top as the grouping factor (right or left). No significant relationships were detected for either hand (all $p > .10$).

Leg-Crossing The Kolmogorov-Smirnov Z test was run separately for the right or left handwith the 2D:4D length ratios as the dependent variable and with the leg placed on top as the grouping factor (right or left). No significant relationships were detected for either hand (all $p > .49$).

6.4 Discussion

The aim of the present study was to replicate the quadratic relationship between degree of linguistic lateralisation and T levels found using neuropsychological techniques. Here, linguistic lateralisation was assessed by means of the fTCD, using the Word Generation task. Functional TCD is a nonivasive diagnostic tool with high temporal resolution that monitors continuous and bilateral event-related changes in blood flow velocity of the basal cerebral arteries, allowing for a convenient and fully automated quantification of linguistic lateralisation. Indeed, further support was provided for the finding that higher T concentrations are associated with a higher degree of lateralisation in a sample of adult males. No associations were found with C, which was used as a control hormone. No associations were found between linguistic laterality and right or left hand 2D:4D length ratios either.

Adult T levels were also investigated with regards to their relationship to a number of behavioural tests that represent well-established differences between left- and right-handers. A significant relationship was detected between recall of the direction of the Queen's head on British coins and T concentrations, with participants correctly recalling the Queen's head as facing right having higher T concentrations than participants recalling the Queen's head as facing left. As discussed earlier, right- and left-handed people tend to be remembering stimuli as left-facing and as right-facing, respectively (Martin and Jones, 1999a;

Viggiano and Vannucci, 2002). In this study, people who exhibited behaviour typical for left-handers (remembering the head facing right) had higher T concentrations. With regards to the 2D:4D length ratios, the only significant relationship was found for the rabbit/duck ambiguous figure. Even though this figure resembles a head in profile, this finding is opposite to the one found for the Queen's head orientation test. In particular, those exhibiting behaviour typical of left-handers, had higher 2D:4D ratio, which is translated as lower pre-natal T levels.

Moreover, three postural lateral preferences were recorded (i.e., Arm-Folding, Leg-Crossing, and Finger-Clasping) and their relationship with adult and prenatal T levels was investigated as well, but no statistically significant relationships were detected.

These findings replicate – if only indirectly – the results of chapter 5 with regards to praxic lateralisation. Participants exhibiting behaviour typical for left-handers (remembering the Queen's head as facing right) had higher T levels. Moreover, the present findings replicate the findings of chapter 5 with respect to linguistic lateralisation, as it was demonstrated that a higher lateralisation index related to higher T levels. Based on the results of this chapter, support for the sexual differentiation hypothesis is again provided.

The relationship of the 2D:4D length ratio with the rabbit/duck ambiguous figure contradicts the above findings, as participants showing behaviour typical for left-handers seem to have lower prenatal T concentrations. This finding might well be a Type 1 error, as a rather large number of comparisons was performed. Another possibility might be that the 2D:4D length ratio might not be as useful as a biomarker of prenatal T levels as Manning et al. (2000) have suggested. In that respect, this failure to demonstrate the expected results further adds to recent work by Grouios and colleagues, who have similarly failed to find expected relationships of the 2D:4D length ratio to conditions such as body

weight (Koidou et al., 2006), sporting excellence (Grouios et al., 2007), and intellectual disability (Ypsilanti et al., 2008).

The findings of both chapters 5 and 6 point to the importance of the degree of linguistic lateralisation. It is proposed that the direction of lateralisation may not be the most useful variable for the study of hemispheric lateralisation for language processes. The right/left dichotomy hides some important information conveyed by the continuous measurement inherent to the degree of lateralisation with regards to the amount of interhemispheric share of information.

Using the Word Generation task, which is the most frequently used activation task for assessing language dominance with the fTCD, means that only one of the multiple dimensions of language was investigated, namely language production. Other aspects of language, such as prosody, were not tested in the study presented here. These aspects could show a different relationship with T levels. Nevertheless, the present findings replicate those that were produced using the VHLD test, a test of language perception. The latter test is based on subtle performance differences between the two hemispheres, whereas the fTCD directly reflects the degree of physiological activation of the language areas in the brain. Moreover, whereas the Word Generation task is expressive in nature, the VHLD is a test of receptive language. Being able to replicate findings using both behavioural and physiological approaches as well as using language tasks with different properties gives a certain degree of confidence in the claim of a quadratic relationship between T concentrations and degree of linguistic lateralisation.

The sample size of the study presents a limitation in detecting relationships with direction of linguistic laterality. Since approximately 4% of right-handers and 27% of left-handers are right hemisphere dominant for language (Knecht et al., 2000), with the present sample size of 35 participants

out of which 12 were right-handers and 23 left-handers for writing hand, one should have expected to find only about seven participants who would be right hemisphere dominant for language. Even though this sample size would be underpowered to detect any relationships with direction of lateralisation, the main purpose of the present experiment was to replicate findings with regards to the degree of linguistic lateralisation. Chapter 5's findings demonstrated that a sample size of 30 males is powerful enough to detect relationships between salivary T and degree of lateralisation. Indeed, results regarding degree of lateralisation were replicated. In addition to the above, it seemed efficient to follow up the male participants that had taken part in the chapter 5's study, so that rich information on their praxic and linguistic laterality patterns would be available. Thus, the participant pool was limited to 70 males that had taken part in the previous study. Including the female participants, which would add another 50 participants to the pool, was not considered useful, since no relationships were detected for females in the study presented in chapter's 5. Moreover, for female participants further restrictions would have to apply, namely participants not having been on the contraceptive pill for six months prior to study participation and being at menses during testing. Nevertheless, female and male data would have needed to be analysed separately, due to female and male T concentrations being so dissimilar.

Overall, the present study was successful in replicating the quadratic relationship between adults T levels and brain lateralisation for language. It provided an improvement to the study presented in chapter 5, with regards to both the measurement of linguistic lateralisation (here measured by means of fTCD using the Word Generation task) as well as with regards to the method of saliva collection (here all saliva samples were collected in a period of one month, at the same evening time for all participants). Further work on the relationship between hormonal levels with linguistic lateralisation should extend

the investigation to female participants. Moreover, other aspects of language (e.g., comprehension or prosody) should be investigated with regards to their association with hormonal concentrations.

Chapter 7

General Discussion

Two aspects of behaviour are characteristic of hominid evolution: one relates to the use of language (Lieberman, 1975, 1984) and the other to the population bias towards right-hand preference for manual praxis (McManus, 1991; Annett, 1996). Praxic lateralisation and the neurobiological substrate for language are, moreover, intimately linked, with praxic lateralisation being an indirect index for linguistic lateralisation in the brain. Knecht et al. (2000) showed, using fTCD, that the incidence of right-hemisphere language dominance increases linearly with the degree of left-handedness, from 4% in strong right-handers, to 15% in ambidextrous individuals, and 27% in strong left-handers. Both praxic and linguistic lateralisation have been further suggested to be sexually dimorphic (e.g., Oldfield, 1971; Hiscock; Voyer, 1996; Knecht, 2000), even though not all studies's findings are in agreement (e.g., Salmaso, 1985; Frost, 1999).

The focus of the present thesis was to examine the putative sex differences in praxic and linguistic lateralisation, to explore the adequacy of competing explanatory theories and to further investigate possible mechanisms underlying these differences. This work gains its importance from the fact that in conditions, such as laterality, where a sex bias exists, information regarding the origin of the sex bias is essential for understanding the aetiology of the condition

(Baron-Cohen et al., 2004). This examination further contributes to the broader question of individual differences in brain organisation and abilities. Individual differences, specifically in the lateralisation of praxis and language, are also important to psychiatric, neurological, and neuropsychological research and practice.

7.1 Overview of the research work

The relationship between praxic and linguistic lateralisation, along with the fact that linguistic lateralisation is difficult to study in large populations, has led to extensive study of handedness (the most important manifestation of praxic lateralisation). Therefore, the present thesis initiated the research into laterality by means of a large-scale meta-analysis on the incidence of handedness in males and females (Papadatou-Pastou et al., 2008). The meta-analysis aimed to provide a definitive test of the hypothesis that there is a sex difference in the incidence of handedness and to estimate the overall magnitude of this difference. In addition to that, it aimed to assess whether systematic variation in the size of the sex difference between different studies exists and, if so, to investigate the sources of any such variance.

The meta-analysis included data on 1,787,629 individuals (831,537 male, 956,092 female) extracted from 144 studies. In the most comprehensive comparison (left-handedness [total]), which included nearly all the data sets, the ratio of male-to-female left-to-right handedness odds was estimated at 1.23 with a 95% confidence interval of 1.19 to 1.27. Moreover, a significant sex difference was detected in each one of four other meta-analyses carried out on smaller sets of data. Three factors were found to moderate significantly the size of the sex difference odds ratio, namely the way in which handedness had been assessed, the year of publication of the study and the ancestry of the participants. The sex difference appeared larger when handedness was

assessed using methods other than the recording of writing hand (or, equivalently, writing hand together with self-report of handedness); in earlier rather than later studies; and in East Asian rather than Caucasian and African samples. Other potential moderating factors that, despite their acclaimed effect on the incidence of handedness, were not shown to be sensitive with regards to sex differences are: the educational status of the participants, the number of questionnaire items used, the type of response categories used, whether the main purpose of the study had been to measure handedness, and whether the data were collected by self-report. Tests of ascertainment bias revealed that there is no evidence the sex difference is a Type 1 error.

A limitation of the meta-analysis was that it did not directly examine what is the cause of the difference in the estimating male-to-female odds ratios when handedness is assessed using writing hand compared to when other measures of handedness are used. For example, it did not examine whether the use of a graded response format in hand preference inventories artificially generates the sex difference, as suggested by Bryden (1977) following the rationale that the two sexes have different reactions to the wording of the response format of a hand preference questionnaire. In order to overcome this limitation, a study was designed to systematically investigate the effect of different response formats of hand preference inventories, while controlling for both handedness and sex (chapter 3). A number of other effects pertinent to the response format of a hand preference questionnaire were also addressed. More specifically, it was investigated whether an “either” response in a 5-point graded response format is translated differently into a binary response format according to the handedness and/or the sex of the individual. It was further investigated whether the EHI in its 5-point graded response format differs significantly in producing “either” responses from the EHI in its graphic graded response format.

It was demonstrated that both the reluctance to give extreme responses and the translation of an “either” response into a binary response questionnaire are subject to one’s handedness and not to one’s sex. It is thus argued that the sex difference in handedness is not artificially produced by the different reactions the two sexes have to the wordings of the response format of handedness questionnaires. Therefore, Bryden’s findings should be rather attributed to the fact that left-handers of both sexes avoid giving extreme responses and at the same time there are more left-handers within the male population. An interesting new finding was that, irrespective of sex, right-handers tend to choose a “right” response in the place of an “either” response more often than left-handers choose a “left”response in the place of an “either” response. Moreover, the rank order of participants in terms of degree of handedness was found not to be significantly dependent upon the questionnaire or upon the response format used.

The meta-analysis did not reveal a significant difference among different hand preference questionnaires in the male-to-female left-handedness odds ratio produced. However, the power of the meta-analysis was limited by the relatively small number of studies employing any individual questionnaire. Therefore, a direct comparison between different hand preference tests was performed (chapter 4) with the aim to inform subsequent studies with regards to which instrument to employ for the study of the sex differences in praxic and linguistic lateralisation. This direct testing gave the opportunity to include relative hand skill tests in the comparison, which assess handedness in terms of performance, and to further include assessments of footedness and eyedness, two other important behavioural asymmetries.

The results of chapter 4’s study confirmed the findings of the meta-analysis that the hand preference questionnaires do not significantly differentiate amongst each other with regards to their sensitivity in capturing a sex difference

in handedness. The foot and eye preference questionnaires also failed to produce significantly different scores between the sexes. The QHPT, though, a behavioural test of hand preference employing card reaching in different locations, did prove to be sensitive in capturing sex differences, at least for right-handed participants. Similar results were obtained for two of the hand skill tests: the Peg-Moving and the Tapping Speed tests. For all these three tests, right-handed females were found to be more skillful with their right hand compared to their left hand (or to prefer the right rather than the left hand for reaching actions) as opposed to right-handed males. These findings lead to the conclusion that behavioural tests of handedness, and specifically the QHPT, the Peg-Moving, and the Tapping Speed test, are more senstive tools than hand preference inventories when it comes to the study of the sex difference in handedness and its correlates.

The findings of the meta-analysis, that is the fact that a sex difference in handedness is present in every comparison representing different conceptions of left-handedness, as well as in all the levels of the different moderator variables, provide support for the notion that the sex difference in praxic lateralisation has its basis in innate biological differences between the two sexes, namely differences in their genetic make-up (e.g., McManus and Bryden, 1992; Jones and Martin, 2000; Annett, 2002), in their rate of somatic maturation (e.g., Maehara et al., 1988), and in their hormonal environment (e.g., Geschwind and Galaburda, 1987). Genetic, maturational, and hormonal theories are not mutually exclusive though, as it could be argued that they focus on different aspects of the same phenomenon, maturation being intertwined with hormonal changes that are controlled by genetic factors, all resulting in the different neural organisation of the two sexes.

While theories discussing the rate of somatic maturation were not investigated further in this thesis, useful information was provided towards

exploring the adequacy of competing genetic and hormonal theories. With regards to genetic theories, the estimate of the RS theory (Annett, 2002) of a displacement of the chance distribution of asymmetry farther to the right in females by about 20% is very close to the most inclusive estimate of the meta-analysis of 1.23 for the ratio of male-to-female left-to-right handedness odds, and falls within the *95% CI* of 1.19 to 1.27. Nevertheless, the sex difference is not integral to the RS theory. The modifier-gene hypothesis by McManus and Bryden (1992) as well as the single-gene recessive model of Jones and Martin (2000) make integral predictions of the occurrence of a sex-difference in handedness, therefore they receive greater support from the present findings than the RS theory does. For the single-gene model in particular, there are quantitative as well as qualitative implications. The odds ratio predicted on the basis of the parameter values estimated for their recessive model by Jones and Martin (2000, 2001) takes the value of 1.70. Because the theoretical odds ratio lies outside the confidence intervals established here, it is apparent that this model needs to be reconsidered.

Theories describing hormonal influences on praxic and linguistic lateralisation were experimentally investigated and the studies were presented in the last two empirical chapters (5 and 6). The study described in chapter 5 was designed to examine the relationship between salivary T concentrations and hand preference, hand skill, and linguistic lateralisation. Salivary C was also measured as a control hormone in order to test if any of the relationships found are specific to T. The three behavioural tests identified in chapter 4 as the most sensitive ones with regards to sex differences in praxic lateralisation (Peg-Moving, Tapping-Speed, and the QHPT) were used. Moreover, hand preference was measured by means of the EHI, which is the most popular measure of hand preference. Linguistic lateralisation was measured by means of two neuropsychological tests, specifcally the CV-DL and the VHLD tests. The study

was designed to overcome certain limitations of previous research, namely: (a) the measurement of handedness mostly as hand preference, (b) the use of a single measure of brain laterality, (c) the failure to exclude female participants that were on oral contraceptives, (d) the failure to control menstrual cycle phase, and (e) the fact that some studies overlooked circadian and circannual changes in the levels of T and C concentrations.

A significant linear relationship was detected between the Peg-Moving test score and T concentrations for males as well as a trend towards a negative linear relationship between the Tapping Speed test and T concentrations, again for males. No relationships were detected between T concentrations and hand preference, as defined by either the EHI or the QHPT. In other words, the male participants who had higher T concentrations took longer to move the pegs with the right hand compared to moving them with the left hand, and they also produced less taps with the right compared to the left hand. In both cases, higher T concentrations were associated with the right hand being less skillful than the left hand. As far as linguistic lateralisation is concerned, a quadratic relationship between the VHLD test accuracy scores and T concentrations was detected over the whole sample. When analyzing data separately for the two sexes, a trend towards a quadratic relationship was detectable only for males. In both cases, more brain asymmetry, or a greater degree of linguistic lateralisation, was associated with higher T levels. For both praxis and language, associations with lateralisation were observed only for T concentrations and did not generalise to C. Therefore, hormonal relationships were specific to T.

One important limitation of the study presented in chapter 5 was the fact that linguistic lateralisation was assessed by means of neuropsychological testing. Neuropsychological tests infer lateralisation through performance differences between the two hemispheres. Thus, they measure lateralisation only indirectly and even though they are adequately reliable in estimating

laterality effects for group studies, they are not considered ideal for individual assessment of linguistic laterality (Krach et al., 2006). Moreover, chapter 5's study measured only adult T concentrations. Therefore, an investigation followed, in order to study whether the results presented in chapter 5 on the relationship between T and praxic and linguistic lateralisation can be replicated by means of the fTCD, using the Word Generation test for the assessment of linguistic lateralisation, a brain imaging technique that is more reliable than neuropsychological testing (chapter 6). Further to the fTCD, a number of behavioural tests were administered within this study (i.e., the Line Bisection, Drawing "H", Drawing a Head in Profile, Verbal Recall of Coin Head Orientation, and the Ambiguous Figures tests), which represent well-established differences between left- and right-handers (Martin and Jones, 1999b; Jewell and McCourt, 2000; Viggiano and Vannucci, 2002) and three postural lateral preferences were recorded (i.e., Arm Folding, Leg-Crossing, Finger-Clasping). The relationships of the behavioural tests and the lateral preferences to T concentrations were investigated. Moreover, in addition to the measurement of adult T levels, prenatal T levels were also measured, albeit indirectly, via a recently proposed somatic marker, the 2D:4D length ratio. Moreover, this study was an improvement compared to chapter 5's study as far as the control for circannual and circadian variations of T concentrations is concerned, in the following two ways: all testing was carried out in a period of one month and all participants gave saliva samples at the same times in the evening. The sample of the study included half of the male participants that had taken part in chapter 5's study.

Further support was provided for the finding that higher T concentrations are associated with a higher degree of linguistic lateralisation in adult males. A significant relationship was further detected between recall of the orientation of the Queen's head on British coins and T concentrations, with participants correctly recalling the Queen's head facing right having higher T concentrations

than participants recalling the Queen's head facing left. Therefore, people who exhibited behaviour typical of left-handers (remembering the head facing right) had higher T levels. No associations were found with C.

With regards to the 2D:4D length ratio, no associations were found between linguistic laterality and right or left 2D:4D length ratios. The only significant relationship for the 2D:4D length ratio was found between the right hand 2D:4D ratio and the rabbit/duck ambiguous figure, but results contradict the ones found for the orientation of the Queen's head test. In this case, those exhibiting behaviour typical of left-handers (recognizing the ambiguous figure by its right-facing image) had higher 2D:4D ratio, which is translated as lower prenatal T levels. Nevertheless, a number of recent studies (e.g., Koidou et al., 2006; Grouios et al., 2007; Ypsilanti et al., 2008) have claimed that the 2D:4D length ratio might not be as useful a marker as previously suggested. No relationships were detected between the three postural lateral preferences and either adult or prenatal hormonal levels.

Throughout the thesis, a number of interesting patterns seem to be emerging. The first pattern concerns the direction/degree dichotomy with regards to the sex differences in praxic and linguistic lateralisation. The meta-analysis showed in a robust manner that males have greater odds of being left-handed, as measured by hand preference tests. Findings presented in chapter 4, further showed that a sex difference in praxic laterality is also present when measured by hand skill tests (i.e., the Peg-Moving and the Tapping Speed tests) as well as by the QHPT (even though this holds true only for right-handers). Moreover, the results of the study presented in chapter 5 showed that males with lower T concentrations are more skilful with their right hand. Similarly, in chapter 6 it was shown that participants who exhibited behaviour typical of left-handers (remembering the Queen's head as facing right) have higher T levels. These findings all point to the same direction: that the defining characteristics of

males (biological sex or higher T concentrations) are associated with left hand preference or with the left hand being more skilful that the right hand. In other words they are associated with direction of laterality.

As far as linguistic laterality is concerned, a quadratic relationship between the VHLD test accuracy scores and T concentrations was detected (chapter 5). When analysing data separately for the two sexes, a trend towards a quadratic relationship was detectable only for males. This quadratic relationship was replicated in the male only sample of chapter 6 when measuring laterality with a new brain imaging technique, the fTCD, using the Word Generation test. In both cases, more brain asymmetry, or greater degree of linguistic lateralisation, was associated with higher T concentrations. Thus, in the case of brain organisation for language, the defining male characteristic of higher T concentration is associated with a higher degree of lateralisation.

These results provide support for the claim that asymmetry for praxic function could be relatively independent of asymmetry for linguistic function and that at the same time the relationship of T with asymmetry for praxis and language could be different if one considers the direction or the degree of that asymmetry (Gadea et al., 2003). It is here claimed that T has indeed independent effects on praxic and linguistic lateralisation, in such a way that when it comes to praxic lateralisation, direction of lateralisation is what is affected, whereas when it comes to linguistic lateralisation, degree is what is affected. More specifically, higher T concentrations (measured directly or inferred from the sex of the individual) are associated with left-handedness and with greater asymmetry of linguistic lateralisation. These results provide support for the sexual differentiation hypothesis for both praxic and linguistic lateralisation.

Another interesting pattern concerns the sex difference in hand skill between the two hands specifically for right-handers. The sex difference in

praxic laterality (as measured by the Peg-Moving test, the Tapping Speed test, and the QHPT) was shown to be larger for right-handed females who were found to be more skilful with the right hand compared to the left hand (or to prefer the right rather than the left hand for reaching actions) than right-handed males (chapter 4). It was then shown that males who have lower T concentrations are more skilful with their right hand (chapter 5). In other words, lower T concentrations (measured directly or inferred from the sex of the individual) exaggerate the difference in hand skill between the right and the left hand, in favour of the right (at least in right-handers). The fact that this difference was found only for right-handers, might be explained by left-handedness being rarely as complete as right-handedness (Inman 1924, Humphrey, 1951; Benton et al., 1962; Steenhuis and Bryden, 1989; Rigal, 1992) as well as by findings that right-handers tend to show greater variability in the skilled performance of the left hand compared to the skilled performance of the right hand (e.g., Peters and Durding, 1978, 1979; Todor et al., 1982; Carlier et al., 1993). Evidence on the tendency of left-handers to be significantly less lateralised and more widely dispersed that their right-handed counterparts on preference measures was also given in chapter 3, where it was shown that right-handers tend to give a “right” response in the place of an “either” response in a graded response format more often than left-handers give a “left” response in the place of an “either” one.

In addition to the above, a pattern can be seen in the discriminatory properties of the two manifestations of handedness: hand preference and hand skill. The findings of both chapters 4 and 5 support the notion that hand preference and relative hand skill have different properties, at least as far as sex differences are concerned. Relative hand skill tests were not only found to be more sensitive in capturing a sex difference, but they were further found to be associated with T concentrations. It would be interesting to note here that Annett’s RS model for handedness argues that genes determine hand skill

rather than hand preference (Annett, 1985). With regards to specific hand skill tests, the sex effect found in chapter 4 was slightly greater for the Peg-Moving test compared to the Tapping Speed test. Similarly, the relationship between T concentrations and the Peg-Moving test score was significant, whereas the same relationship failed to reach significance for the Tapping Speed test. Also in parallel with chapter's 4 findings, where no sex difference was found for the hand preference tests, no relationships were detected between hand preference and sex hormones either. The QHPT, which is a behavioural test of hand preference, seems to be a borderline case between preference and skill; no associations with T concentrations were detected, but the QHPT was found to be sensitive in detecting sex differences. The failure to detect significant relationships between the QHPT scores and T concentrations may be due to the fact that this test was shown to be less powerful in detecting a sex difference compared to the relative hand skill tests.

The differential power between the Peg-Moving and the Tapping Speed tests in detecting a sex difference and in showing significant associations with T concentrations, may be due to factors such as demands on visual guidance and movement type. Whereas the Peg-Moving test requires visual guidance and combines intrinsic and extrinsic hand movements, the Tapping speed test can be executed without visual guidance and requires only intrinsic movements. Moreover, the nature of the intrinsic movements involved in the two tests differs. The Peg-Moving test involves simple synergies and the Tapping Speed test reciprocal ones (Elliot and Connolly, 1984). With regards to the Dot-Filling test not being able to detect a sex difference in hand skill, this is possibly best explained by its proximity to writing, which gave the smallest male-to-female left-handedness odds ratio when compared to other instruments used to measure handedness the meta-analysis. Moreover, the Dot-Filling test is the test most influenced by training, skewing the outcome distribution in favour of the

preferred hand (Peters 1998). This skewing might be concealing an underlying sex difference, by means of a ceiling effect for both sexes.

The reasons why an association with T concentrations was found only for the VHLD test and not the CV-DL test are also of interest. With regards to the modality they engage to study lateralisation, the VHLD, like the Peg-Moving test, employs vision, whereas the CV-DL employs audition. Moreover, these two neuropsychological tests differ in terms of the paradigms used to study language. The VHLD uses word stimuli and the CV-DL uses consonant-vowel syllables, a kind of stimuli that has been criticised in terms of ecological validity (Keith et al., 1985). Nevertheless, the DL procedure further tends to underestimate the proportion of the right-handed population that is left hemisphere dominant for language perception (Segalowitz and Bryden, 1983), probably due to the fact that DL tasks are generally well performed, making differences between the two ears small (Bryden, 1988a).

Suggesting that the sex differences in praxic lateralisation are best explained by biological factors does not preclude the possibility that environmental factors could be moderating the size of male-to-female odds ratios in different populations. In fact, the findings of the meta-analysis provide evidence that social/cultural pressures do moderate the size of the sex differences in handedness. Firstly, the finding that the sex difference was larger in earlier than later studies can be explained by the fact that social pressures against the use of the left-hand were stronger in past years than they are nowadays (e.g., Searleman and Porac, 2003; Martin and Porac, 2007). Moreover, the sex difference was found to be larger in East Asian rather than Caucasian and African samples. Indeed, oriental cultures are known to be less tolerant towards left hand use than Western societies (Medland et al., 2004). The difference was finally found to be larger when handedness was assessed using methods other than the recording of writing hand (or, equivalently, writing

hand together with self-assessment). Writing hand receives more social pressure to favor the right hand compared to other activities measured in hand preference inventories, such as sporting activities, where there might even be encouragement to use the left hand, or bimanual activities such as sweeping with a broom, which are unlikely to be influenced by social pressures.

In order for the results to be explained by social pressures, though, females would have to be the recipients of stronger pressures or they would have to respond to these pressures differently and be more successful at switching over to the left hand (Harris, 1990). This differential level of success could be due to females either being generally more compliant than males (e.g., Gabriel and Gardner, 1999; Van Vugt et al., 2007) or to females being more capable of switching, due to inherent properties related to their greater motoric maturity or to their underlying neurobiological organisation (e.g., Boghi et al., 2006). With regards to sporting activities, the social pressure in favour of left-hand use is likely to be larger for males than females, as more males engage in sport. This is in line with the findings of chapter 3 that males give significantly more extreme responses when it comes to throwing, an action very common in a number of sporting activities.

7.2 Implications

The findings of the present thesis have a number of implications in terms of theory formation as well as of research design.

In terms of theory formation, the present findings provide support to theories proposing innate biological differences in order to explain the sex difference in praxic and linguistic lateralisation, namely genetic theories (e.g., McManus and Bryden, 1992; Jones and Martin, 2000; Annett, 2002), theories concerning the rate of somatic maturation (e.g., Maehara et al., 1988), and hormonal theories (e.g., Geschwind and Galaburda, 1987). With regards to

genetic theories, the modifier-gene hypothesis by McManus and Bryden (1992) as well as the single-gene recessive model of Jones and Martin (2000) receive greater support from the present findings than the RS theory does, as they make integral predictions for the occurrence of a sex difference in handedness. Between the two, the single-gene model, which suggests that a lower level of left-handedness in females than in males could reflect a lower phenotypic penetrance of the CC genotype, is preferred, as there are quantitative as well as qualitative implications for this model, even though the parameter values of this model need to be reconsidered. With regards to theories associating laterality with hormonal concentrations, it seems like the sexual differentiation hypothesis (Hines, 1984) receives support by the present findings for both praxic and linguistic lateralisation. According to this hypothesis higher levels of prenatal T are related to left-handedness and greater cerebral language asymmetry, following conversion to estradiol.

Another important implication of the present findings is that the direction of lateralisation may not be the most useful variable for the study of hemispheric lateralisation for language processes. The right/left dichotomy hides some important information conveyed by the continuous measurement inherent to the degree of lateralisation, with regards to the amount of interhemispheric share of information.

In terms of research design, it was shown that the original response scheme of the EHI is more sensitive to tracing sinistrality than its 5-point graded responses counterpart, by encouraging “either” responses. It was also shown that the rank order of participants in terms of their handedness was not significantly dependent upon which questionnaire was used or upon the response format employed. Moreover, it was demonstrated that left- and right-handers have different reactions towards different response formats of hand preference questionnaires. Since males tend to be more left-handed than

females, one should control both sex and handedness when doing research on the neurological and cognitive correlates of handedness or the sex differences in cognition.

Questionnaire type, response format, and handedness are all factors that affect the scores of the participants in hand preference questionnaires as well as in footedness and eyedness questionnaires in a significant manner. For right-handers the questionnaire and response format interaction was found to be greater than for left-handers. Moreover, for both handedness groups, and especially for right-handers, the difference in the mean scores produced by the different questionnaires was greater for the 5-point response format than for the binary response format. These findings point towards the need to reach a consensus amongst laterality researchers about the hand preference questionnaires and inventories that are employed. If questionnaire type and response format can artificially produce different laterality scores, and if they affect right-handers more than they affect left-handers, then comparisons between studies that have not employed the same laterality measurements can produce misleading conclusions. When it comes to hand skill tests, the effect of using different instruments was found to be greater for right-handers compared to left-handers, similarly to hand preference tests. Again, this suggests that comparing studies that have employed different hand skill instruments should be done with caution.

Furthermore, the present findings suggest that behavioural tests of handedness, and specifically the QHPT, the Peg-Moving test, and the Tapping Speed test, should be preferred when it comes to the study of sex differences in praxic lateralisation and their correlates. Amongst them, the Peg-Moving test was found to have the greatest power to detect sex differences followed by the Tapping Speed test and the QHPT, even though all three effect sizes are small. In practical terms though, it may be the case that the Tapping Speed test is

more convenient for use in large groups of participants: as long as each participant has his/her own tally-counter, the experimenter can just set the starting and finishing time (by saying “go” and “stop”) and the participants can make a note of the number of taps they have produced, as displayed on the counter. Nevertheless, it would be recommended that when doing research on handedness, one should provide information on the writing hand and the score of the participants on the EHI in addition to their score on any skill test, for the purposes of comparison between studies. Both writing hand and the EHI are quick and easy to record and administer and they are the most popular hand preference instruments used in the literature, providing a solid basis for comparisons.

7.3 Caveats and limitations

Some remarks with regards to the most important limitations of the present work need to be made. Firstly, it should be stressed that praxic lateralisation is only an indirect and developmentally labile index of anatomical asymmetry and linguistic laterality. Left-handers might have significantly less chances of being left-hemisphere dominant for language than right-handers, but the majority of left-handers still have left-hemisphere dependence of language functions.

With respect to the meta-analysis presented in chapter 2, it was limited by the fact that it did not include information on handedness derived from hand skill tests, but only included studies having assessed handedness in terms of hand preference. Moreover, it could not disentangle between degree and direction of handedness, as these two properties are confounded in studies which use statistical tests that are unable to differentiate between degree and direction, or that report just mean laterality scores across males and females. Another limitation of the meta-analysis comes from the nature of the moderating

variables analysis itself: the crucial characteristic of this analysis is the number of data sets reporting pertinent information and not the number of participants included (Hunter and Schmidt, 1990). Therefore, only large moderating effects could have reached significance given the number of the data sets.

Regarding the experimental work, measuring adult T concentrations limits what may be inferred regarding prenatal concentrations. Prenatal T concentrations were measured in the last study, albeit indirectly, by means of the 2D:4D length ratio, but this measure was not proven powerful enough to provide significant results for the present sample size (apart from an association with the ambiguous figure rabbit/duck which contradicted previous findings). With regards to the collection of saliva samples, it was not feasible to check whether any blood contamination existed below visibility levels.

Another potential limitation of the study is that females were tested only at menses and not re-tested at the mid-luteal phase. Testing females at menses might have provided the advantage of assuring homogeneity in the phase of the menstrual cycle for all participants without having to specifically measure progesterone levels. At the same time it may have hindered the power of the study to detect relationships of T levels with praxic and linguistic laterality.

Furthermore, only a few of the multiple specialised subcomponents of language were investigated within the present thesis. The CV-DL test measures primarily phonology, while the VHLD measures semantics and the Word Generation task measures language production. Other aspects of language, such as prosody, were not tested. Moreover, there is a debate on whether language can be treated as a separate mental faculty or if it should be approached as part of a more general cognitive system (Fodor, 1983) intertwined with prosody, memory, and attention (Knecht et al., 1996; Binder et al., 1997). For all the above reasons, the assessment of linguistic lateralisation based on only these three tests cannot be considered fully adequate for

elucidating the factors underlying the diversity in large-scale neural language organisation.

7.4 Future directions

There are many ways in which this work can be carried forward. For example, it would be interesting to perform a meta-analysis on the sex differences in handedness, as measured by hand skill tests. Moreover, it would be useful to include children in a future meta-analysis, in order for developmental effects to be investigated.

Future studies need to consider possible differences in brain lateralisation related to the menstrual cycle. It might be more fruitful to have a repeated measures design, whereby laterality will be assessed at both menses and the mid-luteal phase of the menstrual cycle. This might be informative with regards to the reasons why different studies have produced contradictory results to date. Further work on the relationships between hormonal levels and linguistic lateralisation as measured by brain imaging should extend the investigation to female participants. Moreover, the assessment of linguistic laterality could include a larger number of tests covering a wider range of language sub-components.

The present findings indicate that it may be of future interest to compare explicitly the role of handedness in influencing the performance of unimanual versus bimanual activities in the two sexes, as these kind of activities are subject to differential levels of social pressure. Moreover, writing and gesturing during speech should be compared to nonverbal actions in terms of the handedness scores they produce between the two sexes, since it has been suggested that they result from separate etiologies.

Theories on the different rate of somatic maturation were not investigated in this thesis. This kind of investigation would be very informative, as it would

add a developmental account to the study of the sex differences in praxic and linguistic lateralisation. It would be particularly interesting to study how hormonal effects are intertwined with the rate of somatic maturation. Longitudinal studies would moreover help disentangle the organisational from the activational effects of sex hormones.

7.5 Conclusions

Overall, the present thesis clearly demonstrates that the sex difference in praxic lateralisation is robust, it quantifies the difference in the magnitude of 1.23 for the ratio of male-to-female left-to-right handedness odds and it reveals three factors that moderate this magnitude: the way in which handedness is assessed, the year of publication of the study, and the ancestry of the participants. Moreover, it shows that the sex difference is not associated with a male tendency to avoid extreme responses in hand preference questionnaire. It is argued that – even though there is evidence that environmental factors exert moderating influences – the sex difference in handedness is underlined by innate biological differences between the two sexes, such as genetic, hormonal, and somatic maturation differences. Furthermore, it is shown that the most sensitive instruments for assessing the sex difference in praxic lateralisation are the Peg-Moving, the Tapping-Speed, and the QHPT tests. Lastly, higher concentrations of T are found to be associated with a praxic intrahemispheric organisation located at the right hemisphere and with a more symmetrical linguistic organisation, indicating greater interhemispheric share of information.

As a conclusion, it is argued that there is no single causative factor for the sex differences in laterality, but that the sex differences praxic and linguistic lateralisation are determined by multiple biological factors, with the sex difference in praxic laterality being further influenced by a number of environmental factors.

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Appendices

Appendix 2.1. Summary of the Studies Included in the Meta-Analysis

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Aggleton, J.P., Kentridge, R.W. & Good, J.M.M. (1994)	1	1,538 musicians	Writing hand	R-L	12.55	12.52	12.59	Data also reported from 10-item EHI
Aggleton, J.P. & Wood, C.J. (1990)	2	(a) 344 professional ten-pin bowling players (b) 363 undergraduates in a variety of subjects at the University of Durham	(a) Hand throwing a ten-pin bowl (information from official records) (b) As above (information by self-report)	(a) R-L (b) R-M-L (Mixed represents either hand)	7.85 11.02	9.92 8.04	6.57 14.63	-
Annett, M. (1973)	2	(a) 3644 students at the universities of Aberdeen & Hull and service recruits in samples described in Annett (1967,1970), and other similar samples	(a) and (b) Writing hand	(a) R-L (b) R-L	11.64 4.05	11.76 4.39	11.45 3.70	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		(b) 7288 parents of the above students						
Annett, M. (1979)	4	(a), (b) 804 students at the Open University (c) wives and husbands of the above (690 individuals) (d) parents of the above (1540 individuals)	(a) Writing hand (b) 12-item AHPQ (c) Report of writing hand by the wives and husbands (d) Filial report of writing hand	(a) R-L (b) R-nonR R: all right nonR: any left (c) R-L (d) R-L	7.59 36.44 8.41 6.17	6.55 32.75 12.73 6.35	8.60 40.05 4.62 5.99	Information on the handedness of siblings reported as well, but age was unknown, possibly under 16 years old
Annett, M. (1985)	4	(a) 642 Parents (b) 747 offspring (c) 224 tennis players in Wimbledon 1978 (d) 66 tennis champions 1947-1978	(a), (b) measure not reported (c), (d) hand holding the racket	(a) R-L (b) R-L (c) R-L (d) R-L	7.59 36.44 8.41 6.17	6.55 32.75 12.73 6.35	8.60 40.05 4.62 5.99	Data reported in Annett (2002) and Raymond et al. (1996)
Annett, M. (2002)	1	100 men and 100 women top ranking tennis players for November 1999 (ATP and WTA guides)	Playing hand	R-L	10.61	15.15	6.06	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Annett, M. (2007)	3	(a) 578 parents of schoolchildren (b) 1670 students at the University of Leicester (c) 3364 parents of the above students	(a) – (c) writing hand	R-L	13.32 11.02 10.85	14.88 10.97 12.19	11.76 11.03 9.51	Participants in the first two data sets are reported to have completed the AHPQ, but only information on writng hand is given in the article
Annett, M. & Kilshaw, D. (1982)	2	1550 students at Hull University, students in a girls school, undergraduates in Warwick University and Coventry (Lancaster) Polytechnic, A-level schoolchildren and teachers of mathematics in various Universities	(a) Writing hand (b) 8-item and 12-item AHPQ	(a) R-L R: all right (b) R-nonR nonR: any left	8.19 37.03	7.80 34.78	8.49 38.73	-
Ardila, A. & Rossellini, O. (2001)	1	6941 Colombians participating in a	Self-classification	R-M-L	4.51	4.99	4.21	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		large neuroepidemiological study						
Ashton, G.C. (1982)	3	3625 parents of nuclear families living in the environs of Honolulu in the period 1972-1976: (a) 2027 Europeans (b) 840 Japanese people (c) 758 other	Writing hand	(a)-(c) R-L	7.10 1.31 5.41	7.09 1.01 5.17	7.11 1.58 5.66	Data reported on hand usage as well (“which hand do you use the most?”)
Azémar, G. & Stein, J.F. (1994)	1	2490 athletes of fencing (champions 1979-1993)	Hand holding sword/foil	R-L	27.63	28.41	26.00	Data reported in Raymond et al. (1996)
Bakan, P. & Putnam, W. (1974)	1	400 undergraduate students at the University of Burnaby, British Columbia, Canada	Writing hand	R-L	12.25	18.54	8.43	-
Barut, C., Ozer, C.M., Sevinc, O., Gumus, M. & Yunten, Z.	1	633 Tuirkish participants	10-item EHI	5 groups, here R-M-L R: 20 to 100	15.63	18.95	11.72	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
(2007)				M: -75 to 15 L: -75 to -100				
Beckman, L. & Elston, R. (1962)	1	981 individuals from different parts of Sweden	-	R-L	5.50	5.28	5.73	-
Betancur, C., Velez, A., Cabanieu, G., LeMoal, M. & Neveu, P.J. (1990)	1	205 patients who consulted the radiology department	Modified version of the 10-item EHI	R-M-L R: LQ>70 M: LQ between 0-70 L: <70	9.76	9.68	9.82	The participants were controls to allergic patients
Birkett, P. (1981)	1	125 people drawn from schools, colleges and the general public in the Bolton area of Lancashire	10-item EHI	R-L R: LQ>0 L: LQ<0	41.60	38.89	43.66	
Briggs, G.G. & Nebes, R.D. (1975)	1	1599 undergraduate students at Duke University	12-item Briggs-Nebes modification of the AHPQ	R-M-L R: 9 to 24 M: -8 to 8 L: -24 to -9	9.13	8.90	9.38	-
Brito, G.N.O., Brito, L.S.O., Paumgartten, F.J.R. & Lins, M.F.C (1989)	4	959 faculty, staff and students from the Universidade Federal Fluminense, Niteroi,	10-item EHI	(a) R-L (whole group) R: LQ>0 L: LQ<0	6.88	8.49	5.33	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		Brazil and Staff from an engineering company and two elementary schools. Data also broken down in age groups (20-29, 30-39, 40+) for the R-M-L classification		(b)-(d) R-M-L R/L: all activities with the right/left hand M: mixed preferences	4.42 2.39 1.97	6.13 2.14 1.79	3.02 2.61 2.21	
Bryden, M.P. (1977)	1	1106 undergraduate students at the University of Columbia	Writing hand	R-L	10.76	12.10	9.05	1. Data also reported for self-classification 2. The subjects were also administered the Crovitz-Zener questionnaire and the EHI, but only mean scores for each question for M-F were given
Bryden, M.P. (1989)	1	794 undergraduate students at the	8 items from EHI	R-L R: LQ>0	8.94	11.08	7.39	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		University of Waterloo		L: LQ<0				
Bryden, P.J. & Roy, E.A. (2005)	1	153 undergraduate students from the University of Waterloo and Wilfrid Laurier University	Writing hand	R-L	11.11	17.02	8.49	-
Buchtel, H.A. & Rueckert, L. (1984)	1	740 undergraduate students from the University of Michigan	Selection of one of four figures showing a hand with pencil writing in four modes: right normal/ right inverted/ left normal/ left inverted	R-L	13.38	13.70	13.07	-
Cannon, M., Byrne, M. Cassidy, B., Larkin, C., Horgan, R., Sheppard, N.P. & O'Callaghan, E. (1995)	1	43 medical, secretarial and domestic staff members in a large rural psychiatric hospital and an outpatient clinic at an	10-item EHI	R-M-L R: LQ= +100 L: LQ= -100 M: the rest	6.98	4.76	9.09	The participants were controls to schizophrenics

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		urban community psychiatric centre						
Carriere, S. & Raymond, M. (2000)	1	246 inhabitants in the village of Nkong Meyos, among 27 households	Observation of which hand is used to hold the machete	R-L	8.13	9.02	7.08	Children are also included in the sample, but the age variable was not significant
Casey, M.B. & Brabeck, M.M. (1989)	1	433 undergraduates from two eastern USA Universities	10-item EHI	R-nonR R: LQ ≥ 40 nonR: LQ <40	25.87	26.89	25.48	-
Chamberlain, H.D. (1928)	1	4354 parents of male students at the Ohio State University	Writing hand (reported by the students)	R-L	3.56	4.18	2.94	The reporter's data were not included, as they were all male as well data on their sibling's handedness because their age was unknown
Chapman, D. & Walsh, R.J. (1973)	1	923 students and staff of the University of New South Wales who used the	Throwing a ball	R-M-L (Mixed: ambidextrous with regards to	6.52	6.89	6.19	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		Physical Education and Recreation Centre facilities		throwing hand)				
Chapman, L.J. & Chapman, J.P. (1987)	1	5825 college students at the University of Wisconsin	13-item questionnaire	R-M-L R: 13≤LQ≤17 M: 18≤LQ≤32 L: 33≤LQ≤39	9.05	9.78	8.32	-
Coren, S. (1989)	1	1896 students from the University of British Columbia	4-items for handedness from the Lateral Preference Inventory by Coren	R-L	9.49	10.37	8.84	Cut-off point not reported
Coren, S. (1993)	1	3307 volunteers recruited from the campus of the University of British Columbia in Vancouver, Canada	4-items for handedness from the Lateral Preference Inventory by Coren	R-L R: LQ>0 L: LQ≤0	10.28	11.78	9.21	-
Coren, S. (1995)	1	2596 parents of individuals residing in Vancouver	4-items for handedness from the Lateral Preference	R-L R: LQ>0 L: LQ≤0	9.05	9.78	8.32	The data on the handedness of the reporters and their siblings are

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
			Inventory by Coren					not broken down by sex
Coren, S. & Porac, C. (1979)	1	1758 residents of the Provins of British Columbia	Selection of one of four figures showing a hand with pencil writing in four modes: right normal/ right inverted/ left normal/ left inverted	R-L	10.86	11.35	10.46	-
Coren, S. & Porac, C. (1980)	2	(a) 2761 responders from two Canadian provinces, Quebec and British Columbia (b) 1410 general population of the Province of British Columbia	4-items for handedness from the Lateral Preference Inventory by Coren	(a) R-L R: LQ>0, L: LQ<0 (b) R-L, as above	10.94 11.13	11.45 12.43	10.49 9.92	-
Coren, S., Searleman, A., Porac, C. (1986)	1	1180 students at the University of Victoria and the University of British Columbia	4 items on handedness from Porac and Coren's Lateral	R-L R: LQ>0 L: LQ<0	10.17	12.85	8.42	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
			Preferences Inventory					
Cornell, E.R. & McManus, I.C. (1992)	1	266 students in the University College and Middlesex School of Medicine	Writing hand	R-L	10.53	7.75	13.71	-
Cosenza, R.M. & Mingoti, S.A. (1993)	2	16590 applicants to the Federal University of Minas Gerais (a) 1961 excepted applicants (b) 14629 rejected applicants	10-item EHI	(a) R-L R: LQ>0 L: LQ<0 (b) As above	9.48 7.88	10.96 8.88	7.82 7.14	-
Cosenza, R.M. & Mingoti, S.A. (1995)	1	15389 applicants for admission to the courses offered by the Federal University of Minas Gerais	10-item EHI	R-L R: LQ>0 L: LQ≤0	7.87	8.79	7.17	-
Cuff, N.B. (1931)	1	109 college students	8-item questionnaire	R-L R: 4 items or more with the	7.34	5.88	7.61	The paper reports data on children as well,

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				right hand L: the rest				not used here
Curt, F., deAgostini, M., Maccario, J. & Dellatolas, G (1995)	1	1609 parents of the children from 9 preschools of the Paris suburbs	12-item hand preference questionnaire	R-L R: LQ <20 L: LQ≥ 20	8.76	8.75	8.77	-
Dane, S. & Erzerumluoğlu, A. (2003)	1	326 handball players	10-item EHI	R-L R: LQ>0 L: LQ <0	17.18	19.38	15.06	-
Dargent-Paré. C., de Agostini, M., Meshbah, Mounir, Dellatolas, G. (1992)	5	(a) 652 Algerians, (b) 685 Greeks, (c) 701 Italians (d) 725 Spaniards (e) 2301 French people (mainly students and employees)	12-item questionnaire (items taken from Dellatolas et al. (1988)	(a) – (e): R-L R: LQ<20 L: LQ ≥20	5.67 6.28 7.28 6.48 9.04	5.45 6.68 8.37 8.00 8.50	5.88 5.79 4.52 4.86 9.48	-
De Agostini, M., Khamis, A.H., Ahui, A.M. & Dellatolas, G. (1997)	3	(a) 764 parents of secondary French-speaking schools in Abidjan (b) 755 undergraduates at4	(a) Filial report: "is your mother/father R-L-unknown?" (b) 10-item questionnaire	(a) R-L (b) R-L L: equal or greater than the mid interval scores were	7.07 5.03	9.16 5.04	4.97 5.03	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		universities in Khartoum, Sudan (c) the parents of the latter (1470)	(c) filial report "is your mother/father R-L-unknown?"	classified as left-handers (c) R-L	5.71	6.40	5.03	
DeLisi, L.E., Svetina, C., Razi, K., Shields, G., Wellman, N, & Crow, T.J. (2002)	1	288 unaffected members of families with schizophrenia or schizoaffective disorder	23-item questionnaire developed by Annett (1985)	R-M-L R: right-handed for all actions or for all but minor actions, M: write with right hand but use their left hand for four minor actions, or use their right hand for writing but left hand for any five items, or use their left hand for writing, but right hand for any other items.	5.48	6.55	3.19	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				L: left hand for writing and all primary items, but could use their right for any other items				
Demura, S., Tada, N., Matsuzawa, J., Mikami, H., Ohuchi, T., Shirane, H., Nagasawa, Y. & Uchiyama, M. (2006)	1	3557 people from 7 prefectures in Japan	10-item EHI	R-M-L R: LQ>0 M: LQ=0 L: LQ<0	4.99	6.18	3.33	Data also reported on each participant's dominant hand for various sports
Downey, J.E. (1927)	1	721 members of the American Psychological Association, scientists, professional men, college and high school students	5-item questionnaire	RRR/ RRL/ RLL/ RLR/ LLL/ LLR/ LRR/ LRL (here classified as R-L)	4.99	6.18	3.33	Data reported on a group of adult and juvenile delinquents, inmates of institutions for the feebleminded and insane and boys and girls in special classes for subnormal

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
								children, but not used here
Dronamraju, K.R. (1975)	2	(a) 431 tribal people of the state of Andhra Pradesh in south-eastern India (Koya Doras, Sugelis and Konda Reddis) (b) 86 non-Tribal (Hindus)	Hand used to hold a brush	(a) R-L (b) R-L	11.60 5.81	15.49 6.98	7.8 4.65	-
Elalmis, D.D. & Tan, Ü (2005)	1	22461 Turkish students, their siblings and their parents	Self-classification	R-M-L	7.59	7.96	7.19	-
Elias, L.J., Saucier, D.M. & Guylee, M.S. (2001)	1	541 undergraduate students at the University of Waterloo, Canada	Self-classification	R-L	9.80	14.53	8.96	-
Ellis, S.J., Ellis, P.J. & Marshall, E. (1988)	1	The register of the major group practice (general medical practitioner) in a small town in	10-item EHI	R-L R: LQ>0 L: LQ<0	7.30	7.79	6.87	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		Lancashire, UK (6577 participants)						
Fry, C.J. (1990)	2	(a) 366 upper division students (juniors, seniors and graduate students) enrolled at the Ohio State University (b) The parents of the above students (721 individuals)	(a) 10-item EHI (b) Filial report of writing hand	(a) R-L R: LQ>0 L: LQ<0 (b) R-L	14.48 11.79	15.64 11.70	12.90 11.88	Data on siblings' handedness, but excluded because age was not reported
Genetta-Wadley, A. & Swirsky-Sacchetti, T. (1990)	1	60 undergraduate students at Drexel University	12-item AHPQ	R-L L: pure left-handers R: the rest	6.67	10.00	3.33	Cut-off point not reported
Gilbert, A. N. & Wusocki, C.J. (1992)	1	1,177,507 subscribers to the National Geographic	Writing hand and throwing hand	R-nonR R: both write and throw with the right hand	11.08	12.60	9.90	-
Gladue, B.A. & Bailey, J.M. (1995)	1	149 individuals recruited via advertisement	10-item AHPQ	R - non R R: all right nonR: any left	32.21	35.53	28.77	The participants were controls to homosexuals
Götenstam, K.O.	2	60 students of	(a) Writing hand	(a) R-M-L	9.36	9.09	9.60	Percentages are

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
(1990)		architecture, School of Architecture at Trondheim Institute of Technology, 88 students of music at Trondheim Music Conservatory and the Department of music at the University of Trondheim, and 87 students from the general student group from Ringre High School	(b) 4-item inventory	(b) R-L	11.49	10.00	12.80	given when reported results on writing hand, adding up to 99.1% for males and 96.8% for females. It was therefore assumed that 0.9% of males and 3.2% of females used equally both hands for writing, making up the mixed category
Green, R. & Young, R. (2001)	1	284 undergraduate and graduate students	6-item questionnaire	R-M-L R: all tasked performed with the right hand M: one task not with the right hand	25.35	23.61	27.14	The participants are controls to transsexuals

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				L: two more tasks not with the right hand				
Grouios, G., Tsorbatzoudis, H., Alexandris, K. & Barkoukis, V. (2000)	2	(a) 1112 class A athletes from Northern Greece (b) 1187 non-sporting university students registered for social sciences, economic and law in the Aristotelian university of Thessaloniki	12-item Briggs-Nebes modification of AHPQ	(a) R-L (b) As above	14.84 9.10	15.92 10.11	13.67 7.80	-
Gunstad, J., Spitznagel, M.B., Luyster, F., Cohen, R.A. & Paul, R.H. (2007)	1	643 healthy community-dwelling individuals, from the Brain Resource International Database (BRID)	Computerised modification of the 10- item EHI	Left/Mixed, Moderately Right, Strongly right (Here: R-nonR)	16.48	16.61	16.36	-
Gur, R.E. & Gur, R.C. (1977)	1	200 workers and non-psychiatric patients at the Philadelphia General Hospital	23-item questionnaire (1974)	R-L (cut-off point was chosen on the basis of an	11.00	16.00	6.00	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				inspection of the distribution of scores)				
Halpern, D.F., Haviland, M.G. & Killian, C.D. (1988)	1	152,653 test-takers (first time) of the Medical College Admission Test (MAT)	Writing hand	R-L	11.63	12.60	10.40	-
Hannay, H.J., Ciaccia, P.J., Kerr, J.W., Barrett, D. (1990)	1	1185 undergraduate students at Auburn University	10-item questionnaire Varney & Benton (1975)	StrongR-Mixed-StrongL StrR-StrL: 9 or 10 questions answered right or left respectively the subject M: the rest	4.39	4.33	4.45	-
Harburg, E., Feldstein, A. & Papsdorf, J. (1978)	2	748 married couples (a) 735 Africans (b) 761 Whites	Self-classification	(a) R-L (b) As above	7.36 6.67	7.69 8.24	7.03 5.12	Data from survey interviews from a larger project conducted in

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
								Detroit in 1968-1969
Harburg, E., Roeper, P., Ozgoren, F. & Feldstein, M. (1981)	2	1153 residents of Tecumseh, Michigan	Selection of one of four figures showing a hand with pencil writing in four modes: right normal/ right inverted/ left normal/ left inverted	(a) R-L (18-39) (b) As above	13.21 6.57	14.39 7.69	12.33 5.49	-
Harris, L.J. & Gitterman, S.R. (1978)	1	356 faculty members listed in the faculty directory at Michigan State University (assistant professors or above)	12-item handedness questionnaire Briggs & Nebbes (1975)	R-L L: LQ<2 R: LQ≥2	7.30	7.26	7.69	8 additional female left-handers were added to provide more power to the results of the study, but are subtracted from the numbers reported here
Harvey, T.J. (1988)	1	398 undergraduate students at the	10-item EHI	R-L R: LQ>0	15.58	17.14	11.86	Data are also reported on 838

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		University of Bath		L: LQ≤0				5th year pupils as well as to 1000 6th year pupils, which were excluded from the study
Hatta, T. & Kawakamai, A. (2007	1	1700 Japanese students in two Universities and two junior Colleges	10-item Inventory	R-M-L R: "right hand" for more than 8 tasks L: "left hand" for more than 4 tasks M: the rest	4.82	6.19	4.23	-
Hatta, T. & Nakatsuka, Z. (1976)	1	1199 Individuals from several colleges and offices in Osaka, Japan	10-item inventory	R-L	3.09	4.30	2.25	Cut-off point not reported
Heim, A.W. & Watts, K.P. (1976)	2	(a) 398 students at 3 coeducational Colleges of Education	Writing hand	(a) R-L	11.56	16.51	9.69	Data on younger participants as well
		(b) 492 students of technical colleges		(b) As above	9.15	10.59	5.92	

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Hicks, R., Dusek, C., Larsen, F. & Pellegrini, R.J. (1980)	1	580 college students at the San Jose State University	12-item handedness questionnaire Briggs and Nebbes (1975)	R-L	11.21	11.28	11.15	Cut-off point not reported
Hicks, R.E. & Kinsbourne, M. (1976)	1	2202 biological parents of college students enrolled in psychology courses at the University of Texas at Austin and the State University of New York at Albany between 1973 and 1975	Filial report of writing hand	R-L	9.36	9.36	9.36	Information about the handedness of the students were also collected, but reported only in the form of laterality quotients
Hicks, R.A., Pellegrini, R.J. & Evans, E.A. (1978)	1	728 at San Jose State University	12-item Briggs-Nebes modification of the AHPQ	R-L R: LQ >9 L: LQ <-9	8.52	11.20	5.80	All ambidextrous participants were excluded from the sample
Holder, M.K. (1992)	1	314 psychology and anthropology students at Rutgers University and	Self-classification	R-M-L (Mixed represents participants	9.24	10.00	9.02	Unpublished M.Phil thesis

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		employees of computer-based information processing in Charlottesville, Virginia		who considered themselves ambidextrous				
Holtzen, D.W. (1994)	1	260 heterosexual parent members of the national support group Parents and Friends of Lesbians and Gays (PFLAG) + parents and siblings of self-identified GLC university students who attend their school's GLB support/social group	5 items from EHI	Left Handed Exclusively/ Left handed mostly/mixed handed/right handed mostly/right handed exclusively but here: R/M/L	7.31	4.88	8.43	The participants were controls to homosexuals
Holtzen, D.W. (2000)	1	1685 tennis players actively competing during 1999	Hand holding the racket	R-L	5.16	5.20	4.98	-
Hoogmartens, M.J. & Caubergh, M.A.A. (1987)	1	102 dental students, 10 nurses, 8 housewives, 4	4-items for handedness from the Lateral	R-L R: LQ>0 L: LQ≤0	9.38	11.54	7.89	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		medical doctors, 3 high school students, 1 medical analyst	Preference Inventory by Coren					
Hoosain, R. (1990)	1	556 undergraduates in the University of Hong Kong	10-item questionnaire	R-M-L R/L: overall preference for the right/left hand, M: either string or mild preference for the right hand for both writing and drawing while indicating an overall preference for the left hand in the remaining eight activities	1.62	2.73	0.89	-
Ida, Y. & Bryden, M.P. (1996)	2	(a) Undergraduate students from Japan (655) (b) Undergraduate	Writing hand	(a), (b) StrR-WeakR-Either-WeakL-StrL (here: R-L, no	1.37 8.55	1.80 9.80	0.93 7.73	Data on 65 other items as well, but no laterality quotient given

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		students from Canada (620)		either responses)				
Inglis, J. & Lawson, J.S. (1984)	1	1880 individuals comprising the standardisation population of the Wechsler Adult Intelligence Scale - Revised (1981)	3 items (self-classification, observation of writing hand and hand usage)	R-L	9.04	9.89	8.19	The cut-off point is not reported
Iwasaki, S., Kaiho, T. & Iseki, K. (1995)	1	1755 outpatients, staff of hospitals and private companies and students, visitors to a college academic exhibition	Writing hand	R-L	0.85	1.15	0.66	Data also reported in a 15-item inventory
Kauranen, K. & Vanharanta, H. (1996)	5	200 randomly selected individuals from the population of Oulu: 5 age groups: (a) 21-30	Self-classification	R-L for all groups	5.0	0.00	10.00	-
		(b) 31-40			12.50	15.00	10.00	
		(c) 41-50			10.00	5.00	15.00	
		(d) 51-60			5.00	10.00	0.00	
		(e) 61-70			2.50	5.00	0.00	

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Lansky, L.M., Feinstein, H. & Peterson, J.M. (1988)	4	2083 random probability sample of adult citizens living in the Cincinnati area (a) 888 Whites 18-39 yr. (b) 853 whites 40-80 yr. (c) 185 Africans 18-39 yr. (d) 157 Africans 40-80 yr.	Writing hand	R-L for all the groups	10.47 11.84 11.89 5.73	12.63 5.20 12.16 7.81	8.86 15.97 11.71 4.30	1. The classification by the authors was R/R mixed/L mixed/ L, using a 5-item questionnaire , (L: left hand for all 5 activities, L mixed: write with the left hand, but do any other activities with the right hand or write most of the time with the left hand, and corresponding categories for the R.) It was broken to R-L, thus using writing hand as the

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
								measure
Lee-Feldstein, A. & Harburg, E. (1982)	1	1153 residents of Tecumseh, Michigan	Selection of one of four figures showing a hand with pencil writing in four modes: right normal/right inverted/left normal/left inverted	R-L	10.32	11.24	9.55	-
Leiber, L. & Axelrod, S. (1981)	2	(a) 1766 undergraduate and medical students at the state University of New York at Buffalo (b) 711 faculty members at the state University of New York at Buffalo	Self-classification	(a) R-M-L (b) As above	10.48 8.30	12.00 9.06	9.01 5.11	-
Lester, D., Werlinen, N. & Heinle, N.H. (1982)	1	2168 individuals	-	R-L	7.66	10.90	6.21	

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Levander, M. & Schalling, D. (1988)	1	921 students in a junior college in a suburb north of Stockholm	Writing hand	R-M-L	8.79	7.91	9.88	The same participants were also classified with the Karolinska Hospital hand preference inventory (constructed by Schalling 1982,using 7 items from theEHI) as R-M-L
Lippa, R.A. (2003)	2	1056 students and staff at California State University, Fullerton	(a) Self-classification (b) 3-item questionnaire	(a) R-nonR R: mostly use right/ exclusively use right NonR: exclusively use left/mostly use left/equally use both	11.84	11.43	12.04	The participants were controls to homosexuals

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				(b) 5-point classification based on the 5 scale points used (here: R-M-L)	7.67	6.86	8.07	
Maehara, K., Negishi, N., Tsai, A., Iizuka, R., Otsuki, N., Suzuki, S., Takahashi, T. & Sumiyoshi, Y. (1988)	1	2459 students of a high school, a university and industrial workers	10-item EHI	R-NonR R: LQ>90	15.05	15.53	14.01	This study had 8693 subjects from 6 to 94 years old. Only reported here is the percentage given for the age group 25-40, since the total average could not be used, due to the age limitation
Marchant-Haycox, S.E., McManus, I.C. & Wilson, G.D. (1991)	1	396 individuals recruited at clinics for treatment of venereal disease, at hospices and clinics for AIDS	9-item inventory	R-L R: LQ>0 L: LQ<0	7.32	7.67	6.42	The participants are controls to homosexuals

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		patients in London and N.Y.						
Martin, W.L.B. & Porac, C. (2007)	1	1635 residents in Belém, Brazil	Self-classification	R-L	10.58	11.08	10.18	Participants also completed the Paraense Lateral Preference Inventory
Mascie-Taylor, C.G.N. (1980)	2	193 husband and wife pairs living in a Cambridge suburb	(a) Writing hand (b) 7-item questionnaire	(a) R-L (b) R-M-L R/L: all activities performed with one hand M: all other patterns of activity	8.03 6.08	8.81 7.06	7.25 5.21	The handedness of the offspring was also measured, but their data were not included, as they were probably below 16
Mascie-Taylor, C.G., MacLarno, A.M. & Lanigan, P.M. (1981)	1	141 Undergraduate students at the University of Cambridge	Writing hand	R-L	16.31	21.52	9.68	-
McFarland, K. & Anderson, J. (1980)	1	181 students at two Universities	Writing hand	StrR-WeakR-Either-WeakL-StrL (here: R-L)	6.08	7.06	5.21	Data on the other items of the EHI reported as well,

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				(no either responses)				but no LI given
McGee, M.G. (1976)	1	112 university students at the University of Minnesota, USA	7 items adapted from the AHPQ (1970)	R-L	16.96	28.26	9.09	Cut off point not reported
McGee, M.G. & Cozad, T. (1980)	1	1230 parents of students from the Universities of Minnesota & Texas	10 items form EHI	R-nonR (nonR: any left)	18.21	19.67	16.75	Also data on the students' and their siblings' data, but were not used, as the siblings' age was not reported
McKeever, W.F. & Rich, D.A. (1990)	1	1690 undergraduate students enrolled at Bowling Green State University and 1390 at Northern Arizona University	Writing hand	R-L	10.94	12.01	10.34	-
McManus, I.C. (1986)[1]	1	2028 students applying to medical school	Self-classification	R-L	10.36	10.04	10.74	Data reported in Sheddon and McManus (1993)
Merrell, D.J. (1957)	2	(a) 123 individuals	(a) Writing hand	R-L	4.07	4.17	3.92	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		(random unrelated group) (b) their parents (497 individuals)	(b) Writing hand (filial report - parents)	R-L	6.64	6.90	6.36	
Meszaros, S., Ferencz, V., Csupor, E., Mester, A., Hosszu, E., Toth, E. & Horvath, C. (2006)	1	150 people referred to the Department of Internal Medicine, Semmelweis University	Structured medical questionnaire	R-L (hand used for the majority of tasks)	27.33	31.82	25.47	-
Morley, R. & Caffrey, E.A. (1994)	2	3814 blood donors in the East Anglian Blood Transfusion Centre	(a) Writing hand (b) Self-classification	(a) R-either-L (b) R- nonR R: right-handed nonR: left-handed or able to use both	11.64 18.75	11.97 20.10	11.34 17.51	-
Mustanski, B.S., Bailey, J.M. & Kaspar, S. (2002)	1	382 undergraduates from Northwester University	Self-classification	R-M-L	9.95	10.17	9.76	The participants are controls to homosexuals
Nalçaci, E., Kalaycioğlu, C., Çiçek, M. & Genç, Y. (2001)	1	310 medical students	13-item questionnaire adapted from Chapman &	R-NonR R: 13≤LQ≤17, NonR: 18≤LQ≤39	28.71	36.31	19.72	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
			Chapman (1987)					
Newcombe, F. & Ratcliff, G. (1973)	1	823 individuals from the normal population of 9 Oxfordshire villages	7-item inventory	R-M-L R,L: uniform pattern for all activities M: the rest	3.16	3.67	2.66	-
Newcombe, F.G., Ratcliffe, G.G., Carrivick, P.J., Hiorns, R.W., Harrison, G.A. & Gibson, J.B (1975)	1	928 people living in a cluster of Oxfordshire villages	7-item questionnaire	R, L, R/l, R/E, L/E, R/L/E (here: R-M-L R: R and R/E M: R/L and R/L/E L: L and L/E)	4.96	5.84	4.08	R: right hand preferred for all items L: left hand preferred for all items R/L: right hand and left hand, each preferred for at least one item, but no either hand responses R/E: right-hand and either hand, but no left-hand responses L/E: left-hand

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
								and either-hand but no right-hand responses R/L/E: right-hand, left-hand, and either – hand, each reported for at least one item
Obrutz, J.E., Dalby, P.R., Boliek, C.A. & Cannon, G.E. (1992)	1	318 university students	The first factor of the Waterloo Handedness Questionnaire (14 items)	R-L R: LQ>0 L: LQ<0	9.12	11.76	8.15	The participants were controls to learning-disabled adults
Ofte, S.H. (2002)	1	393 students at the University of Bergen, Norway	5-item questionnaire	R-L (ambidextrous subjects were so few that they were omitted from the analysis)	13.99	13.73	14.17	-
Oldfield, R.C. (1971)	1	1109 undergraduates of psychology in several English and	10-item EHI	R-L R: LQ>0 L: LQ<0	7.39	10.00	5.92	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		Scottish Universities						
Overby, L.A. (1994)	1	963 undergraduate students enrolled in introductory psychology classes at Texas Tech University	Self-classification	R-M-L	8.10	8.43	7.84	The participants are controls to college students who obtained elevated scores on the BDI ("dysphoric")
Perelle, I.B. & Ehrman, L. (1983)	1	2404 individuals recruited by mail survey	13-item questionnaire	Strong R/ Moderate R/ Mixed/ Moderate L/ Strong L (here classified as R-M-L)	20.01	20.38	19.56	-
Perelle, I.B. & Ehrman, L. (1994)	2	(a) 10781 individuals that ranged from labourer and other blue-collar jobs to highly professional categories (b) their parents (21258 individuals)	(a) Writing hand (b) Writing hand (filial report)	R-L R-L	9.44 5.73	10.59 5.71	8.49 5.75	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Peters, M., Petrie, B., Oddie, D. (1981)	1	365 undergraduate university students at the University of Guelph, Canada	4-item questionnaire	R-NonR R: all items R	11.78	12.31	11.49	-
Peters,M.Reimers, S. & Manning, J.T. (2006)	1	164,230 internet users	Writing hand	5-point classification, here: R-M-L R: right always +mostly right M: either hand L: left always + mostly left	11.68	12.66	10.50	-
Plato, C.C., Fox, K.M. & Garruto, R.M. (1984)	2	705 people who participated in the Baltimore Longitudinal Study of Aging	(a) Writing hand (b) 10-item inventory	(a) R-L (b) R-M-L R, L: uniform pattern for all activities M: the rest	5.96 4.82	6.94 6.07	4.10 2.46	Data also reported on self-classification (R-L)
Porac, C., Coren, S. & Searleman, A. (1983)	1	450 couples living in the province of British Columbia	Writing hand	R-L	7.11	7.56	6.67	Also data from the handedness of their children is available (R-L), but the age in not reported

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Porac, C. (1993)	4	632 Members of the secretarial maintenance and administrative staff of the University of Victoria and community members recruited at temporary research stations established in public shopping areas (a) < 30 yr. (b) 30-45 yr. (c) 46-60 yr. (d) >60 yr.	6-items questionnaire	R-L <3:R 3-5:L (including both ambi-handed and left-handed participants) (under 30 yr.)	11.11 15.52 7.09 2.15	8.16 16.67 10.20 4.76	12.21 14.94 5.13 0.00	-
Porfert, A.R. & Rosenfield, D.B. (1978)	1	2107 students at the University of Massachusetts	Shot questionnaire	R-nonR	14.29	14.56	13.96	
Raymond, M., Pontier, D., Dufour, A.B. & Moller, A.P (1996)	3	(a) 350 sporting students registered for "sport sciences" in Lyon I University in France	(a) Writing hand (students) (b) hand holding discus, javelin, shott put or racket	(a)-(c) R-L	15.71 13.84 22.22	16.35 16.42 20.00	14.79 11.19 25.00	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		(b) 50 discus, javelin and shott put champions 1995/ 100 male and female top 100 tennis players in 1994/ 292 table tennis players, world ranking, top 146, 1994 (c) 36 table tennis players, Danish elite senior	(athletes) (c) hand holding racket (Danish tennis players)					
Reiss, M & Reiss, G. (1997)	1	936 medical students at Hall University	4 items from Porac & Coren's (1981) inventory	R-nonR R: LQ>0 nonR: LQ≤0	8.87	11.26	6.05	-
Reiss, M & Reiss, G. (1998)	1	1223 medical students at Halle University	Self-classification	R-M-L	7.44	7.91	7.05	Data also on 10-item EHI (R-M-L)
Rife, D.C. (1940)	2	(a) 2178 students at the Ohio State + (b) their parents (1374 individuals)	10-item questionnaire	(a) R-nonR nonR=left preference for any of the 10 items	8.77	9.59	7.59	It is not known how many are the students and how many the siblings
				(b) As above	5.24	5.39	5.09	

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Risch, N. & Pringle, G. (1985)	2	(a) 4263 college students during the period 1979 to 1981 at New York University and siblings (b) parents of the above students (3128 individuals)	(a) 10-item EHI + self classification (and classification by siblings) as R-M-L (b) filial report as R-M-L	(a) R-L (all the M where classified as R) (b) R-L (all the M where classified as R)	12.46 9.81	13.05 12.34	11.86 7.29	1. Among the participants it is not clear who is the student i.e. the reporter and who is a siblings 2. Cut-off points were not reported
Rosenstein, L.D. & Bigler, E.D. (1987)	1	50 students in the University of Texas at Austin	10-item EHI	R-L R: LQ>0 L: LQ<0)	6.00	7.14	5.56	The participants were controls to homosexuals
Sakano, N. & Pickenhain, L. (1985)	2	(a) 998 students from 6 Japanese Universities (b) 690 students from the Karl-Marx-Universität Leipzig	5 items from the EHI	(a), (b) R-M-L R: 80<LQ<100 M: 0<LQ<60 L: -100<LQ<-20	3.81 4.20	5.26 7.66	2.84 2.42	It is not clear how the subjects scoring 60-80 or (-20)-0 are classified; possibly they are excluded from the sample
Salmaso, D. & Longoni, A.M. (1985)	1	1694 students in various high schools	20-item EHI	R-L R: Laterality	6.61	6.76	6.41	The cut-off point was arbitrarily

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		and Universities		class >5 L: Laterality Class ≤5)				chosen by the authors
Sanders, B., Wilson, J.R. & Vandenberg, S.G. (1982)	6	(a) 341 European parents (b) 224 European offspring (c) 143 Japanese parents (d) 78 Japanese offspring (e) 55 Chinese parents (f) 38 Chinese offspring	Hand preference questionnaire	(a) – (e) R-M-L 0-4:L 5-16: M 17-18:R	6.45 6.70 2.80 3.85 7.27 2.63	5.78 7.27 4.48 4.17 6.90 0	7.14 6.14 1.32 3.70 7.69 4.76	-
Saunders, D.A. & Campbell, A. (1985)	2	372 Howard university students (USA + Caribbean students; some of unknown origin were also added to the total sample)	10-item EHI	(a) R-L R: LQ>0 L: LQ<0 (b) R-M-L R: LQ ≥ 7 M: -6≤LQ ≤ 6 L: LQ ≤ -7	12.10 10.75	17.89 15.45	9.24 8.43	-
Schachter, S.C., Ransil, B.J. &	1	1117 randomly selected professionals	10-item EHI	R-NonR R: LQ≤70: non-	25.87	27.05	15.97	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Geschwind, N. (1987)				R: LQ>70				
Searleman, A. Tweedy, J. & Springer, S.P. (1979)	1	847 undergraduates at Stony Brook	14-item modified Crovitz & Zener (1962) handedness index	R-M-L	13.46	13.79	13.26	The cut-off point used to discriminate R from M from L is not reported
Searleman, A., Porac, C. & Coren, S. (1984)	1	3709 undergraduates at the University of Victoria and the University of British Columbia	4-items for handedness from the Lateral Preference Inventory by Coren	R-L R: LQ>0 L: LQ<0	10.78	12.37	8.73	-
Searleman, A. & Fugagli, A.K. (1987)	1	277 Individuals responding to advertisements placed around the campus of St Lawrence University Canton, New York	Writing hand	R-L	12.64	14.73	10.81	1. The participants were controls to people with diabetes, Crohn's disease and ulcerative colitis 2. A 7-item questionnaire was also administered to assess strength of

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
								hand preference
Segal, N.L. (1984)	1	1577 high school and college seniors and professional students appearing for one of the standardised examinations e.g., GRE, MCAT	Writing hand	R-L	9.58	9.99	8.98	-
Shan-Ming, Y., Flor, Henry, P., Dayi, C., Tiangi, Li, Shuguang, Q. & Zenxiang, M. (1985)	2	432 hospital staff and workers and administrative staff from neighbouring factories (a) 16-25 yr. (b) 26-73 yr.	10-item demonstration	(a), (b) R-NonR nonR: any left	 6.47 7.36	 8.82 8.16	 4.04 6.77	The participants are controls to schizophrenics
Sherman, J. (1979)	1	98 11th grade students	14-item Crovitz & Zener questionnaire (1962)	R-NonR R: 14-40 NonR: 40-70	37.76	49.09	23.26	-
Shettel-Neuber, J. & O'Reilly, J. (1983)	1	218 parents of full-time faculty members in the architecture college art	Filial report	R-L-ambidextrous	7.34	7.34	7.34	Data are also reported on the faculty members, but not broken

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		department, law college & psychology department at the University of Arizona						down by sex
Shimizu, A. & Endo, M. (1983)	1	4282 students at five senior high senior high schools in the Toyama Prefecture	13-item questionnaire	R-M-L R: LQ ≤-13 M: -12≤LQ ≤7 L: LQ ≥8	3.20	4.03	2.36	-
Singh, M. & Bryden, M.P. (1994)	1	729 students at state and private schools in Meerut, India; young adults that were undergraduates and graduate students at several local colleges + some family members of some responders	the first factor from the 59-item version of the waterloo Handedness Questionnaire (10-items)	R-L	8.37	10.79	6.87	-
Smith, J. (1987)|	1	350 individuals, randomly selected from Paddington and King's Cross railway stations (presumed to be representative	10-item EHI	R-L R: LQ>0 L: LQ<0)	8.86	10.98	6.99	The participants were controls to allergic patients, matched for age and sex

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
		of the general population of England)						
Spiegler, B.J. & Yeni-Komshian, G.H. (1983)	2	(a) 1816 undergraduates at the University of Maryland (b) their parents (3632 individuals)	(a) Writing hand (b) Writing hand (filial report)	(a) R-L (either responses were grouped with left) (b) As above	13.77 9.20	15.19 10.19	12.62 8.20	-
Tan, U. (1986)	1	266 students at Atatürk University	12-item AHPQ	4.89	4.89	7.51	0.00	The threshold for R-M-L discrimination is not reported
Tan, Ü. (1988)	1	1100 students in the faculties of nursery, dentistry and medicine at Atatürk University	Turkish adaptation of the EHI	R-M-L R: 0.5 and 1.0 SD L: -2.5 SD M: -2.0 to -0.5 SD	3.36	3.07	4.00	-
Tapley, S.M. & Bryden, M.P. (1985)	1	1511 undergraduate students at the University of Waterloo, Canada	8-item questionnaire	R-L	10.52	11.50	9.71	The threshold for R-L discrimination is not reported

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
Teng, E.L., Lee, P-H. & Yang, K.-S. (1979)	1	2041 students at the several universities of high academic standard	12-item EHI	R-L R: LQ>0 L: LQ<0	4.46	5.95	2.95	Another 2102 subjects were tested, but their mean age was 11 yr., so they were excluded. The percentages of handedness though, have been calculated for the whole sample, but no significant differences were reported in the school and university sample
Thompson, A.L. & Marsh, J.F. (1976)	1	Urban adult stratified probability sample (Los Angeles County) -1299 individuals	4-item questionnaire	Consistent R-M-consistent L consistent R: if the subject considered themselves	37.11	41.26	32.70	-

Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
				right handed, wrote with their right hand, had never had their handedness switched and said they performed no skilled uni-manual tasks better with their left hand/ consistent L: accordingly M: the rest				
Wolf, P.A., D'Agostino, R.B. & Cobb, J. (1991)	1	2,088 participants from the Framingham Study cohort at biennial examinations 14 and 15 in 1976 and 1978	Interview	R-L (ambidextrous participants grouped with left-handed)	9.00	9.78	8.45	-
Wood, C.J. & Aggleton, J.P. (1989)	1	(a) 752 professional tennis players	which hand is used to hold a	R-M-L	12.1	12.2	10.7	-

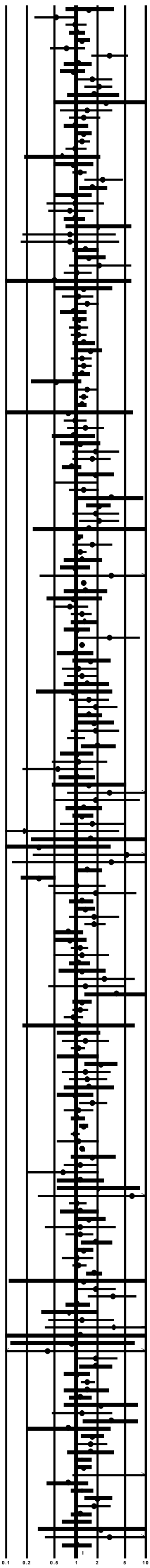
Study	Data sets	Participants	Handedness instrument	Classification of handedness	% LH Total	% LH males	% LH females	Comments
			racket					
Wood, C.J. & Aggleton, J.P. (1991)	3	(a) 257 architects working in architectural firms in London and Newcastle/ (b) 103 architectural students/ (c) 8 80 students at the University of Durham	10-item EHI	(a)-(c): R-L R: LQ>0 L: LQ<0) (architects)	9.73 9.71 11.59	10.17 11.54 11.93	4.76 4.00 11.08	-

[1]Unpublished data set reported in Sheddon, B.M. & McManus, I.C. (1993). The incidence of left-handedness: a meta-analysis.

Unpublished manuscript

Appendix 2.2 Forest plot of the male-to-female odds ratios for the total left-handedness (total) comparison. In the plot the 95% confidence interval for each study is represented by a horizontal line and the point estimate is represented by a circle. The confidence intervals for totals are represented by a diamond shape at the bottom of the plot.

Study name	Odds ratio	Lower limit	Upper limit	Z-Value	p-Value
Aggleton 1990a	1.566	0.712	3.445	1.115	0.265
Aggleton 1990b	0.510	0.261	0.996	-1.970	0.049
Aggleton 1994	0.994	0.724	1.364	-0.039	0.969
Annett 1973a	1.031	0.838	1.267	0.286	0.775
Annett 1973b	1.194	0.945	1.508	1.484	0.138
Annett 1979a	0.745	0.440	1.262	-1.095	0.274
Annett 1979b	3.013	1.675	5.417	3.684	0.000
Annett 1979c	1.063	0.702	1.610	0.289	0.773
Annett 1982	0.911	0.630	1.317	-0.496	0.620
Annett 1985a	1.735	0.947	3.181	1.783	0.075
Annett 1985b	2.115	1.351	3.311	3.277	0.001
Annett 1985c	1.790	0.776	4.129	1.365	0.172
Annett 1985d	2.768	0.497	15.420	1.162	0.245
Annett 2002	1.428	0.621	3.284	0.838	0.402
Annett 2007a	1.311	0.809	2.124	1.099	0.272
Annett 2007b	0.993	0.690	1.430	-0.037	0.971
Annett 2007c	1.320	1.061	1.643	2.489	0.013
Ardila 2001	1.196	0.951	1.504	1.527	0.127
Ashton 1982a	0.997	0.710	1.399	-0.017	0.986
Ashton 1982b	0.634	0.184	2.182	-0.723	0.470
Ashton 1982c	0.903	0.484	1.705	-0.300	0.765
Azemar 1994	1.130	0.934	1.366	1.260	0.208
Bakan 1974	2.472	1.347	4.534	2.923	0.003
Barut 2007	1.760	1.125	2.755	2.473	0.013
Beckman 1962	0.919	0.530	1.591	-0.303	0.762
Betancur 1990	0.984	0.389	2.487	-0.035	0.972
Birkett 1981	0.821	0.399	1.688	-0.536	0.592
Briggs 1975	0.945	0.672	1.328	-0.326	0.744
Brito 1989a	2.102	0.747	5.913	1.408	0.159
Brito 1989b	0.816	0.179	3.710	-0.264	0.792
Brito 1989c	0.806	0.160	4.059	-0.261	0.794
Bryden 1977	1.382	0.933	2.047	1.616	0.106
Bryden 1989	1.561	0.958	2.544	1.786	0.074
Bryden 2005	2.211	0.795	6.145	1.521	0.128
Buchtel 1984	1.055	0.692	1.613	0.252	0.801
Cannon 1995	0.500	0.042	5.966	-0.548	0.584
Carriere 2000	1.302	0.513	3.306	0.554	0.579
Casey 1989	1.076	0.667	1.735	0.300	0.764
Chamberlain 1928	1.440	1.040	1.994	2.197	0.028
Chapman 1973	0.918	0.606	1.392	-0.401	0.688
Chapman 1987	1.122	0.912	1.382	1.088	0.276
Coren 1979	1.095	0.811	1.480	0.595	0.552
Coren 1980	1.103	0.868	1.401	0.801	0.423
Coren 1980b	1.289	0.924	1.798	1.494	0.135
Coren 1986	1.604	1.099	2.343	2.447	0.014
Coren 1989	1.193	0.877	1.624	1.124	0.261
Coren 1993	1.316	1.051	1.648	2.392	0.017
Coren 1995	1.195	0.913	1.564	1.298	0.194
Correll 1992	0.529	0.237	1.177	-1.552	0.118
Cosenza 1993a	1.452	1.065	1.978	2.361	0.018
Cosenza 1993b	1.268	1.124	1.430	3.859	0.000
Cosenza 1995	1.249	1.110	1.404	3.703	0.000
Cuff 1931	0.759	0.087	6.596	-0.250	0.803
Curt 1995	0.997	0.706	1.409	-0.016	0.987
Dane 2003	1.355	0.760	2.417	1.030	0.303
Dargent-Pare 1992a	0.922	0.474	1.794	-0.239	0.811
Dargent-Pare 1992b	1.165	0.624	2.179	0.481	0.630
Dargent-Pare 1992c	1.928	0.920	4.038	1.739	0.082
Dargent-Pare 1992d	1.703	0.922	3.147	1.701	0.089
Dargent-Pare 1992e	0.887	0.665	1.184	-0.814	0.416
De Agostini 1997a	1.927	1.082	3.433	2.226	0.026
De Agostini 1997b	1.002	0.521	1.926	0.006	0.995
De Agostini 1997c	1.292	0.830	2.014	1.134	0.257
De Lis 2002	3.154	1.094	9.094	2.126	0.033
Demura 2006	2.125	1.469	3.073	4.004	0.000
Downey 1927	1.909	0.906	4.020	1.701	0.089
Dronamraju 1975a	2.168	1.168	4.024	2.451	0.014
Dronamraju 1975b	1.538	0.244	9.695	0.458	0.647
Elalmis 2005	1.116	1.011	1.232	2.175	0.030
Elias 2001	1.727	0.936	3.187	1.747	0.081
Ellis 1998	1.144	0.950	1.378	1.419	0.155
Fry 1990a	1.251	0.688	2.277	0.734	0.463
Fry 1990b	0.983	0.625	1.546	-0.075	0.940
Geneta-Wadley 1990	3.222	0.316	32.889	0.987	0.324
Gilbert 1992	1.312	1.297	1.327	46.194	0.000
Gladue 1995	1.364	0.684	2.723	0.881	0.378
Gotenstam 1990 2	0.942	0.390	2.273	-0.134	0.894
Green 2001	0.830	0.486	1.417	-0.684	0.494
Grouios 2000a	1.195	0.857	1.667	1.052	0.293
Grouios 2000b	1.330	0.888	1.990	1.385	0.166
Gunstad 2007	1.019	0.672	1.545	0.088	0.930
Gur 1977	2.984	1.116	7.978	2.179	0.029
Halpern 1998	1.242	1.203	1.282	13.291	0.000
Harnay 1990	0.971	0.557	1.694	-0.103	0.918
Harburg 1978a	1.664	0.919	3.013	1.681	0.093
Harburg 1978b	1.102	0.639	1.899	0.349	0.727
Harburg 1981a	1.195	0.758	1.884	0.766	0.444
Harburg 1981b	1.435	0.703	2.929	0.991	0.322
Harris 1978	0.939	0.268	3.283	-0.099	0.921
Harvey 1988	1.537	0.811	2.911	1.319	0.187
Hatta 1976	1.953	1.009	3.783	1.986	0.047
Hatta 2007	1.495	0.947	2.360	1.728	0.084
Heim 1976a	1.844	0.974	3.491	1.878	0.060
Heim 1976b	1.882	0.883	4.011	1.637	0.102
Hicks 1976	1.000	0.751	1.332	0.000	1.000
Hicks 1978	2.048	1.185	3.542	2.567	0.010
Hicks 1980	1.014	0.603	1.704	0.053	0.958
Hobler 1992	1.121	0.458	2.745	0.250	0.802
Hotzen 1994	0.557	0.179	1.735	-1.009	0.313
Hotzen 2000	1.046	0.582	1.881	0.150	0.881
Hoogmartens 1987	1.522	0.462	5.008	0.691	0.490
Hoosain 1990	3.112	0.770	12.576	1.593	0.111
Ida 1996a	1.951	0.484	7.868	0.939	0.348
Ida 1996b	1.296	0.735	2.283	0.896	0.370
Ingls 1984	1.231	0.897	1.689	1.285	0.199
Iwasaki 1995	1.748	0.631	4.841	1.074	0.283
Kauranen 1996a	0.180	0.008	4.009	-1.082	0.279
Kauranen 1996b	1.588	0.236	10.704	0.475	0.635
Kauranen 1996c	0.298	0.028	3.146	-1.007	0.314
Kauranen 1996d	5.541	0.249	123.079	1.082	0.279
Kauranen 1996e	3.154	0.121	82.165	0.691	0.490
Lansky 1988a	1.488	0.967	2.288	1.808	0.071
Lansky 1988b	0.289	0.168	0.496	-4.502	0.000
Lansky 1988c	1.044	0.422	2.582	0.093	0.926
Lansky 1988d	1.886	0.486	7.312	0.917	0.359
Lee-Feldstein 1982	1.199	0.820	1.752	0.935	0.350
Leiber 1981a	1.377	1.013	1.871	2.042	0.041
Leiber 1981b	1.850	0.821	4.168	1.485	0.138
Lester 1982	1.847	1.340	2.547	3.746	0.000
Levander 1988	0.783	0.496	1.236	-1.051	0.293
Lippa 2003	0.838	0.511	1.375	-0.699	0.485
Maehara 1988	1.128	0.886	1.437	0.978	0.328
Marchant-Haycox 1991	1.210	0.501	2.918	0.424	0.672
Martin 2007	1.100	0.802	1.509	0.591	0.555
Mascie Taylor 1980	1.235	0.591	2.582	0.561	0.575
Mascie Taylor 1981	2.559	0.943	6.945	1.845	0.065
McFarland 1980	1.382	0.406	4.703	0.518	0.604
McGee 1976	3.939	1.370	11.331	2.543	0.011
McGee 1980	1.218	0.911	1.628	1.329	0.184
McKeever 1990	1.184	0.939	1.492	1.427	0.154
McManus 1986	0.927	0.697	1.235	-0.516	0.606
Merrell 1957a	1.065	0.172	6.616	0.068	0.946
Merrell 1957b	1.091	0.537	2.218	0.242	0.809
Meszaros 2006	1.365	0.632	2.950	0.793	0.428
Morley 1994	1.063	0.872	1.296	0.608	0.543
Mustanski 2002	1.047	0.535	2.049	0.135	0.893
Nalbaci 2001	2.321	1.381	3.902	3.177	0.001
Newcombe 1973	1.395	0.633	3.074	0.825	0.409
Newcombe 1975	1.460	0.800	2.665	1.234	0.217
Obrutz 1992	1.502	0.658	3.375	0.984	0.325
Offe 2002	0.964	0.536	1.732	-0.123	0.902
Oldfield 1971	1.765	1.123	2.772	2.465	0.014
Overby 1994	1.083	0.681	1.723	0.336	0.737
Perelle 1983	1.053	0.861	1.287	0.501	0.616
Perelle 1994a	1.277	1.122	1.453	3.706	0.000
Perelle 1994b	0.993	0.885	1.115	-0.119	0.905
Peters 1981	1.081	0.559	2.090	0.232	0.816
Peters 2006	1.236	1.199	1.274	13.573	0.000
Plato 1984	1.745	0.843	3.614	1.500	0.134
Porac 1983	1.144	0.688	1.904	0.518	0.604
Porac 1993a	0.639	0.203	2.015	-0.765	0.445
Porac 1993b	1.139	0.542	2.393	0.344	0.731
Porac 1993c	2.102	0.536	8.246	1.056	0.287
Porac 1993d	6.358	0.297	136.163	1.183	0.237
Porfert 1978	1.050	0.822	1.343	0.393	0.694
Raymond 1996a	1.126	0.623	2.034	0.393	0.694
Raymond 1996b	1.559	0.949	2.561	1.753	0.080
Raymond 1996c	1.157	0.367	3.649	0.249	0.803
Reiss 1997	1.134	0.739	1.738	0.575	0.565
Reiss 1998	1.973	1.217	3.197	2.757	0.006
Rife 1940a	1.292	0.948	1.761	1.625	0.104
Rife 1940b	1.060	0.660	1.705	0.242	0.809
Risch 1985a	1.115	0.930	1.338	1.176	0.240
Risch 1985b	1.791	1.404	2.283	4.698	0.000
Rosenstein 1987	1.306	0.109	15.679	0.212	0.832
Sakano 1985a	1.902	0.991	3.652	1.931	0.053
Sakano 1985b	3.348	1.554	7.213	3.086	0.002
Salmaso 1985	1.059	0.718	1.561	0.289	0.773
Sanders 1982a	0.798	0.335	1.899	-0.511	0.609
Sanders 1982b	1.199	0.420	3.426	0.339	0.735
Sanders 1982c	3.516	0.357	34.634	1.077	0.281
Sanders 1982d	1.130	0.098	13.101	0.098	0.922
Sanders 1982e	0.889	0.116	6.806	-0.113	0.910
Sanders 1982f	0.390	0.015	10.208	-0.565	0.572
Saunders 1985	1.984	1.023	3.847	2.026	0.043
Schachter 1987	1.952	1.172	3.251	2.570	0.010
Searleman 1979	1.047	0.698	1.571	0.221	0.825
Searleman 1984	1.476	1.189	1.832	3.525	0.000
Searleman 1987	1.425	0.700	2.903	0.976	0.329
Segal 1984	1.125	0.797	1.588	0.671	0.502
Shan-Ming 1985a	2.298	0.684	7.723	1.346	0.178
Shan-Ming 1985b	1.225	0.455	3.297	0.401	0.688
Sherman 1979	3.182	1.316	7.696	2.569	0.010
Shettel-Neuber 1983	0.792	0.207	3.034	-0.340	0.734
Shmizu 1983	1.741	1.223	2.478	3.077	0.002
Singh 1994	1.639	0.969	2.773	1.841	0.065
Smith 1987	1.641	0.778	3.462	1.300	0.194
Spiegler 1983a	1.239	0.949	1.619	1.573	0.116
Spiegler 1983b	1.269	1.012	1.591	2.064	0.039
Tan 1985	15.729	0.924	267.647	1.906	0.057
Tan 1988	0.759	0.386	1.494	-0.797	0.425
Tapley 1985	1.208	0.870	1.679	1.128	0.259
Teng 1979	2.080	1.331	3.249	3.218	0.001
Thompson 1976	1.786	1.025	3.111	2.047	0.041
Wolf 1991	1.175	0.869	1.588	1.047	0.295
Wood 1989	1.028	0.645	1.638	0.117	0.907
Wood 1991a	2.264	0.291	17.627	0.780	0.435
Wood 1991b	3.130	0.377	26.016	1.056	0.291
Wood 1991c	1.028	0.645	1.638	0.117	0.907
	1.284	1.272	1.297	51.394	0.000



Appendix 3.1 Questionnaire used for the screening of the participants taking part in the study described in chapter 3.

Please take some time and complete the following questionnaire:

Are you male or female?

…….

What is your date of birth?

…….

Do you write with your right or left hand?

……

Are you a native English speaker?

……

Are you bilingual? (i.e. have been raised having two languages as mother tongues)

……

Do you have any neurological problems (e.g. epilepsy, meningitis, encephalitis, multiple sclerosis, stroke)

……

Have you ever suffered any severe head trauma?

……

Do you have any medical condition interfering with hand function? (e.g. arthritis?)

……

Thank you for your time!

Appendix 3.2 Information sheet for the participants taking part in the study described in chapter 3.

INFORMATION SHEET

You are being invited to take part in a research project. Here is some information to help you decide whether to do so. Please take time to read this information carefully. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part.

This study will involve you coming to the Department of Experimental Psychology for about half an hour on a day and time to suit you. On this day you will be asked to complete questionnaires which include questions about your hand preferences, e.g. which hand do you use to screw a lid or to brush your teeth.

Exclusion criteria
People with a history of neurological problems or with any medical conditions interfering with hand function cannot take part in the study. Moreover, participants will have to be native, monolingual English speakers and not be taking any medication.

Written consent
You will be asked to give written consent before taking part in the study. However, signing the consent form will not commit you to completing the study. You remain free to leave the study at any time and without having to give any reason for doing so.

Storage and disposal of data
Data will be stored at the researchers locked office for at least 10 years.

This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

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Appendix 3.3 Item included in the questionnaire used in the study described in chapter 3.

In brackets, the questionnaire in which each item was included is marked.

A = Annett's Hand Preference Questionnaire (AHPQ)

B = Edinburgh Handedness Inventory (EHI)

C = Waterloo Handedness Questionnaire (WHQ)

D = Healy, Liederman and Geschwind Inventory (HLGI)

Which hand do you use:

To write a letter legibly? (A,B,C,D)

To throw a ball to hit a target? (A,B,D)

To hold a racket in tennis, squash or badminton? (A,C,D)

To hold a match whilst striking it? (A,B,C,D)

To cut with scissors? (A,B,C,D)

To guide a thread through the eye of a needle (or guide needle on to thread)? (A,C,D)

At the top of a broom while sweeping? (A,B)

At the top of a shovel when moving sand? (A,D)

To deal playing card? (A,D)

To hammer a nail into wood? (A,C,D)

To hold a toothbrush while cleaning your teeth? (A,B,C,D)

To unscrew the lid of a jar? (A,B,C)

To draw (B,C,D)

To hold a knife (without a fork) (B,D)

To hold a spoon (B)

With which hand would you turn on a water tap? (C)

With which hand would you throw a dart? (C,D)

In which hand would you hold a heavy object? (C)

With which hand would you pick up a penny off a desk? (C)

On which shoulder do you rest a baseball bat when batting? (C)

With which hand do you throw a baseball? (C)

With which hand would you pet a cat or a dog? (C)

In which hand would you carry a heavy suitcase? (C,D)

With which hand would you pick up a glass of water? (C)

Which hand would you use to dial a number on a push button phone? (C,D)

Over which shoulder would you swing an axe? (C,D)

With which hand would you point to a distant object? (C,D)

Which hand would you use to catch a ball if you were bare-handed? (C,D)

With which hand would you pick up a screw? (C)

With which hand would you hit someone? (C)

In which hand would you hold a fly-swatter when killing flies? (C)

With which hand do you use a pair of tweezers? (C,D)

With which hand would you throw a spear? (C)

With which hand would you tighten a screw by hand? (C,D)

Which hand do you put down on the floor first when doing a cartwheel? (C,D)

With which hand would you hold a cloth when dusting the furniture? (C)

With which hand would you hold the razor when shaving? (C,D)

With which hand do you flip a coin? (C,D)

Which shoulder would you use to push open a pair of swinging doors (café style) when your arms are full? (C)

With which hand do you wind a stop-watch? (C,D)

With which hand would you pick up a paperclip off a desk? (C)

With which hand do you use the eraser on the end of a pencil? (C,D)

With which hand would you insert a pin into material? (C)

With which hand would you pick up a piece of paper off a desk? (C)

With which hand would you shoot a marble? (C)

With which hand would you wash your face with a cloth? (C)

Which hand would you use to wave goodbye? (C,D)

Which hand would you use to snap your fingers? (C,D)

Which hand would you use to pick up a marble? (C)

Which hand would you use to bat in baseball? (C)

In which hand would you hold the paperclip when clipping papers together? (C)

Which hand would you use to screw in a light bulb? (C)

With which hand do you hold a comb when combing your hair? (C,D)

With which hand would you pick up a book? (C)

With which hand would you pick up a pin? (C)

With which hand would you extract a small object from a tight space? (C)

With which hand would you shoot a basketball? (C)

With which hand would you pick up a heavy suitcase? (C)

With which hand would you erase a blackboard? (C,D)

Which hand is the most adept at picking up a small object? (C)

Do you consider yourself a left-handed or a right-handed baseball player? (C)

If both hands were empty which hand would you use to break your fall if you slipper on ice? (C)

Which hand do you use to manipulate implements such as tools? (C)

Which hand do you consider the strongest? (C)

In which hand would you hold a knife to cut bread? (C)

Which hand would you use to pick up a nut or a washer? (C)

Which hand would you use to pick up a comb? (C)

With which hand would you pick up a bat? (C)

With which hand would you pick up a toothbrush? (C)

In which hand would you carry a briefcase full of books? (C)

With which hand would you pick up a jar? (C)

With which hand would you pick up a pen? (C)

Which hand would you use to put a nut washer on a bolt? (C)

With which hand would you pick up a baseball? (C)

Which fist would you use to pound on the table to express anger? (D)

Which hand do you use to:

Use a screwdriver? (D)

Eat with a fork (without a knife)? (D)

Operate a corkscrew? (D)

Peel an apple? (D)

Pull a trigger on a gun? (D)

Saw a piece of wood? (D)

Open a letter with a letter opener? (D)

Wash a dish (which hand washes the dish?) (D)

Pour a cup of coffee? (D)

Set a time on a clock? (D)

Paint a wall? (D)

Throw a bowling ball? (D)

Turn a doorknob? (D)

Type with one hand if you could use only one? (D)

Press the buttons on a calculator? (D)

Color or paint a picture? (D)

Pour water from a pitcher? (D)

Beat time to music? (D)

Dial a phone? (D)

Use a bottle opener? (D)

Iron a shirt? (D)

Screw a light bulb? (D)

Write on a blackboard? (D)

Sew? (D)

Hold a bat in baseball? (D)

Appendix 3.4 The Edinburgh Handedness Inventory in the its original graded graphic response

Please indicate your preferences in the use of hands in the following activities *by putting* + in the appropriate column. Where the preference is so strong that you would never try to use the other hand unless absolutely forced to, *put* ++. If in any case you are really indifferent *put* + *in both columns*.

Some of the activities require both hands. In these cases the part of the tasks, or the object, for which hand preference in wanted is indicated in brackets.

Please try to answer all the questions, and only leave a blank if you have no experience at all of the object or task.

	Left	Right
Writing		
Drawing		
Throwing		
Scissors		
Toothbrush		
Knife (without fork)		
Spoon		
Broom (upper hand)		
Striking Match (match)		
Opening box (lid)		

Appendix 4.1. Questionnaire used for the screening of the participants taking part in the study described in chapter 4.

Please take some time and complete the following questionnaire:

Are you male or female?

…….

What is your date of birth?

…….

Do you write with your right or left hand?

……

Are you a native English speaker?

……

Are you bilingual? (i.e. have been raised having two languages as mother tongues)

……

Have you been taking any medicine including contraceptive pills in the last 6 months?

……

Do you have any neurological problems (e.g. epilepsy, meningitis, encephalitis, multiple sclerosis, stroke)

……

Have you ever suffered any severe head trauma?

……

Do you have any medical condition interfering with hand function? (e.g. arthritis?)

……

Thank you for your time!

Appendix 4.2 Information sheet for the participants taking part in the study described in chapter 4, who were administered all laterality test.

INFORMATION SHEET

You are being invited to take part in a research project. Here is some information to help you decide whether to do so. Please take time to read this information carefully. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part. This study will involve you coming to the Department of Experimental Psychology for about an hour on a day and time to suit you. On this day you will be asked to complete questionnaires asking about your hand preferences, to perform some easy tasks, give saliva samples and do some computer-based tests. We are interested to see how these different measures correlate with each other in right- and left-handers.

Questionnaires
The questionnaires you will be asked to complete include questions about demographic data as well as your hand preferences, e.g. which hand do you use to screw a lid or to brush your teeth.

Tasks
The tasks you will be asked to perform are fun and easy. You will be asked, for example, to tap using a tally counter. Moreover, you will be asked to do some computer-based tests.

Exclusion criteria
People with a history of neurological problems cannot take part in the study, as we are interested in the function of the intact brain. Moreover, you will have to be a native, monolingual English speaker and not be taking any medication, including contraceptive pills. All participants have to have normal or corrected vision and normal hearing from both ears.

Written consent
You will be asked to give written consent before taking part in the study. However, signing the consent form will not commit you to completing the study. You remain free to leave the study at any time and without having to give any reason for doing so.

Storage and disposal of data
Data will be stored at the researchers locked office for at least 10 years.

This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Ms Marietta Papadatou-Pastou Prof Maryanne Martin
Department of Experimental Psychology
University of Oxford

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Appendix 5.1. Questionnaire used for the screening of the participants taking part in the study described in chapter 5.

Please take some time and complete the following questionnaire:

Are you male or female?

……

Do you write with your right or left hand?

……

Are you a native English speaker?

……

Are you bilingual? (i.e., have been raised having two languages as mother tongues)

……

Have you been taking any medicine including contraceptive pills in the last 6 months?

……

Do you have any neurological problems (e.g. epilepsy, meningitis, encephalitis, multiple sclerosis, stroke)

……

Have you ever suffered any severe head trauma?

……

Do you have normal or corrected vision?

……

Do you have normal hearing from both ears?

……..

Do you have any medical condition interfering with hand function? (e.g. arthritis?)

……

For women:

Do you have a normal period cycle?

……

When do you expect your next period?

…….

Thank you for your time!

Appendix 5.2 Information sheet for the participants taking part in the study described in chapter 5.

INFORMATION SHEET

You are being invited to take part in a research project. Here is some information to help you decide whether to do so. Please take time to read this information carefully. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part.

This study will involve you coming to the Department of Experimental Psychology for about an hour on a day and time to suit you. On this day you will be asked to complete questionnaires asking about your hand preferences, to perform some easy tasks, give saliva samples and do some computer-based tests. We are interested to see how these different measures correlate with each other in right- and left-handers.

Questionnaires

The questionnaires you will be asked to complete include questions about demographic data as well as your hand preferences, e.g. which hand do you use to screw a lid or to brush your teeth.

Tasks

The tasks you will be asked to perform are fun and easy. You will be asked, for example, to tap using a tally counter. Moreover, you will be asked to do some computer-based tests.

Saliva samples

You will be asked to give saliva samples. This will be done by spitting in a testing tube. You will be asked in the consent form if you agree to the collection and analysis of this sample for this particular study for hormone levels. Should you agree, samples will be anonymised (labelled with an identifying number rather than personal information).You also retain the right to request this sample to be destroyed at any point. Samples will be destroyed after they have been analysed. If you suffer from any disease that might be transmittable by saliva, then it would be better if you didn't take part in the study.

Exclusion criteria

People with a history of neurological problems cannot take part in the study, as we are interested in the function of the intact brain. Moreover, you will have to be a native, monolingual English speaker and not be taking any medication, including contraceptive pills. All participants have to have normal or corrected vision and normal hearing from both ears.

Written consent

You will be asked to give written consent before taking part in the study. However, signing the consent form will not commit you to completing the study. You remain free to leave the study at any time and without having to give any reason for doing so.

Storage and disposal of data

The saliva samples will be disposed of as soon as they are analysed for hormonal levels. All other data will be stored at the researchers locked office for at least 10 years.

This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Ms Marietta Papadatou-Pastou Prof Maryanne Martin
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Appendix 5.3 Full list of stimuli used in the lexical decision test.

word / non-word pairs

1. guest	snold
2. belc	dumb
3. broad	telth
4. broke	codge
5. bronk	pause
6. build	thirt
7. burnt	gloot
8. cheer	thist
9. chust	sharp
10. cloth	stath
11. crowd	swerm
12. debt	kirg
13. drug	vieg
14. flood	thomp
15. gench	shelf
16. glad	tulf
17. grey	jund
18. grud	wrap
19. praud	scrap
20. print	whard
21. quick	smald
22. snaid	vague
23. thimp	trust
24. waird	twice

non-word / non-word pairs

1. balch	wrisp
2. blol	tulp
3. blumb	cluel
4. boarl	thrub
5. chonk	whall
6. dway	glon
7. dweet	quask
8. flawn	chich
9. goug	onch
10. holve	spune
11. jadge	plent
12. nulch	shrob
13. sagu	frug
14. shomp	turge
15. smaid	thort
16. snole	stach
17. mirm	ferf
18. swif	grik
19. swote	stife
20. tihe	rulg
21. glunk	troil
22. vamb	drin
23. wagu	twag
24. wrowl	woond

Appendix 6.1. Questionnaire used for the screening of the participants taking part in the study described in chapter 6.

Please take some time and complete the following questionnaire:

Have you been taking any medicine in the last 6 months?

……

Have any neurological problems (e.g., epilepsy, meningitis, encephalitis, multiple sclerosis, stroke) become known to you since taking part in the study on Trinity 2006?

……

Have you suffered any severe head trauma since taking part in the study on Trinity 2006?

……

Have any medical condition interfering with hand function appeared since taking part in the study on Trinity 2006? (e.g., arthritis?)

……

Thank you for your time!

Appendix 6.2 Information sheet for the participants taking part in the study described in chapter 6.

INFORMATION SHEET

You are being invited to take part in a research project. Here is some information to help you decide whether to do so. Please take time to read this information carefully. If there is anything you do not understand, or if you would like more information, please ask us. Take time to decide whether you wish to take part.

This study will involve you coming to the Department of Experimental Psychology for about two hours on a day and time to suit you. On this day you will be asked to undergo Doppler Sonography, perform some easy tasks and give saliva samples. We are interested to see how these different measures correlate with each other in right- and left-handers.

Functional TCD

Functional Transcranial Doppler Ultrasonography (fTCD) is a test that measures the velocity of blood flow through the brain's blood vessels. Two probes will be placed approximately on your side cheeks and some jelly will be used to help place the probes. You will then be asked to perform some easy language tasks. The procedure is totally painless and safe – ultrasonography is a routine examination even for unborn babies.

Tasks

The tasks you will be asked to perform are fun and easy. You will be asked, for example, to try and bisect a line at midline and draw a quick profile of your mother.

Saliva samples

You will be asked to give saliva samples in the evening of the day of the testing. This will be done by spitting in a testing tube provided to you by the experimenter. You will then have to store the samples in you freezer and return them to the Department of Experimental Psychology on the following morning. You will be asked in the consent form if you agree to the collection and analysis of this sample for hormonal levels. Should you agree, samples will be anonymised (labelled with an identification number rather than personal information).You also retain the right to request this sample to be destroyed at any point. Samples will be destroyed after they have been analysed. If you suffer from any disease that might be transmittable by saliva, then it would be better if you didn't take part in the study.

Exclusion criteria

People with a history of neurological problems cannot take part in the study, as we are interested in the function of the intact brain. Moreover, you will have to be a native, monolingual English speaker and not be taking any medication. All participants have to have normal or corrected vision.

Written consent

You will be asked to give written consent before taking part in the study. However, signing the consent form will not commit you to completing the study. You remain free to leave the study at any time and without having to give any reason for doing so.

Storage and disposal of data

The saliva samples will be disposed of as soon as they are analysed for hormonal levels. All other data will be stored at the researchers locked office for at least 10 years.

This project has been reviewed by, and received ethics clearance through, the University of Oxford Central University Research Ethics Committee. Maintenance of confidentiality of information is subject to normal legal requirements.

Ms Marietta Papadatou-Pastou Prof Maryanne Martin
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Appendix 6.3 Instructions for the collection of saliva samples.

Dear participant,

Please try to follow the instructions –it is very important that everything gets done correctly!

It's very easy –all you need to do is the following:

1. **At 5 p.m. TODAY, spit into the tubes labelled T1 and C1.**
2. **At 5.15 p.m. TODAY, spit into the tubes labelled T2 and C2**
3. **Store the samples in your fridge**
4. **First thing tomorrow morning bring back the samples in the Department of Experimental Psychology.**

… some tips:

- Do not collect saliva 30 minutes after eating or drinking or gum chewing.
- Do not collect saliva within 15 minutes after brushing teeth or use dental floss.
- In case of any doubt rinse your mouth with pure mineral water or tap water before collecting saliva
- If you have problems with producing saliva, then just chew the parafilm provided –but don't swallow it! At best don't chew anything.
- You should try to provide enough saliva until the middle of the test tube (1ml), which is marked by a line. There is also a stick provided for stirring if needed!
- Place the tubes in the bag provided and then put the bag in your fridge.
- The following morning put the bag in the envelope provided and return it to the Department of Experimental Psychology or St Edmund Hall.
- You must discard any sample, which shows even a slightly red colour. In this case, you should rinse the tube 2 times with tap water, wait for another 10 minutes and sample again.

Thanks!