Bangor University

DOCTOR OF PHILOSOPHY

Hemispheric asymmetries: behavioural, kinematic, and electrophysiological predictors of cerebral organisation

Johnstone, Leah

Award date:
2016

Awarding institution:
Bangor University

PRIFYSGOL
BANGOR
UNIVERSITY

Hemispheric asymmetries: Behavioural, kinematic, and electrophysiological predictors of cerebral organisation

Leah T. Johnstone

School of Psychology
Bangor University
November 2015

Thesis submitted to the School of Psychology Bangor University in partial fulfillment of the requirements for the degree of Doctor of Philosophy

Acknowledgements

Firstly, I would like to thank my examiners for taking the time out of their schedules to read and assess this body of work.

Huge thanks go to all Brigantia staff and PhD students in Psychology for making my time here entertaining as well as educational. Particular gratitude extends to Patricia ‘the Beast’ Bestelmeyer, Paul ‘Mulman’ Mullins, and my private dancer Bronson Harry for teaching me all I know about neuroimaging. Thank you all for your patience in answering my tedious questions. Alongside Kami Kold(e)wyn, Manon ‘I’m not being funny right’ Jones, and Chris ‘cup of tea?’ Saville, you also provided some pretty great tea breaks and lunchtime gossip. Thanks to Paul Downing for letting me stick around.

Obviously I owe a big thank you to my family. Mum and Dad, you always kept the door open for me to run back for some home comforts and a big moan whenever I needed it! Cheers for teaching me how to adult. It’s hard but I’m getting better at it. Eve – thanks for doing all the things only a big sister can. It meant a lot. Andrew – you got me into this mess, so I hope you’re happy!

To Maz, Lucy and Jemma – thanks for only being a message away. Without pizza squad I doubt I would have made it to the finish line. I owe you all a slice.

Luke – well let’s face it, I wouldn’t have lasted without you! Who would have done spider duty and remembered when it was bin day? More importantly, how would I have relaxed in the evenings without a kitchen-washing-up-cooking-dance-sing-off with Sam Smith, Jess Glynne, Whitney, Miguel, and Mariah…and a good old startle before bed? Didn’t think I’d start a PhD and finish with more family. Cheers pal.

Finally I thank my supervisor, who has put at least as much time and energy into this line of research as I have. I hope we both continue to do so for many years to come. David – don't worry, I’ll keep it short and sweet. I don’t think I’d find a better mentor, not only in terms of my academic pursuits but also for offering a new perspective (and your unfiltered opinion) on most aspects of my life. I doubt I would have been anywhere near as productive as I have been without your gentle, laid-back management style (“JOHNSTONE?…REPORT!”), and your various motivational songs (“this girl is on fire”, “Johnstone is doing it for herself”, and “there’s only one Leah Johnstone” to name but a few). I don’t quite feel ready to snatch the pebble from your hand, but you seem to think I am and that’ll do for me.

Summary

Our best estimates suggest that ~95% of dextrals and ~70% of adextrals have left hemisphere language dominance. Currently the only way to determine language lateralisation is to use invasive hemispheric anaesthetising procedures, or expensive functional neuroimaging methods. This lack of identification has led to adextrals being studied as an 'atypical' group in terms of functional lateralisation, despite the vast majority of them sharing the same brain organisation as dextral subjects. Therefore research into brain asymmetries or atypical dominance could progress much more quickly if a more successful predictor (or combination of predictors) of cerebral lateralisation than handedness were available.

This body of work investigates the potential usefulness of behavioural, kinematic, and electrophysiological measures to predict cerebral asymmetries. These data are discussed in the first three experimental chapters, and the fourth chapter contains a neuroimaging project. In this final study language, face, and body processing asymmetries are identified in dextral and adextral participants who had taken part in the initial lab-based tests. The results from this thesis suggest that a consonant-vowel dichotic listening task, as well as strength of left-sidedness, may increase successful identification of 'atypical' language dominance beyond the 15% success of left-handed writing. Additionally, ear advantage on a further listening paradigm, the Octave illusion, differentiates between dextral and adextral subjects in a way that appears related to language lateralisation. Kinematic measures may be related to brain organisation, but the relationship is less clear than in the more successful behavioural lab tests. Finally, asymmetries in electrophysiological components are a poor predictor of functional lateralisation. This thesis advocates against the exclusive use of measures of central tendency, promoting alternative proportional and individual level analyses. This assessment has implications for laterality researchers using any methodology from behavioural neuropsychology to functional neuroimaging.

Table of Contents

List of tables and figures

Chapter 1 – General introduction

1.1 Is handedness innate?

All humans have a preferred hand for writing. Usually this hand is also favoured for almost all other manual tasks, such as throwing a ball or brushing teeth. This depth of preference is unheard of in other species, even other great apes (Marchant & McGrew, 2013). This uniqueness has inspired many conflicting theories as to why Homo sapiens developed a dominant hand, but a fact that remains undisputed is that around 90% of people prefer to use the right hand for skilled tasks (Coren & Porac, 1977).

The anthropology literature has searched for manual asymmetries in non-human animals, and primates in particular. Primatologists have claimed that chimpanzees, bonobos, and baboons show population-level right-handedness for various skilled tasks (Lonsdorf & Hopkins, 2005; Hopkins, 2006; Meguerditchian & Vauclair, 2006; Hopkins, 2007). There have even been claims for leftward asymmetries in homologues of Broca's and Wernicke's area (Hopkins & Cantalupo, 2004; Hopkins, Russell, & Catalupo, 2007). Other research, however, has repeatedly revealed methodological issues in making these claims, including insufficient task validity, small sample sizes, and varied or over specified categorisation of skilled hand uses (Warren, 1980; Cashmore, Uomini, & Chapelain, 2008; Holder, 1999; Marchant & McGrew, 1991).

If strong right hand preference is relatively restricted to homo sapiens, its origins are of considerable theoretical interest. A colleague who works in the genetics of handedness once told us that it was difficult to get grants to look for alleles related to handedness in large samples of dextrals and adextrals because "handedness is learned". The least sophisticated of this type of argument fails to appreciate the extreme skew in handedness; that is if hand preference is determined by chance, then the proportions of left and right handers in the world should be *roughly* equal. For example, it may appear by chance choices in infants, or may be biased, consciously or unconsciously by the hand preference of parents via shaping or mimicry. A slightly more sophisticated form of the "handedness is learned" argument acknowledges the extreme asymmetry in incidence of right and left handedness, but claims that it is mainly the result of social pressure against left-sidedness (Watson & Watson, 1921; Blau, 1946; Ashton, 1982). It is certainly true that many human societies have had subtle (and not so subtle) biases against the sinistral minority (Corballis, 1991).

Although there has been such a bias in Western cultures, there is evidence that it is largely disappearing (McManus, 2004). Coren and Halpern (1991) present analyses of a large data series (collected by Porac & Coren, 1981) where incidence of left handedness is compared across participant birth years. There are fewer left handers in the sample with early birth years, and at the time of publication this was interpreted as “reduced longevity of left handers” (Coren & Halpern, 1991). This conclusion sparked multiple investigations into left handed life expectancy (e.g. Harrell, 1991; Gilbert & Wysocki, 1992; Aggleton, Kentridge, & Neave, 1993; Harris, 1993; Hugdahl, Satz, Mitrushina, & Miller, 1993; Salive, Guralnik, & Glynn, 1993; Persson & Allebeck, 1994; Ellis, Marshall, Windridge, Jones, & Ellis, 1998; Steenhuis, Østbye, & Walton, 2001). Several of these studies came to the conclusion that the data actually indicate a gradual decrease in anti-sinistral bias. McManus (2004) plotted Porac and Coren’s (1981) dataset reporting incidence of left handedness as a function of birth year (see figure 1.1). Left handedness gradually increased from the turn of the 20th century, a symptom of the decrease in cultural anti-sinistral bias. From this figure that from post-war birth years onwards, the prevalence of left handedness has remained largely stable for both sexes. A crucial additional observation from these data is that the sex difference in left handedness is remarkably stable, and does not seem to be decreasing with the hypothesised decreased in anti-sinistral bias.

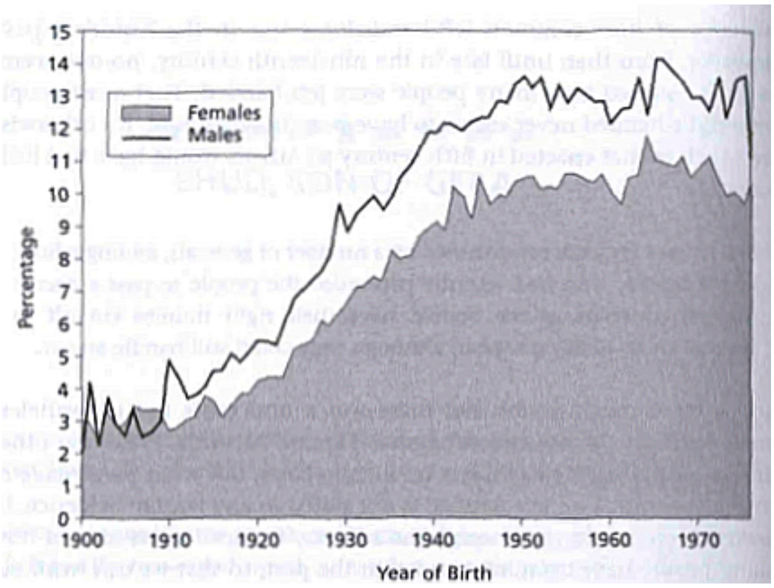


Figure 1.1 – Incidence of left handedness in cohorts with different birth dates. Percentage of left handedness appears on the *y*-axis and clearly increases up until the 1940s/50s, then remains relatively stable. Also note the 4-5% increase in the incidence of left handedness in men compared with women. (taken from McManus, 2004)

This sex difference in incidence of left-handedness is also suggestive of a biological component driving hand preference. A few authors have suggested that this too is due to social factors; young girls may be more compliant to attempts to switch their hand preference than equivalently aged boys (Sato, Demura, Sugano, Mikami, & Ohuchi, 2008). If this is the case convergence of the two curves above might be expected (figure 1.1), as the century progressed. Carey, Hirnstein and Westerhausen (*in progress*) are finding an even larger sex difference in the same direction in footedness in football players, an asymmetry unlikely to have been influenced by any pressure against left sidedness. In fact, left footedness is valuable in football tactics (Carey et al., 2001). Therefore a parent or coach should be more likely to encourage left foot preference than right. These considerations and others encouraged more research on possible biological underpinnings of handedness.

The most notable of these is the literature on the planum temporale. There are multiple claims that this superior surface of the posterior temporal lobe is larger in the left hemisphere, and it is thought to contain Wernicke's area in people with conventional cerebral dominance (Geschwind & Levitsky, 1968; Wada, Clarke & Hamm, 1975; Steinmetz & Galaburda, 1991; Steinmetz & Setiz, 1991; Galaburda, Corsiglia, Rosen, & Sherman, 1987; Kulnych, Vladar, Jones, & Weinberger, 1993; Foundas, Leonard, Gilmore, Fennell, & Heilman, 1994). Just as most individuals are right handed, most are also left hemisphere dominant for speech (Rasmussen & Milner, 1977). Therefore, a language-related region larger in the left hemisphere was an attractive piece of evidence linking handedness with anatomy. Some planum temporale research suggests that the region is somewhat less asymmetrical in left handed individuals (Hochberg & Le May, 1974; Le May & Kido, 1978). A key finding was that of Steinmetz, Volkmann, Jäncke and Freund (1991) who used MRI measures to show that both right and left handers had a leftward asymmetry, but that the magnitude of this asymmetry was greater in the right handers. This literature, however, is fraught with problems surrounding measurement methods, and often reports a much lower incidence of leftward planum asymmetry than the proportion of the population with leftward language lateralisation (Beaton, 1997). More direct evidence of a biological bases for handedness has been searched for by geneticists.

Early population and pedigree studies indicated that the traditional, Mendelian logic of genetic inheritance could not explain handedness (Ramaley, 1913; Jordan, 1914;

Chamberlain, 1928; Rife, 1940)[1]. Annett (1964) proposed a genetic model developed to include an explanation of 'mixed-handedness' – defined as the preference for one hand for some unimanual tasks, and the other for others (as opposed to use of either hand for a unimanual task). Annett (1964) suggested that majority of sinistrals were 'mixed-handers', and that most of the difficulty in explaining hemispheric and hand dominance may be due to heterozygotes developing preference for *either* hand, and speech in *either* hemisphere. Evidence from aphasia incidence after unilateral brain damage had long suggested a relationship between lesion side and the patient's handedness, dating back to research by Broca (1865). This genetic hypothesis is known as the 'right-shift theory' (Annett, 1978). This theory suggests that manual asymmetries depend upon accidental differences, but that a 'right-shift gene' (RS+) weights these accidental chance factors in favour of right hand preference. As well as the initial asymmetry in congenital development and a weighting towards dextrality in humans, the theory includes a third factor affecting handedness; culturally imposed enhancements of dextral biases (Annett, 2002).

Other researchers have attempted to develop more complex models that involve more deterministic factors than a 'weighted chance' process (Levy & Nagylaki, 1972), however, models such as this one can be largely explained away by relatively low concordance of handedness between either monozygotic or dizygotic twins (Collins, 1970). Of course, this is a criticism of any genetic model, but those which include appreciation of some nongenetic factors are better equipped to deal with such arguments. McManus and Bryden (1992) analysed surveys from 72,600 children, and found that 90.5% of children from two right-handed parents were also right handed. This proportion dropped to 80.5% if one parent was left handed, and further decreased to 73.9% if both parents were adextral. These percentage estimations are the current 'gold standard' in handedness genetics, suggesting a strong biological contribution to hand preference, but one which is complex and likely polygenetic.

Other labs have worked to actually identify the gene(s) responsible for handedness. Some have found relationships between a gene and language lateralisation but not handedness (Ocklenburg et al., 2011), while others have identified

---

[1] It is important to acknowledge that as in Coren & Halpern (1991), cultural anti-sinistral bias could have confounded data from these early genetic studies.

[2] It has been demonstrated, however, that Paul Broca never explicitly made such claims (Eling,

polymorphisms that relate to degree but not direction of handedness (Arning et al., 2013). Although efforts are ongoing, currently no specific gene or combination of genes has been identified as responsible for an individual's hand preference.

1.2 Handedness and functional cerebral asymmetries

There is various evidence suggesting that an individual's handedness is related to their brain asymmetry for speech and language processes. Neurosurgical advances led to the development of the Wada test to uncover an individual's language lateralisation (Wada, 1949). This procedure involves injecting sodium amytal into the carotid artery to anaesthetise one hemisphere independent of the other, and then testing the patient's speech functioning. This test was carried out on large numbers of neurosurgical patients, particularly patients with chronic epilepsy who were to undergo temporal lobe surgery to remove their epileptic foci, where surgeons should attempt to avoid removing areas important for speech. Since the development of this test much research has centred on its applications for brain surgery, as well as what it can tell us about hemispheric asymmetries in general. Rasmussen and Milner (1977) collected Wada test data from a large case series of epileptic patients. Data from this huge sample suggests that 96% of right-handers are left lateralised for language.

This result suggests fairly obviously that there is a relationship between handedness and language asymmetry, the hemisphere controlling speech and language is the same hemisphere that controls the dominant hand. One link suggested by this near-perfect relationship is implied by the motor control requirements for speech. Motor theories of speech perception come in various guises, but they tend to have in common the notion that substrates for speech perception will have substantial overlap with the substrates necessary for speech production (e.g. Kimura, 1993). These kinds of perspectives look for common links between conditions such as limb apraxia and aphasia, and how they overlap and may reveal something about left hemispheric specialisation for certain aspects of sensory motor control. For example, Kimura and her collaborators have made much of motor sequencing deficits in patients with left hemisphere damage, whether they have apraxia or aphasia (Kimura & Archibald, 1974; Kimura, 1993). Of course these arguments work best for dextral people.

According to motor theories of speech perception the vast majority of left handers should be right-hemisphere dominant for language. These people should be the mirror image of right handers in terms of language dominance as well as manual and perceptual asymmetries. This concept became known as "Broca's rule" (Hécaen & Piercy, 1956; Maly, Turnheim, Heiss, & Gloning, 1977; Strauss & Wada, 1983)[2]. This pattern of lateralisation appears not to be the case, as Rasmussen and Milner (1977) also found that 70% of left-handers' had speech arrest after left-hemisphere anaesthetisation. Dysphasia after anaesthetising the right hemisphere occurred in 4% of the right-handed sample and 15% of the left-handed sample, with the remaining 15% of left-handers having bilateral language abilities. The relationship between handedness and hemispheric language asymmetry is therefore far from linear, but a relationship is clearly present, as these figures suggest a right brain dominant individual is three times more likely to come from a left-handed sample.

Some researchers have suggested that perhaps estimates taken from patients with epilepsy will not reflect the proportions of left and right language dominance in healthy individuals (Kimura, 1993). These patients had epilepsy severe enough that it resisted drug treatment, and temporal lobe surgery was necessary. There is some evidence that perinatal brain damage changes incidence of language dominance (Geschwind & Galaburda, 1985). Nevertheless, it seems plausible that any reversal of inherited speech dominance would be roughly equivalent after left or right brain damage. In spite of this caveat, evidence from non-epileptic samples suggest language dominance estimates in dextrals and adextrals that are fairly equivalent to those provided by the Wada studies. We conducted a meta-analysis in which the proportions of left and right brain dominant dextrals and adextrals were analysed from multiple fMRI, electroconvulsive therapy (ECT), and functional transcranial Doppler sonography (fTDS) studies. The analysis suggests estimates of 90% left brain dominance in dextrals and 73% in adextrals (Carey & Johnstone, 2014), largely reflecting the figures reported by Rasmussen and Milner (1977).

Other sources of evidence are also relatively consistent with the above evidence. Studies of patients with and without aphasia after unilateral strokes were arguably the first datasets to suggest that handedness and hemispheric language dominance were not entirely contralaterally related (Critchley, 1954; Goodglass & Quadfasel, 1954; Zangwill, 1960). Over time, physicians and aphasiologists came to recognise that aphasia in left

---

[2] It has been demonstrated, however, that Paul Broca never explicitly made such claims (Eling, 1984; Harris, 1991).

handers was also more common after left hemisphere than right hemisphere insult, unlike what was predicted by "Broca's rule" (Critchley, 1954, Hécaen & Piercy, 1956; Bryden, Hécaen, & DeAgostini, 1983). These findings tend to also support the Rasmussen and Milner data. Using meta analysis we examined aphasia incidence after unilateral brain damage, and found that dextrals and adextrals are similarly prone to aphasia after a left hemisphere stroke, but that a right hemisphere stroke is seven times more likely to produce aphasia in adextrals (Carey & Johnstone, 2014).

Clearly, a relationship between handedness and cerebral language dominance is present, but is extremely complex. Interestingly, early research proposed that adextrals were more likely to have problems with language functioning after brain damage than dextrals (Chesher, 1936; Gloning, Gloning, Haub, & Quatember, 1969), however, when comparing prognosis between dextrals and adextrals, adextrals appear to recover earlier and more completely (Subirana, 1969). The first of these findings could be explained by the increased incidence in aphasia after a right hemisphere stroke in adextrals (Carey & Johnstone, 2014). The difference in prognosis could be explained perhaps by the phenomenon of bilateral speech representation, which appears to be present in the adextral population but not in dextrals (Rasmussen & Milner, 1977).

Whilst it is probably the most striking, language function is not the only longstanding functional asymmetry suggested by neuropsychological evidence. As post-stroke or brain injury patients can present with aphasia, they can also present with a face-processing disturbance. Acquired prosopagnosia is the inability to recognise faces after brain damage. It is a complex condition to assess, as patients with prosopagnosia can still identify persons using their voice, body, or other non-biological cues (Humphreys & Riddoch, 1987). As there is no universal set of faces that everyone would recognise, currently no standardised neuropsychological test given routinely to all patients exists (as there are for aphasia and motor/attentional disorders). Therefore our estimates of its incidence after left or right brain damage, in adextrals in particular, are much weaker than that of aphasia.

Original hypotheses surrounding the cause of prosopagnosia was that it occurred after damage to posterior regions of the right hemisphere (Hécaen & Angelergues, 1962; Benton & Van Allen, 1968), however this theory was refuted by scientists reporting that most prosopagnosic patients had suffered bilateral brain damage (Meadows, 1974; Damasio, Damasio & van Hoesen, 1982). However, as medical neuroimaging techniques improved, so did the evidence for the original right-hemisphere hypothesis, with many prosopagnosic patients reported as having spared left hemispheres (De Renzi, 1986; Sergent & Villemure, 1989, Benton, 1990; De Renzi, Perani, Carlesimo, Silveri & Fazio, 1994; Wada & Yamamoto, 2001 – see figure 1.2). This patient work provides evidence that face processing and perception have an asymmetric representation in the brain. Due to the fact that adextrals are rare, there is simply less literature surrounding adextral patients. Mattson, Levin and Grafman (2000), however, provide a case report of a single adextral patient who developed prosopagnosia after a closed head injury resulting in a left hemisphere focal lesion, suggesting the reverse of the commonly reported functional organisation.

Unfortunately, there are no large case series datasets reporting the incidences of prosopagnosia after left or right unilateral lesions (as there is in the language literature, mentioned above). Therefore we have to rely on experimental research in face processing using typically functioning dextrals and adextrals. Functional magnetic resonance imaging (fMRI) can now be used to identify differences in activity between the two hemispheres in response to different stimuli (for example language presentation, or images of faces). This research can not only shed light on the anatomy of normal language or face processing (as opposed to relying on patients who are unusual by nature), but can also tell us more about the relationship of handedness to these cerebral asymmetries.

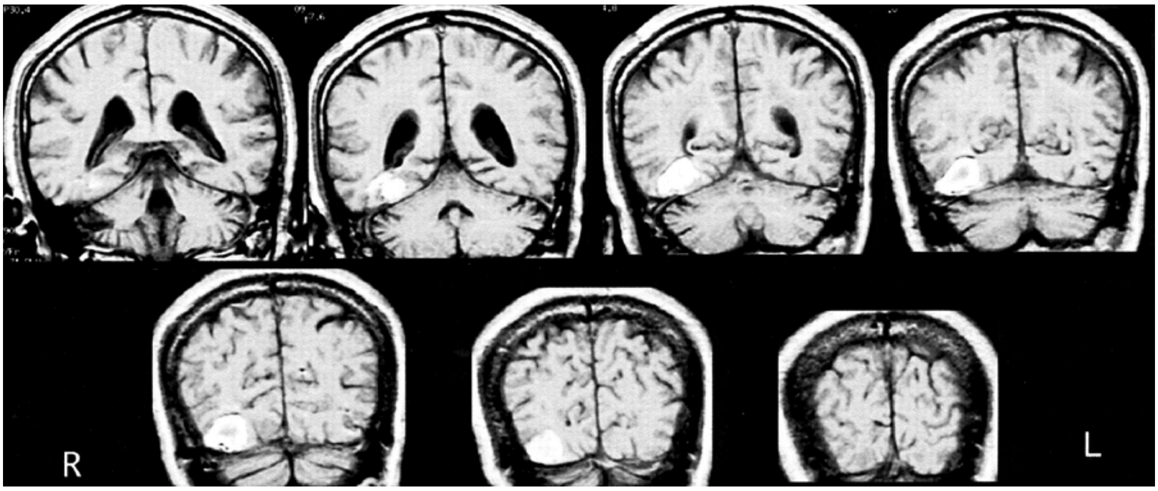


Figure 1.2 – Coronal slices of the structural scan in Wada and Yamamoto (2001) In these images taken from a prosopagnosic patient, there is a lesion in the right fusiform but no damage in the left homologous region.

1.3 fMRI and cerebral asymmetries

fMRI is a non-invasive imaging technique which quantifies neurological activity using a blood oxygen level dependent (BOLD) signal. The idea is that the more activity neurons are undertaking, the more oxygen (and therefore blood) this brain area will require.

There have been many efforts to establish fMRI's ability to determine language lateralisation at an individual level. Most research reports the results of fMRI designs from individuals who have undergone the Wada procedure, and evaluate concordance between the two methods of assessing dominance. There are several papers of this type (Binder et al., 1996; Sabsevitz et al., 2003; Janecek et al., 2013), and all support the use of fMRI for determining cerebral language dominance. Again, we encounter the caveat that these participants are mostly drug-resistant epilepsy patients, and may have congenital brain damage. However, data from our meta analysis suggests that the proportions of participants with left language lateralisation from fMRI, fTDS and ECT studies are similar to those found by Wada test data (90% dextrals and 73% adextrals; Carey & Johnstone, 2014), and therefore we do not regard this issue as overly problematic.

Using this method to classify hemispheric asymmetries in patients is ideal in clinical settings where running costs are covered. For academic research into individuals with uncommon hemispheric asymmetries, however, this pre-screen measure is largely impractical. fMRI scanning is extremely expensive and time consuming, and identifying a sample of 15 right-brain language dominant individuals would theoretically require scanning 100 left-handed participants. This financial hindrance is less of a problem for research areas such as typical language function, where only (relatively) small numbers of dextrals are required in the first place. In these instances, fMRI has largely overtaken all other research methods.

Consequently there is a huge literature on the cognitive neuroscience of typical language functions. However there is little agreement about which tasks are the best suited to elicit language-related activations (Binder, Swanson, Hammeke, & Sabsevitz, 2008), let alone which tasks promote the most lateralised responses (the most relevant task qualities for the research in this thesis). Unfortunately most fMRI researchers are more interested in particular networks or brain regions associated with language and their responses to certain linguistic features, rather than the asymmetry of the responses (Scott & Johnsrude, 2003; Karuza, Newport, Aslin, Starling, Tivarus, & Bavelier, 2013; McGettigan, Eisner, Agnew, Manly, Wisbey, & Scott, 2013). These studies often include small samples of only dextral participants, and present only group averaged data.

A minority of research teams have recognised the potential value of using neuroimaging to answer unresolved questions regarding cerebral asymmetry. Brysbaert and colleagues have had success in classifying individual participants with a sub-vocal verbal fluency task (Hunter & Brysbaert, 2008; Van der Haegen et al., 2011; Cai, Van der Haegen, & Brysbaert, 2013), which elicits strongly lateralised responses in a majority of participants.

In addition to language asymmetry, fMRI can be used to assess localised responses for many cerebral functions. Several of these processes are occasionally reported as being right hemisphere dominant; including face processing, visuospatial/attention processes, some emotion processing, prosody, music (Kanwisher, McDermott, & Chun, 1997; Cai, Van der Haegen, & Brysbaert, 2013; Buchanan et al., 2000; Riecker, Wildgruber, Dogil, Grodd, & Ackermann, 2002; Riecker, Ackermann, Wildgruber, Dogil, & Grodd, 2000). These asymmetries that appear opposite to the strong leftward asymmetry for language in most individuals, have led to hypotheses of complementary hemispheric specialisation. This concept suggests that if an individual has language functions lateralised to one hemisphere, face processing (and other typically right-hemispheric processes) will lateralise to the opposite hemisphere. There are two proposed mechanisms resulting in this outcome: the causal hypothesis, and the statistical hypothesis (Bryden, Hécaen, & DeAgostini, 1983).

Causal hypotheses of complimentary specialisation suggest that one function lateralises first, and is strongly biologically predetermined (Plaut & Behrmann, 2011; Behrmann & Plaut, 2015). The later developing functions lateralise to the opposite hemisphere *because* the first functions are in the other hemisphere (Kosslyn, 1987; Hellige, 1990). Cai, Van der Haegen, & Brysbaert (2013) support this model, as they showed leftward organisation of visuospatial abilities (as measured by fMRI activations in response to a landmark task) in all of the individuals they studied who had right hemisphere language dominance.

The statistical account of hemispheric specialisation proposes that lateralisation of functions is driven by independent, probabilistic biases (Bryden, Hécaen, &

DeAgostini, 1983). This argument states that there is (more often than not) a bias for language to be lateralised to the left hemisphere, and processes such as visuospatial skills and face perception to the right, but that these biases are driven by probabilities in underlying unrelated sources. The crossed aphasia literature supports this argument in that there are several documented cases where patients who have suffered a unilateral brain lesion suffer deficits in both language and a different, typically 'right hemisphere' function (Bryden, Hécaen, & DeAgostini, 1983). Other evidence for this model comes in the form of fTDS measures where data suggests participants can have two 'opposing' functions lateralised in the same hemisphere (e.g. Whitehouse & Bishop, 2009).

Whilst studies investigating face perception are not usually focussed on asymmetry, it does appear that most dextrals have a rightward asymmetry of the fusiform face area (FFA). This is a region of BOLD activation that responds more strongly to face stimuli than to any other stimulus category (Kanwisher, McDermott, & Chun, 1997). Kanwisher, McDermott, and Chun (1997) used fMRI to identify a face selective region of human extrastriate cortex. Data from 12 participants (10 right-handed and two left-handed writers) were collected during passive viewing images of faces as well as assorted common objects whilst in the scanner. Of the 10 right-handed subjects, half had fusiform activation in the *right hemisphere only*, while in all the remaining dextrals the right fusiform activation was *bigger than the left* (see fig. 1.3). One left-handed subject showed only a left fusiform activation, whereas the other had bilateral representation, but with larger activation in the right fusiform. Whilst this experiment only used a very small sample (of both dextrals and of course adextrals), this paper provides evidence for a rightward asymmetry for face perception in dextrals, at least.

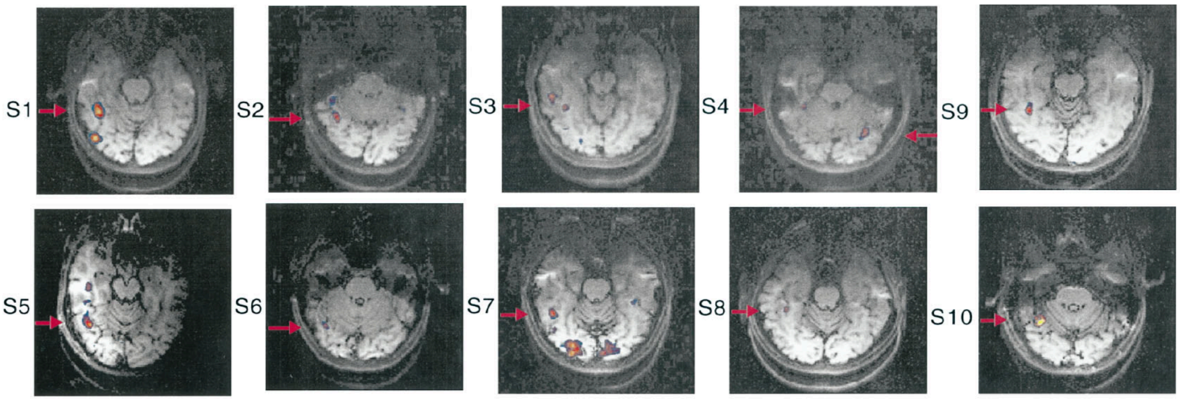


Figure 1.3 – Structural images overlaid with statistical maps from 10 right-handed subjects in Kanwisher, McDermott and Chun (1997). In these individuals, more right than left fusiform activation is present for faces. These images are in radiological convention and therefore the right hemisphere is on the left of the image.

Willems, Peelen and Hagoort (2010) investigated the lateralisation of face and selective brain regions in 16 dextrals and 16 adextrals. They found that the dextral group had significantly larger activations in the right FFA, whereas the adextral group showed no significant difference between the hemispheres. Unfortunately, they did not report how many of their participants followed the average pattern.

Bukowksi, Dricot, Hanseeuw and Rossion (2013) scanned 11 adextrals whilst they passively viewed faces and non-face stimuli. They reported that the FFA was left lateralised at a group level. In this paper, individual data are reported, showing that 3 of their sample had a bilateral FFA (as defined by the proportion of active voxels in each hemisphere being 45-55%), 5 showed a left dominant FFA, and the remaining 3 had a right dominant FFA. They infer from this that "there is a substantial proportion of left-handers who present with a larger FFA in the left than the right hemisphere" (pg. 2585). This study, like much other handedness research, may be underpowered to make such claims from such a small sample size. Proportions that are reported as though they differ, when that difference is two participants, is not convincing enough evidence that most adextrals have a left lateralised FFA.

Averaging data across adextral samples, where the variability between participants' underlying cortical organisation is higher than within dextral samples, is a common weakness in laterality research. If a small proportion of an adextral sample had right hemisphere language dominance and the remaining majority were left lateralised, the result in averaged fMRI data would be a more bilateral language representation. Therefore when researchers conclude that adextrals are 'less asymmetrical' than dextrals, it is hard to interpret whether the majority of adextrals as individuals are less asymmetrical, or whether this is an artefact of a central tendency analysis (the minority subgroup reduce the mean bias provided by the majority). The pitfalls of averaged data can apply to most datasets of course, but are particularly relevant in small sample sizes; the norm in neuroimaging studies. Averaging across dextrals with strongly left-lateralised activations and some with weaker left-lateralised activations could produce an activation map that is not representative of any individual in the sample. At the individual level however, fMRI could potentially be more useful than the Wada test and other dichotomous left/right measures, as it enables continuous measurement; i.e. estimates of degree of lateralisation can be recorded. Despite this strength, neuroimaging analysis is fraught with problems when comparing activations between hemispheres in one individual, due to the dependence of left versus right calculations on statistical thresholds. This problem will be discussed in detail in Chapter 5 of this thesis.

Although fMRI can be used to determine an individual's language lateralisation, it may not be the most economic means of doing so. If a sample of 20 right-hemisphere dominant individuals were required for a research project, the experimenters would need to scan ~130 adextral subjects on average, in order to find them. As neuroimaging is expensive and time-consuming, it is rare that a research team could complete such a costly pre-screen measure. Therefore the study of atypical language representation has unfortunately been largely neglected.

Atypical cerebral organisation of language within 'normal' healthy individuals could aid our understanding of language functions in both hemispheres, improving outcomes for dysphasics and other individuals with speech and language difficulties. With limited means of identifying people with atypical cortical organisation, these lines of research cannot move forward. Therefore, an alternative and reliable way of classifying individuals as left or right hemisphere dominant for functions such as language (and face processing, visuospatial attentional functions, etc) is both desirable and essential to advancing this field. Developing a classification method is the core aim of this thesis, which attempts to identify predictive markers of an individual's cerebral organisation using behavioural, electrophysiological and kinematics data, as well as fMRI to determine functional brain asymmetries.

Amongst these potential predictive markers are scores on perceptual asymmetry tasks, using dichotic listening and visual half field (VHF) paradigms. What is unfortunate in the progress of laterality research, is that wide scale availability of neuroimaging techniques came after attempts to use these perceptual, behavioural asymmetries to identify cerebral dominance for language functions had been largely left behind. These earlier 'indirect' perceptual measures of cerebral asymmetry were extremely popular in the 1970s and 1980s, but there was at that time no simple way to validate their success in identifying left or right language dominance.

1.4 Perceptual asymmetries relating to cerebral asymmetries

Since early experiments by Broadbent (1956), several neuropsychologists including Doreen Kimura and Philip Bryden recognised that verbal stimuli presented dichotically (that is two differing stimuli presented one to each headphone channel simultaneously), tended to produce right-ear advantages (REA) in dextral university undergraduates (reviewed in Bryden, 1988). According to Kimura (1967), the REA is caused by the anatomy of the auditory projections from the cochlear nucleus to the primary auditory cortex in the temporal lobes, alongside a left hemisphere advantage in processing language-related stimuli. The auditory system projects excitatory and inhibitory impulses bilaterally to the dorsal and ventral nuclei of the lateral lemniscus, but from here to the inferior colliculus (and beyond, to the pulvinar thalamus and auditory cortex), projections from the lateral lemniscus nuclei are mainly contralateral (Price et al., 1992). Although auditory signals from both ears reach each hemisphere's auditory cortex, the contralateral projections from the inferior colliculus are represented more strongly (Hugdahl, 1995).

The classic model of dichotic listening suggests that the REA may be a measure of left hemisphere language dominance. The model proposes that the REA is caused by the improved projection of contralateral information, a left hemisphere specialisation for language, and the suppression of ipsilateral pathways by the contralateral information, at least under dichotic conditions (Kimura, 1967; Sparks & Geschwind, 1968). Milner, Taylor and Sperry (1968) supported this argument, reporting almost entire extinction of the left channel syllable in split-brain patients after dichotic stimulation. Hugdahl, Bodner, Weiss and Benke (2003) carried out a dichotic listening paradigm with frontal lobe lesioned, but non-aphasic patients. On average, healthy controls and the right lesioned patients had an REA of the same magnitude, whilst the left lesioned patients had no ear advantage (NEA). In fact, only three of the left-hemisphere patients showed NEA, with the remaining 13 falling in either REA or LEA subgroups. Following this classic model, a left ear advantage (LEA) should suggest right hemisphere language dominance, and NEA (in an individual) would indicate a more bilateral language representation.[3]

In some of the early studies, small to medium sized groups of non-right handers were also tested. They also tended to show right ear advantages for these sorts of material; sometimes smaller than that obtained in the right handers (e.g. Curry, 1967; Bryden, 1970), sometimes not (e.g. Briggs & Nebes, 1976). Many of these studies actually provide data on the number of individuals in each group who show a right ear

---

[3] The boundaries of 'no asymmetry' on perceptual tests such as dichotic listening, as well as in neuroimaging studies, turns out to be a rather important consideration which has rarely been addressed with much vigour since early days of perceptual asymmetry.

advantage, at least in early days of this research field. In our meta analysis, we included these studies plus a smaller number of VHF experiments on verbal material. We found that dextrals were approximately 22% more likely to show a right visual field (RVF) bias or REA in reporting verbal material (Carey & Johnstone, 2014). These data suggest that verbal dichotic listening could be a useful predictor in a battery of behaviours designed to predict an individual person's cerebral asymmetry for speech and language.

Some studies, including some with relatively large samples of dextrals and adextrals, do not find a statistically significant difference between the two groups in the average magnitude of the right ear effect (Sequeira et al., 2006; Hugdahl et al., 2009). Of course, typical null hypothesis significance testing makes some assumptions about normally distributed data which may not be true when it comes to ear advantages in dextrals and adextrals. Additionally, perceptual asymmetries in some individuals might be predictors of their cerebral dominance (for example in people with extreme ear dominances not accounted for by hearing difficulties or attentional fluctuations), even if for many other individual people this particular perceptual test may not be not sensitive enough.

Furthermore, right ear advantages in individuals can be rather unreliable in test-retest experiments (Blumstein, Goodglass, & Tartter, 1975). Some of that unreliability may be related to the fact that individuals can selectively attend to one ear or the other with relative ease, and may do so in unpredictable ways during tests. For example, particularly compliant participants might note the ear that their previous response originated in, and then explicitly or implicitly attend more to the opposite ear, in an attempt to 'attend to both ears'. Unless particular care is taken to try to ensure individuals do not actively move the focus of their attention, performance on dichotic listening in the same individual may vary considerably from test to test (reviewed in Hugdahl, 1988). As a result of these limitations, scientists using dichotic listening tend to focus on dextrals and are more interested in exploring attentional manipulations (Hugdahl et al., 2009), or stimuli eliciting non-right ear responses (e.g. Efron & Yund, 1974), and have become less interested in its use as a predictor of cerebral asymmetry.

Another paradigm for assessing perceptual asymmetries is the VHF task. These experiments involve the brief presentation of a stimulus to a participant's left or right VHF, and assess participants' speed/accuracy as a function of presentation location. Due to the crossing of the nasal optic fibers in the optic chiasm, information presented in the RVF projects initially to the left hemisphere, whereas stimuli presented in the left visual field (LVF) is processed initially by the right hemisphere (Horton & Hoyt, 1991). Therefore responses to the presentation of a stimulus associated with a typically left or right hemisphere function (e.g. words/consonant-vowel pairs, or faces), might reveal information about a participant's cerebral lateralisation of those functions. Less is known about the ease at which people can voluntarily shift attention from one VHF to the other.

Regardless of possible attentional biases affecting results, one potential limitation for using VHF experiments as part of a multi-test behavioural battery is the claim by Hunter and Brysbaert (2008), who suggest that a large number of trials is necessary in order to get a stable visual field advantage, at least for word reading. As a pre-screen measure for cerebral asymmetry, a battery of shorter tests, ideally administered in one session, is attractive (see Chapter 4). Fortunately, in spite of the Hunter and Brysbaert (2008) caveat, experiments with a shorter number of trials (e.g. Hugdahl & Franzon, 1985) have had some success in distinguishing between dextrals and adextrals with a language related task.

Other experiments in the visual domain have depended upon perceptual bias but employ free-viewing techniques, the most popular of which is the use of chimeric faces. Chimeric faces are composite images of two different faces, where each side of the face has an independent characteristic, e.g. one side of the face is happy and the other is sad (Levy, Heller, Banich, & Burton, 1983). Participants tend to be biased towards the side of the face presented on the left side, and this bias has been reported as larger in dextrals than adextrals (Levy, Heller, Banich, & Burton, 1983; David, 1989; Bourne, 2008). Therefore various tasks that test both left and right hemisphere related processes have been shown to differentiate dextral and adextral participants.

Many other behavioural tests of laterality were published in the 1980s and 1990s, some of which enjoyed some popularity for a short period of time, and others have faded into obscurity rather quickly. In chapter four a battery of six perceptual asymmetry tests is presented, alongside a more in depth introduction to the literature behind each task. Selecting from the multitude of different indirect perceptual experiments present in the literature was difficult. Nevertheless, we tended to be biased towards tests where dextrals and adextrals were both lateralised in the same direction, but to a different degree. More explicitly, the particular behavioural asymmetry (especially if related to speech and language) would be reduced in adextrals, paralleling the reduced incidence of left hemisphere language dominance, as suggested by the epilepsy Wada literature, as well as fMRI, fTDS, ECT, and other techniques (Carey & Johnstone, 2014).

1.5 Other measures linked to underlying cerebral asymmetries

Functional transcranial doppler sonography (fTDS), like fMRI, uses changes in blood flow to identify highly activated brain areas. Instead of the BOLD signal, ultrasound is used to measure changes in cerebral bloodflow velocity through the middle cerebral artery in each hemisphere (Deppe et al., 2000). It is considerably less expensive than fMRI, and has been used as another method of determining cerebral dominance for language functions (Whitehouse & Bishop, 2009; Badcock, Nye, & Bishop, 2012; Groen, Whitehouse, Badcock, & Bishop, 2012), and validated alongside Wada test results (Knecht et al., 1998).

fTDS has also been used with right and left handers. Knecht et al. (2000) used scores on a handedness questionnaire to split data from 326 healthy participants into seven subgroups based on degree of hand preference, ranging from "strong right-handers" to "strong left-handers". They found that the incidence of atypical language representation increased to ~27% in strong left-handers. If this figure were accurate, scanning 60 strong left-handers with fMRI would lead to a sample of 15 right-brain dominant individuals. Although improving significantly upon scanning 100 adextrals to find 15 individuals with atypical language lateralisation, there are some limitations fTDS. Laterality indices (LIs) are calculated based on the peak difference value between the left and right channels while the participant carries out the relevant task (e.g. verbal fluency or picture description; Knecht et al., 2000, Groen, Whitehouse, Badcock, & Bishop, 2012). This would be less of a problem if many trials were undertaken, but typically studies involve ~10 'epochs' of the relevant task.[4]

A further technique that has gained popularity in cognitive neuroscience is that of measuring event-related potentials (ERPs). ERPs are an index of brain electrical activity measured from electrodes set on the scalp. Continuous electroencephalogram (EEG) is recorded whilst a stimulus (the "event" in ERPs) is presented to the participant. The EEG is then broken down into short 'chunks', or epochs, that are time-locked to stimulus onset, and the brain waveforms that appear in this epoch are the ERPs (Rugg &

---

[4] This issue was brought to our attention in a conference talk by Dr Reint Geuze; Durham 11th September 2014.

Coles, 1995). Different categories of visual stimuli manipulate the amplitude of these waveforms, and these changes are used as a quantitative measure of functional activity (Donchin, Ritter, & McCallum, 1978). The N170 measure (so named as it is a negative peak of activity ~170 msec; see chapter 3 for more detail) has been demonstrated to be particularly sensitive to face stimuli as compared to a control stimulus (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Bötzel, Schulze, & Stodieck, 1995; Rossion et al., 2000). This increased amplitude to faces is often larger over right electrode sites than left. Given what we know about the lateralisation of face processing functions, it is tempting to suggest that this N170 asymmetry could be a marker of hemispheric cerebral asymmetries. There is, however, a large literature debating whether the N170 really is face selective.

Thierry, Martin, Downing, and Pegna (2007a) published a study suggesting that the large change in N170 amplitude after face presentation was due to methodological factors. It was claimed that faces were always presented face on, cropped to a uniform outline, occupying the same number of pixels on the screen, etc., whilst stimuli in the object/control categories varying greatly (labelled as uncontrolled interstimulus perceptual variance, or ISPV). This investigation involved face, car, and butterfly stimuli, and controlled for low or high ISPV. The results showed that the N170 was sensitive to ISPV but not to stimulus category.

As a whole field of electrophysiological research had been working on N170 face-specificity for 15 years, research groups made several attempts to oppose with the results of Thierry et al. (2007a). Bentin et al. (2007) immediately published a rebuttal in which they restated N170 effects where ISPV was in fact controlled, stating that “Thierry and colleagues’ claim is wrong and misleading” (pg 801). Rossion and Jacques (2008) claimed that Thierry et al. (2007a) reported data from the wrong electrode sites, and that the modulation of N170 in relation to ISPV probably reflected a biased comparison of different quality sets of images. Following this critique, Dering, Martin, and Thierry (2008) published a study using the recommended electrode sites and followed other methodologies laid out in the criticism. They found that mean N170 amplitude was larger for cars than for faces. What neither side is debating is that the N170 is indeed a response that is affected by face stimuli.

An appealing aspect of the N170 to faces is that it appears to be lateralised to right scalp sites. For our purposes, a rightward asymmetry in a measure that is related to face perception could be a useful marker of a participant's cerebral organisation. In fact, attempts have been made at source analysis of the N170, and results point towards the posterior superior temporal sulcus (Batty & Taylor, 2003; Itier & Taylor, 2004, Nguyen & Cunnington, 2014), an area the human neuroimaging and primate single-cell recording literatures suggest is involved in face and body processing (see Allison, Puce & McCarthy, 2000, for a review).

There is also work suggesting that a larger N170 over left scalp sites can be elicited following word or language-related stimuli (Rossion, Joyce, Cottrell, & Tarr, 2003; Maurer, Bradeis, & McCandliss, 2005; Simon, Petit, Bernard, & Rebai, 2007; Maurer, Zevin, & McCandliss, 2008; Maurer, Rossion, & McCandliss, 2008). However, none of the studies investigating language-related N170s have included adextral subjects, and no N170 studies report the proportions of their sample showing certain asymmetries. Although some of the face N170 work has included adextral subjects, the samples were never large enough for separate analyses, and researchers tended to average their data with that of the dextrals (e.g. Rossion et al., 1999; Batty & Taylor, 2003; Goffaux, Gauthier & Rossion, 2003).

Measures such as these could therefore be useful predictors of cerebral asymmetry, if the N170 asymmetry is robust in individual participants. Throughout this thesis, an emphasis on reporting data from individual participants (in the form of proportions) is present. Across all experiments, the proportions of individuals displaying the typical or atypical pattern of results are reported. Here, typical tends to refer to what we expect from a majority of dextral participants, given their reduced variability in terms of cerebral organisation, relative to adextrals.

A completely different type of data, which may speak to cerebral asymmetries as well, is made possible by modern techniques for measuring movements. The recording of manual actions with high spatial and temporal frequency is now accurate and affordable, but rarely used by laterality researchers. There is a large body of research investigating the specialised role of the left hemisphere in motor control of movement (Kimura & Archibald, 1974; Kimura, 1993; Elliott & Roy, 1996; Goldenberg, 2013). Given the population level right hand preference for skilled motor tasks (such as handwriting and throwing), some scientists argue that a left hemisphere system controlling the muscular requirements of speech would give some motor advantages to the limbs controlled by the same hemisphere (Goodale, 1988; Kimura, 1993; Rushworth, Krams, & Passingham, 2001; Carey et al., 2009).

In dextral participants, the most robust of these advantages is a shorter right hand movement duration (Fisk & Goodale, 1985; Carson et al., 1993; Elliott, Chua, & Pollock, 1994), recorded in visually-guided aiming experiments. In these studies participants make reaching movements to suddenly-appearing visual targets. Under these conditions, dominant hand peak velocity advantages are also often reported (Carey, Hargreaves, & Goodale, 1996). Accuracy also tends to favour the right hand, suggesting that these shorter movement times (and higher peak velocities) are not obviously related to a speed-accuracy trade off.

As well as these dominant hand advantages in dextrals, multiple studies report finding a left hand advantage in reaction time (Brown et al., 1989; Bradshaw, Bradshaw, & Nettledon, 1990; Carson, Chua, Elliott, & Goodman, 1990; Carson et al., 1992; Elliott et al., 1993; Carson et al., 1995; Carson, 1996; Boulinguez, Nougier, & Velay, 2001ab; Carey et al., 2015). This phenomenon is often linked to a potential right hemisphere advantage in visuospatial or movement planning processes, providing a reaction time (RT) advantage to its controlled hand (Elliott et al., 1993; Barthélémy & Boulinguez, 2001ab; Barthélémy & Boulinguez, 2002; Carey et al., 2015). Due to the 'privileged access' of each hand's motor output to other mechanisms in the contralateral hemisphere, theoretically, differences between the hands in terms of motor performance should reflect the specialisations of each hemisphere (Goodale, 1988; 1990; Poizner, 1990; Bagesteiro & Sainburg, 2002). Less is known about these manual asymmetries in adextral subjects, as few studies include these participants.

Goodale (1990) tested a small sample of adextral participants on a visually-guided aiming experiment and claimed that, on average, adextrals generally have slower movement times, and present with a left hand RT advantage. His averaged adextral data shows no difference between the hands for peak velocity, duration, or deceleration duration. This is an apt example of the commonly encountered caveat of averaging adextral data. As his adextral sample is more likely to be heterogeneous in terms of cerebral organisation, it is hard to interpret from averaged data whether individual adextral participants are less asymmetrical than the dextrals, or if a certain proportion of them behave just as the dextrals, with a subgroup showing a reversed pattern of equal magnitude.

Given that a majority of adextrals have language functions dominant in their left hemisphere (Rasmussen & Milner, 1974), if the praxis system is dominant in the same hemisphere as language processing, most left handers would have a dominant praxis system supporting their non-dominant hand (Main & Carey, 2014). Therefore, we might expect most left handers to have duration or peak velocity advantages with their non-dominant *right* hand. In addition, if visuospatial functions are complementarily organised with language or motor systems, we might expect the *left* hand reaction time to present in a majority of adextrals. If these manual asymmetries are dependent upon functional hemispheric asymmetries, then they may be useful in identifying an individual's cerebral asymmetry for such functions. Therefore to determine this possibility, assessment at the individual level is necessary, estimating what proportion of dextral or adextral participants display these differing hand advantages.

1.6 The current body of research

There is a gap in the brain asymmetry literature in terms of a proportional approach to assessing predictors of cerebral organisation. It would be useful to identify individuals with atypical organisation for various reasons. Any hypotheses relating to language asymmetry, which are commonly based on observations in 'typical' participants, could be tested in atypical individuals. This is also true for any theories of complementary hemispheric specialisation. Additionally, this subgroup of individuals could help assess genetic models of asymmetry versus hand preference inheritance.

Questions about handedness could also be better assessed if easier identification of typical/atypical adextrals were possible. For example, typical dextrals and adextrals (both groups having left hemisphere dominance for speech and language, and by implication, some aspects of motor function) could be compared to identify what the neural consequences are of preferential use of one hand that come from experience and practice. It would also be possible to tease apart whether the praxis system and language processing network overlap in the same hemisphere in typically-organised adextrals.

This enterprise is exciting for the cognitive neuroscience of language and handedness, and could be interesting for the aphasia literature. The claim by Subirana (1969) that adextrals have better recovery from aphasia most likely relates to some bilateral organisation of language functions. Right hemisphere language regions could be investigated using some of the same techniques that have been validated in left-brain dominant dextrals, the only group routinely studied in this field to date. For example, it is largely unknown whether right hemisphere language functions depend upon homologues of the left hemisphere language regions. This research could have implications for post-stroke rehabilitation.

In order for research into atypical lateralisation of functions to advance, participants with atypical cerebral organisation must be more easily identifiable. We have begun a line of research into factors that may be predictive of functional brain asymmetries. In this thesis, I will describe a series of experiments where we tested whether each outcome measure may be related to the lateralisation of language.

The logic behind all the experiments included is the same. If a particular measure were predictive of an individual's brain asymmetry, we would expect a large majority of dextrals, and a smaller majority of adextrals, to behave in the same way, i.e. in the same direction of the asymmetry of their responses. The decreased majority showing any given behaviour in adextrals relative to dextrals reflects the difference in prevalence of left hemisphere language dominance between dextral and adextral samples. Similarly, if the proportions of each sample showing an effect are different, we might also expect a difference in mean scores between the groups on that measure.

This proportional approach provides a crude assessment of whether a certain task may be tapping into asymmetries in functional organisation. If a clear majority of dextrals, who we expect to be ~95% left lateralised for language (Rasmussen & Milner, 1977), do not show the same asymmetry in their responses (e.g. an REA or a RVF advantage), we might conclude that measure is not successful in aiding prediction of functional lateralisation. This logic translates to adextrals participants too, but we would expect a marked decrease in the 'typical' proportion when compared to the dextral sample.

In Chapter 2 a very large-scale visually-guided aiming experiment investigating manual asymmetries in dextrals and adextrals is reported. We report the proportions of each sample displaying manual asymmetries that may be related to brain asymmetry, as well as measures of central tendency, and correlations between the movement measures.

Chapter 3 contains an ERP study of the lateralisation of N170 waveforms. The asymmetry of this waveform in both dextrals and adextrals is assessed across two experiments. Again, particular attention is paid to the proportion of each sample showing a rightward N170 in response to faces and a leftward N170 in response to words, but averaged responses are also reported.

In Chapter 4, our indirect perceptual test battery is presented. This is a set of six indirect perceptual asymmetry tests, including dichotic listening and VHF paradigms thought to be related to both left and right hemisphere processes. Statistical analysis of both the proportions and measures of central tendency are reported, as well as correlations between these six measures.

The above methodologies were employed due to their potential usefulness for providing markers of cerebral asymmetries. The indirect perceptual tasks described in Chapter 4 have traditionally been associated with investigations into cerebral lateralisation, but their combined predictive power has not been systematically tested. In contrast, the use of kinematics and electrophysiology to answer questions relating to functional lateralisation remains largely unexplored. There are, however, good theoretical reasons outlined above to anticipate a relationship between the results from these experiments and cortical organisation.

Finally our fMRI project is reported in Chapter 5. Brain activity relating to language, face and body perception was obtained from each participant, so that we could determine their cerebral asymmetry for these three functions. These participants had also taken part in multiple experiments from earlier chapters in this thesis. Therefore preliminary commentary upon the relationships of these measures to functional cerebral asymmetries is provided.

This is an appropriate time to undertake such a project. Although the collection of behavioural data from large numbers of participants is time-consuming, it is not costly (at least relative to fMRI). In addition, the availability of fMRI allows for actual examination of how successful a combination of indirect measures may be in predicting functional lateralisation.

Chapter 2 – Are manual asymmetries a consequence of cerebral asymmetries?

2.1 Introduction

As both hands are controlled contralaterally (that is, the left hemisphere is largely responsible for the motor control of the right hand, and the right hemisphere the left hand), it has been suggested that subtle asymmetries in manual motor performance should be consistent with specialisations of each hemisphere (Goodale, 1988, 1990; Carey et al., 2015).

Neurologists and neuropsychologists interested in limb apraxia and related phenomena have amassed a large literature on the specialised role of the left hemisphere in motor control of movement (Kimura & Archibald, 1974; Kimura, 1993; Elliott & Roy, 1996; Goldenberg, 2013). As a right hand preference for skilled motor tasks (such as handwriting and throwing) is present at a population level in humans, and considering what is known about incidences of left hemisphere language lateralisation in the population, some scientists argue that perhaps a left hemisphere system involving control of the articulatory requirements of speaking would give some motor advantages to the limbs controlled by the same hemisphere (Goodale, 1988; Kimura, 1993; Rushworth, Krams, & Passingham, 2001; Carey et al., 2009). Evidence from the visually-guided aiming literature supports this hypothesis. Experiments with dextral participants have found a robust right hand advantage for movement duration (Fisk & Goodale, 1985; Carson et al., 1993; Elliott, Chua, & Pollock, 1994; Carnahan, 1998), as well as peak velocity (Carey, Hargreaves, & Goodale, 1996; Carey et al., 2015).

Given that a majority of adextrals have language functions dominant in their left hemisphere (Rasmussen & Milner, 1974), if the praxis system does 'co-organise' to the same hemisphere as language processing, the majority of left handers would have a praxis system arranged to support their *non-dominant* hand (Main & Carey, 2014). Whether such a system would advantage the non-dominant hand, disadvantage the dominant hand, or both, is unknown.

As well as a right hand superiority in some measurements of movement times (Fisk & Goodale, 1985; Elliott et al., 1993; Carnahan, 1998), a left hand advantage is often present in reaction time (RT; Brown et al., 1989; Bradshaw, Bradshaw, & Nettledon, 1990; Carson, Chua, Elliott, & Goodman, 1990; Goodale, 1990; Carson et al., 1992; Elliott et al., 1993; Carson et al., 1995; Carson, 1996; Boulingue, Nougier, &

Velay, 2001ab; Carey et al., 2015). This left hand RT advantage is usually explained as a product of a right hemispheric process related to movement planning, visuospatial attention, or localising visual stimuli (Elliott et al., 1993; Barthélémy & Boulinguez, 2001; Barthélémy & Boulinguez, 2002; Carey et al., 2015). Studies of motor control in patients with unilateral brain lesions largely agree with a right hemisphere explanation of this finding, providing evidence that patients with right hemisphere lesions have delayed movement initiation when compared to those with left hemisphere damage (Fisk & Goodale, 1988; Haaland & Harrington, 1989).

Carson et al. (1992) attempted to manipulate the left hand RT by adding to the "spatial complexity" of a reaching task, in which participants would identify the final position of a target array to complete a complex figure. It was hypothesised that the more complex the figure, the more demanding the task was on visuospatial processes (therefore a change in RT was anticipated); however no effect of figure complexity was found.

Another attempt to manipulate RT was made by Elliott et al. (1993), where participants were asked to point to the centre of multiple circle stimuli that varied in diameter. Again perceived task difficulty did not have an effect on motor outcomes. These tasks varied in difficulty in a cognitive sense, but in terms of localising or motor performance, the conditions were matched, as the target or endpoint where participants were expected to reach to did not vary across condition. The endpoint of the complex figures in Carson et al. (1992) was always the same location, and there were only three unique centre points of the stimuli in Elliott et al. (1993). If the left hand RT advantage is related to visuospatial demands in relation to movement, then the complexity of the visuospatial task should have an outcome for the motor response, that is, if the task varies in the visual domain, but does not require varied motor responses, a participant can largely ignore any stimuli manipulations, as after a few trials they offer no new information for the motor response.

Researchers have also manipulated movement durations using attention-taxing Posner cueing paradigms. Bestelmeyer and Carey (2004) reported that while the right hand of dextrals was unaffected by invalid cues, the left hand was significantly slowed.

If manual asymmetries in movement duration, peak velocity, and RT are related to cerebral organisation of specific functions, the effect might be reduced in an adextral sample. It is thought that ~70% of adextrals share the same cerebral organisation as

~95% of dextrals (at least in terms of language lateralisation). Therefore, if manual responses were a consequence of related functional cerebral asymmetries, a decreased prevalence amongst a sample of adextrals would also be predicted. This hypothesis assumes some level of complementary specialisation when considering right hemispheric contributions to left hand advantages. There are no estimates for the proportion of dextrals who have right lateralisation of the processes underlying the left hand RT advantage, let alone estimates for adextrals.

There have been a small number of visually-guided aiming experiments that included adextral participants. Goodale (1990) claimed that adextrals are slower to initiate movements, and reach lower peak velocities than their dextral counterparts, but also presented with a mean left hand RT advantage (see figure 2.1). Notable in this particular experiment is that the dextral sample showed a RT advantage with their dominant hand, opposing the usual finding. These data showed that adextrals, on

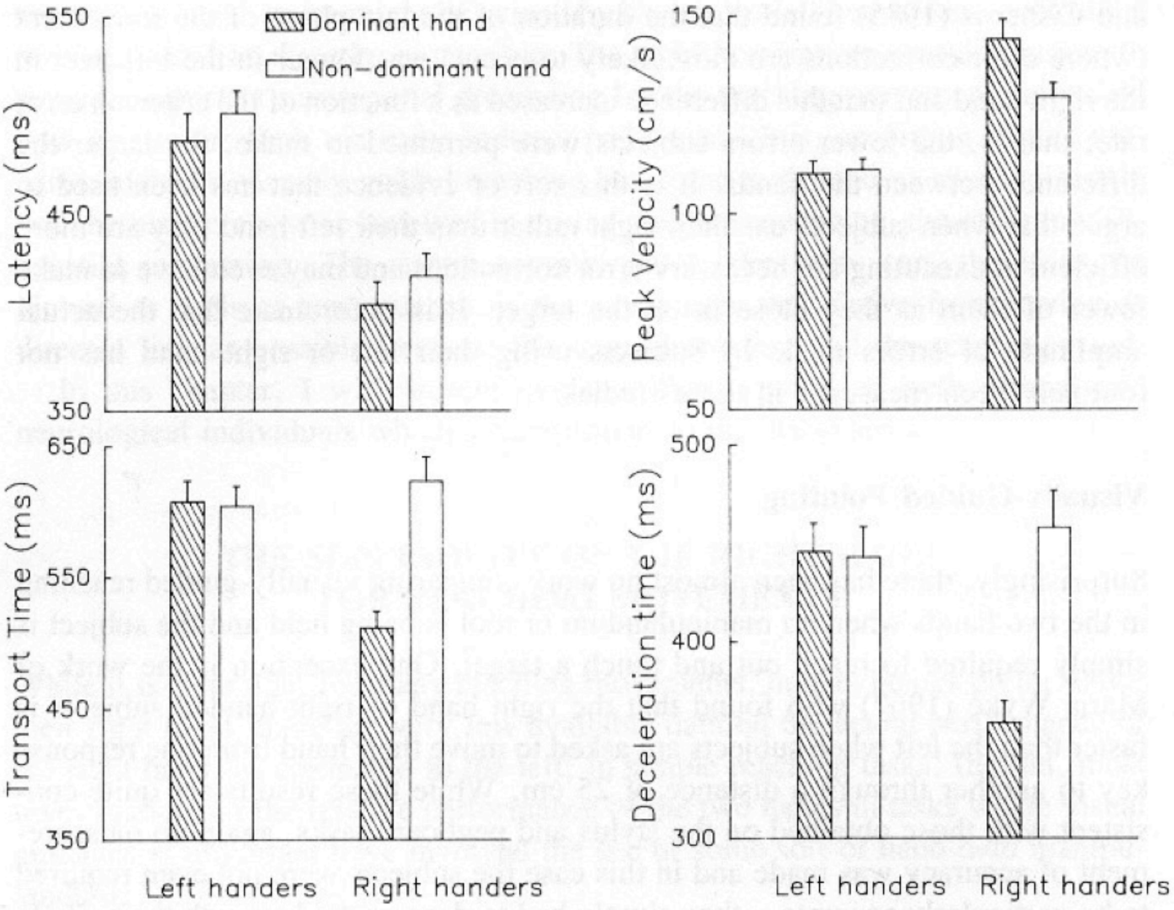


Figure 2.1 – Figure taken from Goodale (1990) displaying data from dextral and adextral samples on four different measures of speed during manual aiming movements. What is apparent from this figure is that adextrals are generally slower, as well as less asymmetric than the dextral participants.

average, were far less asymmetrical than dextrals in terms of their manual asymmetries, with no differences between the hands other than in RT. Goodale (1990) stated that these results are consistent with the idea that adextrals would, on average, have less pronounced hemispheric lateralisation than in typical dextral participants. What cannot be inferred from this paper, is whether adextral participants, as individuals, are less asymmetrical in terms of their manual responses, or whether a certain proportion of the sample show an asymmetry in one direction, with the reverse response present in the rest of the sample. These alternatives have rather different theoretical implications; the former suggests a mixture between inherited dominance and practice of skilled movements with the preferred hand, the latter links hand differences quite directly to hemispheric dominance.

The inability to assess this result highlights a real limitation of reporting measures of central tendency exclusively; valuable information about the individuals in the sample is lost. It is entirely possible that none of the adextral participants in this study were symmetrical in terms of their motor responses, and yet that is the finding at the group level. One aim of this chapter is to analyse patterns of behaviour in terms of proportions of the samples showing an effect, as well as at the group level, in order to gain more information about adextrals' manual symmetries or asymmetries.

Boulinguez, Velay and Nougier (2001a,b), in a very similar experiment (published as two separate papers for the dextral and adextral samples), report conflicting results where an overall RT advantage favouring the left hand was found in dextrals and adextrals. Their interpretation of these results in terms of functional hemispheric asymmetries, however, is similar to that of Goodale (1990). In this case Boulinguez and colleagues emphasise the probable majority of adextrals being lateralised in the same way as dextrals, whereas Goodale (1990) emphasised the probable minority that would have reversed lateralisation.

These two studies, however, have some methodological issues, in particular a very small sample of adextrals (Goodale (1990) $n = 8$; Boulinguez, Velay & Nougier (2001b) $n = 7$). Studies of adextrals are particularly susceptible to sampling error given the increased heterogeneity of brain organisation when compared to dextrals (Kim, 1994). With such small *n*s these studies could contain only typically lateralised individuals, or a small number of atypicals who would have a large effect on any measures of central tendency.

As a demonstration of this problem, I created a dataset containing 1000 dummy cases; 700 "typical" and 300 "atypical" participants, to simulate an adextral sample. I randomly sampled eight cases from this dataset 50 times, and obtained the percentage of typical participants in each random sample. Of fifty samples, seventeen had 75% typical participants, 5/50 samples had 100% typical samples and 4/50 samples had ≤50% typical participants (see figure 2.2). The results of this analysis are not devastating for small *n* studies of adextrals, but ~40% of samples had a largely over- or under-representative numbers of "typical" participants. We would like to do more sophisticated power analyses of real datasets to establish how many *trials* or *participants* are appropriate for visually-guided aiming experiments, and these will be discussed later in this chapter.

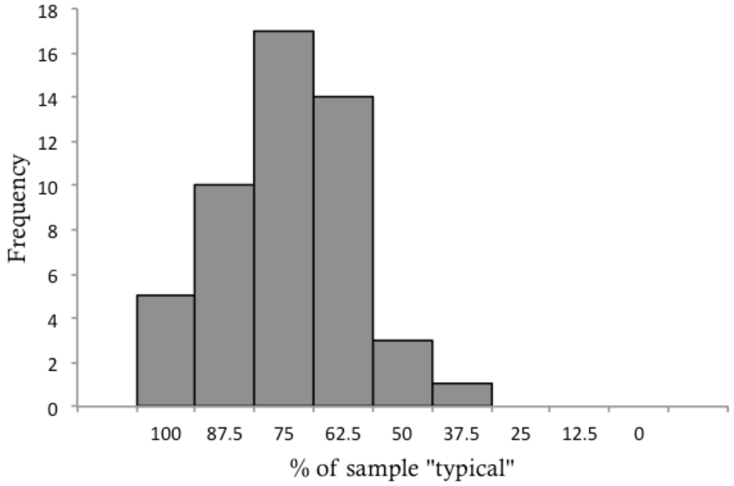


Figure 2.2 – Frequency histogram displaying prevalence of typical dominance across 50 random samples of 8 participants. These samples were taken from a theoretical dataset of 1000 cases (including 70% typical and 30% atypical cases).

As well as a small number of participants, Goodale (1990) and Boulinguez, Velay, and Nougier (2001a,b), include only a small number of targets (four; two on each side of fixation/participant's midline). These target locations would be easy for participants to identify, learn, and even mentally label (i.e. "the far left target", "the near right target"). These paradigms might not "push" any potential localisation/ visuospatial attention functions of the right hemisphere. Additionally, in the paradigm adopted by Boulinguez, Velay, and Nougier (2001a,b), the participants made the pointing movements using a stylus. Manipulating such an implement involves movements that are extremely over practiced for our dominant writing hand. However, since their adextral sample behaved similarly to the dextral sample, and both samples had a left hand RT advantage, this tool appears not to have caused dominant hand differences between dextrals and adextrals.

Despite considerable theorising, there is remarkably little evidence to connect left hand RT effects with a specific right-hemispheric process. An indirect source of evidence is that if manual asymmetries were related to practice of fine motor movements with the dominant hand, adextral participants would present as the reverse of dextrals; this pattern of results is clearly not the case (from the small *n* studies cited above, at least). For the purposes of the present chapter, what is crucial is whether or not manual asymmetries in adextrals, when assessed at the individual level, mimic hand differences in dextrals. It was anticipated that the 'typical' asymmetries (i.e. those shown by a majority of dextrals and thought to be indicative of typical cerebral organisation) would be present in a majority of participants, but that this majority would still be smaller than the number of dextrals showing the effect. In other words, if a specific hand marker was a 'perfect' predictor of cerebral asymmetry, then ~95% of dextrals would show this specific hand advantage, as would roughly 70% of adextrals (by specific I mean the right or left hand, as opposed to the dominant or non dominant hand). If manual asymmetries are related to right and left hemisphere processes, it is assumed that the proportions of dextrals that are right/left brain dominant for these processes are related to our estimates of language lateralisation proportions.

The present study is a large-scale attempt to make definitive conclusions about hand differences in visually guided aiming between dextral and adextral participants. This study is an improvement on the previous ones in a number of ways. First, and most obviously, sample size is substantially increased, which will not only allow for more reliable and representative average data, but will also allow for estimating the proportion of dextral and adextral samples presenting with relevant manual asymmetries. Secondly, we have included a wider range of target locations, as compared to the often limited number of target positions used in this literature. In addition, target position was varied in two dimensions rather than one. It was anticipated that varied movement distances, and multiple endpoints within an expansive two-dimensional target array would tax localisation related processes (i.e. visuospatial attention). It was predicted that a higher proportion of dextrals would present with a left hand RT advantage than adextrals. If the left hand RT advantage is indeed related to a functional cerebral asymmetry, it was expected that both groups would have a majority of participants with a *left hand* RT advantage (as opposed to a non dominant hand advantage), but that this majority would be higher in the dextrals. As commonly reported right hand advantages in movement duration, peak velocity, and deceleration duration are taken as evidence for a left hemispheric specialisation for motor functions, it was anticipated that these advantages would occur in the majority of both dextral and adextral samples, but with that proportion being higher in the dextrals.

2.2 Method

2.2.1 Participants

Participants were 102 undergraduates, postgraduates, and staff members in the Psychology departments of the University of Aberdeen and Bangor University. Two equal groups of dextral and adextrals, were devised based on handwriting hand and score on a modified version of the Waterloo Handedness Questionnaire (WHQ; Steenhuis & Bryden, 1989). For our purposes, adextrals were any participant who preferred to write or throw a ball with their left hand, or who reported as having been pressured to switch from writing with their left hand as a child (this classification is used throughout this thesis). Dextrals had a mean score of +28.29 on the WHQ, and adextrals had a mean score of –18.40. Within the dextral group there were 27 females and 24 males with an age range of 20-52 and a mean age of 28.29. The adextral group contained 25 females and 26 males, an age range of 18-54 and a mean age of 30.10. Eye and foot dominance was also recorded from most participants (*n*=97), which are thought to be weak predictors of brain asymmetry (McManus, 1991; Carey, 2001; Carey et al., 2001; McManus, 2004). Of 48 dextrals, 45 were right-footed and 30 were right eye dominant. Of 49 adextrals, 17 were right-footed and 24 were right-eyed.

2.2.2 Apparatus and stimuli

Movements were recorded using a Qualisys Oqus motion capture system with a three camera set-up (Qualisys, Sweden) recording at a frequency of 240 Hz. This was a substantial improvement on the 25 Hz capture frequency reported in Goodale (1990). Recording 25 frames per second will allow each data point to be recorded to the nearest 40 msec, whereas recording with 240 Hz allows for accuracy within 4 msec. To estimate the spatial accuracy of our camera system, ten trials were collected of a static infrared marker (with a duration of five seconds). The biggest difference in the position data across trials was 3, 2.8, and 3.3 mm in the *x, y* and *z* dimensions.

The forty targets used were white filled circles with a diameter of 1cm (although participants' height affected individual viewing distance, we estimated an average viewing height of 55 cm, which would give the targets a visual angle of 1°). The target grid was arranged with horizontal (14 targets) and vertical (10 targets) meridians, with targets separated from one another by 5 cm. There were also four additional targets positioned in a 10 cm square in each quadrant (see figure 2.3). Targets were displayed on a black background.

These stimuli were presented to the underside of a bespoke glass top table (140 x 106 cm) using a short-throw Sanyo PDG-DWL2500 Multimedia Projector. The projector mirrored a computer running EPrime 2.0 software (Psychology Software Tools, Pittsburgh, PA) to present the stimuli, and a second computer collected infrared marker data. The start position for participants was a Velcro pad located in the centre of the closest table edge, 30 cm from the central fixation point. The most peripheral of the targets were 35 cm (or 35°) lateral to fixation. An infrared reflective marker with a diameter of 1 cm was attached to the nail of participants' index fingers using adhesive Velcro.

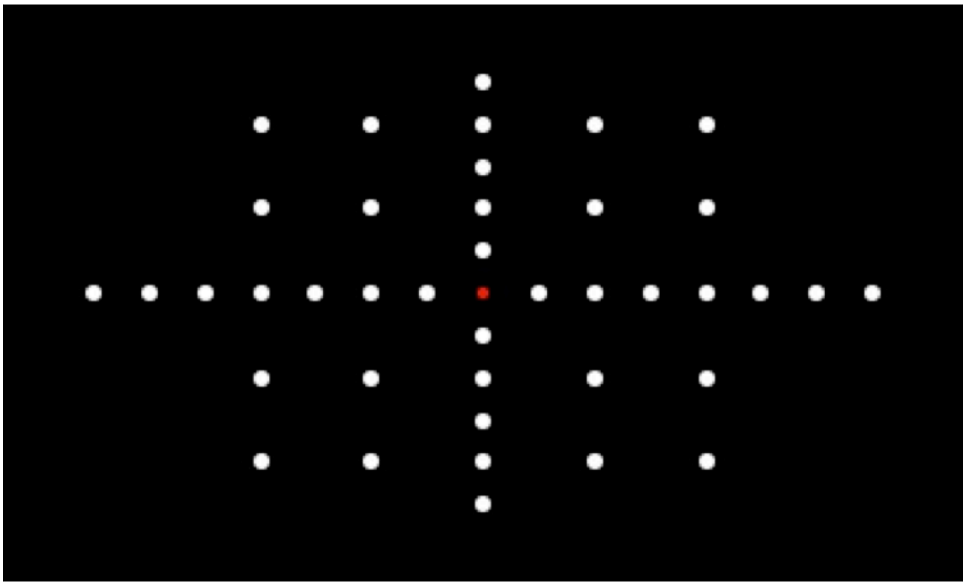


Figure 2.3 – A representation of the two-dimensional target grid. The red circle represents fixation location.

2.2.3 Procedure

Participants sat oriented to the middle of the table. A central fixation cross was presented at the start of every trial. A verbal cue from the experimenter would precede the start of each trial to ensure participants were focused and prepared. The experimenter would then initiate the trial with an audible key-press; the fixation cross would disappear, a variable delay of 200, 400, or 600 msec would follow before the target would appear for 400 msec. This brief duration has been used in previous experiments to encourage rapid responding (Carey, Hargreaves, & Goodale, 1996). A trigger was sent to the cameras to begin collection simultaneously with target presentation. Participants were instructed to reach as quickly and as accurately as possible to the target location and to remain where they landed until instructed to return to their starting point. After target offset there was a 1600 msec delay before the fixation cross for the next trial appeared. Infrared cameras recorded movement at 240 Hz for two seconds from target onset, resulting in 480 frames of movement data. Participants completed three 80-trial block pairs in each of two sessions (resulting in a total of 480 trials). All 40 targets appeared once in each block, and each hand carried out one block in each pair. Two different target orders were used, which, across session with counterbalancing, meant both hands reached to targets in the same sequence within blocks.

The room was dimly lit for maximum target visibility. To control for order effects, across the two sessions both hands completed the identical target order as each other. After both sessions were completed experimenters asked participants which hand they thought was "faster", which was "more accurate", and how many target locations they thought there were.

2.2.4 Analysis

We used a suite of LabVIEW programs (3Wave) for data processing. Raw position data were differentiated into a three-dimensional format and filtered with a 10 Hz, low-pass filter, to remove high-frequency noise from the data. From the filtered files we extracted RT (i.e. msec from target onset to movement onset), peak velocity (mm/sec), movement duration (msec), and deceleration duration, which was calculated as a proportion of duration. This is an improvement upon Goodale (1990) where deceleration duration was calculated as time to peak velocity subtracted from duration, therefore being entirely confounded with duration. We used a velocity of 30 mm/s as a threshold for both movement onset and offset (Carey & Liddle, 2013; see figure 2.4). Side of space was not included as a factor in analyses as we have controlled for this variable by ensuring equal numbers of reaches by each hand into each side of space.

Often in the visually-guided aiming literature, researchers report separate ANOVA analyses for each of these dependent variables separately (e.g. Carson, Chua, Goodman, Byblow, & Elliott, 1993; Carey, Hargreaves, & Goodale, 1996; Barthélémy & Boulinguez, 2002). It is very likely, however, that these measures are correlated with one other. For the current project, correlations between these variables are reported. MANOVA was used to analyse group means, as it is a more appropriate analysis of multiple, related, dependent measures (Cole, Maxwell, Arvey, & Salas, 1994). Post hoc 2x2 ANOVAs were also run between handedness group and hand (dominant/non dominant) for each of the four dependent variables, to investigate group differences that may be present within each measure.

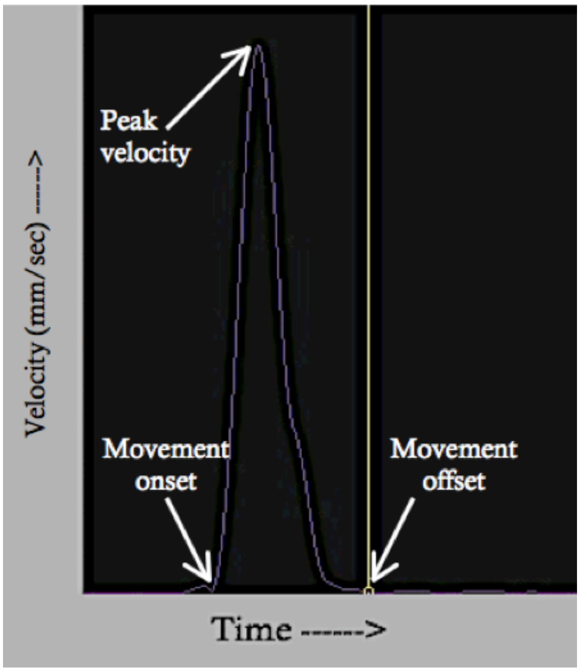


Figure 2.4 – A typical velocity profile for one aiming movement. Duration was calculated as offset – onset.

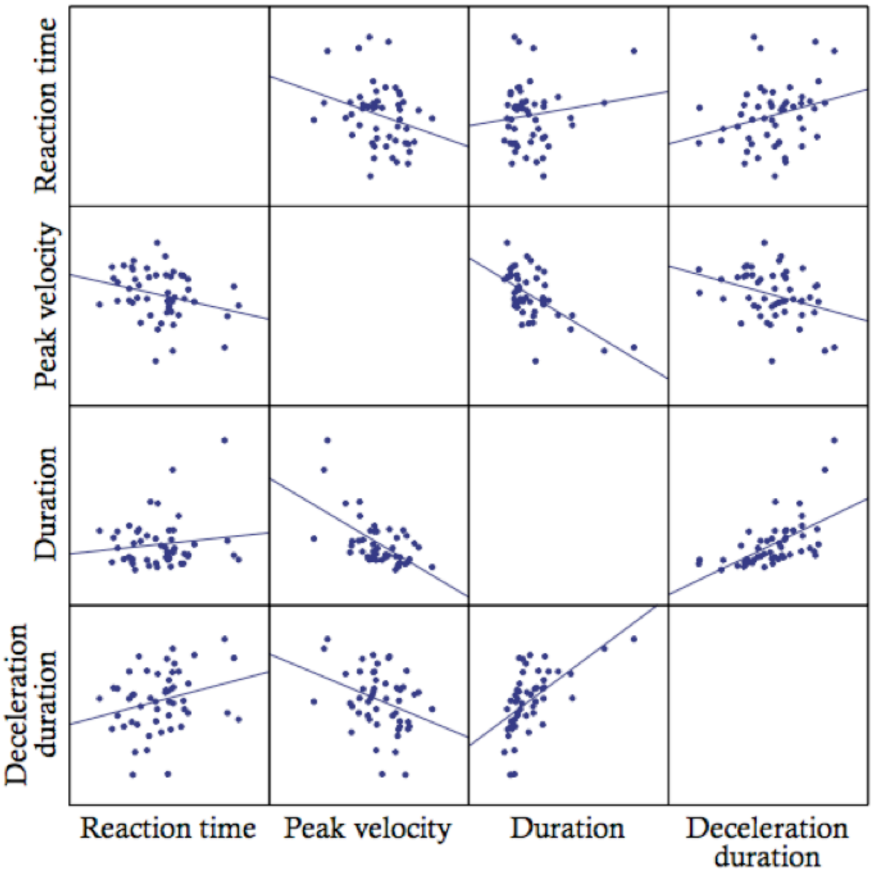
It was predicted that a higher proportion of dextrals than adextrals would display a left hand RT advantage, or a right hand peak velocity/duration/deceleration duration advantage. Therefore z-tests were used to calculate whether the proportions of the two groups displaying these manual asymmetries are different to one another.

2.3 Results

2.3.1 Correlations

Bivariate correlations between the four dependent variables (RT, peak velocity, duration, and deceleration duration) are reported separately for the dextral and adextral groups. In the dextrals significant negative correlations were found between peak velocity and RT ($r = -.28$, $p<.05$), peak velocity and duration ($r = -.60$, $p<.001$), and peak velocity and deceleration duration ($r = -.34$, $p<.02$), as well as a significant positive correlation between duration and deceleration duration (*r* = .60, *p*<.001). In the adextral sample, however, significant correlations were only found between duration and peak velocity (*r* = -.39, *p*<.01), and duration and RT (*r* = .34, *p*>.01; see figure 2.5 and 2.6 for the dextral and adextral scatterplots respectively).

Despite some non-significant correlational relationships, the data suggest these dependent variables are not independent sources of variance, and therefore provide evidence to warrant the use of MANOVA. In fact for both samples there were non significant correlations with *r* values of .27 (dextrals: RT x deceleration duration, *r* =.27, *p* =.056; adextrals, duration x deceleration duration, *r* =.27, *p* =.052).



<u>*Figure 2.5* – Matrix scatterplot showing the relationship between each of the four dependent variables in the dextral group.</u> Peak velocity correlates negatively with all other measures as it is the only variable where a higher is 'better'.

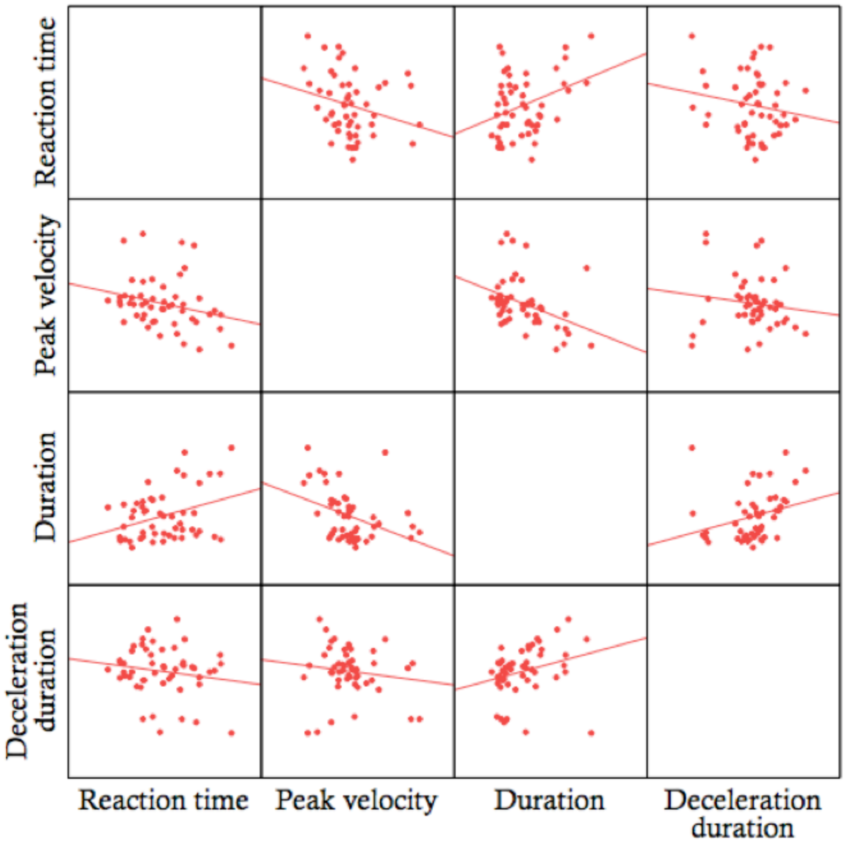


Figure 2.6 – Matrix scatterplot showing the relationship between each of the four dependent variables in the adextral group. The only significant correlations in this figure are between duration and RT, and duration and peak velocity.

2.3.2 Measures of central tendency

2.3.2.1 MANOVA

A MANOVA analysis of all four dependent measures broken down by dominant/non dominant hand, with handedness group as the fixed factor was run. A Box's M statistic of 81.95 and an associated *p* value of <.001 was obtained, suggesting the covariance matrices between the group are not equal. It is commonly reported, however, that this test is highly sensitive and if the group samples are large enough, and equal, the violation can be largely ignored (Tabachnick & Fidell, 2001; Field, 2009). The multivariate result was significant for group (Pillai's Trace=.33, *F*(8,93)=5.69, *p*<.001, ηp^2=.33). Pillai's trace is reported as it is cited as the most robust to violations of test assumptions (Tabachnick & Fidell, 2001). The univariate *F* tests showed significant differences between participant groups only for dominant hand durations (*F*(1,100)=6.06, *p*<.02, ηp^2=.06, obs power=.68), with dextrals having lower movement durations using their dominant hand than adextrals. See figure 2.7 for mean scores broken down by dominant or non-dominant hand for each handedness group on each dependent measure. ANOVAs were run on each of the dependent measures to assess the hand effects as a function of group.

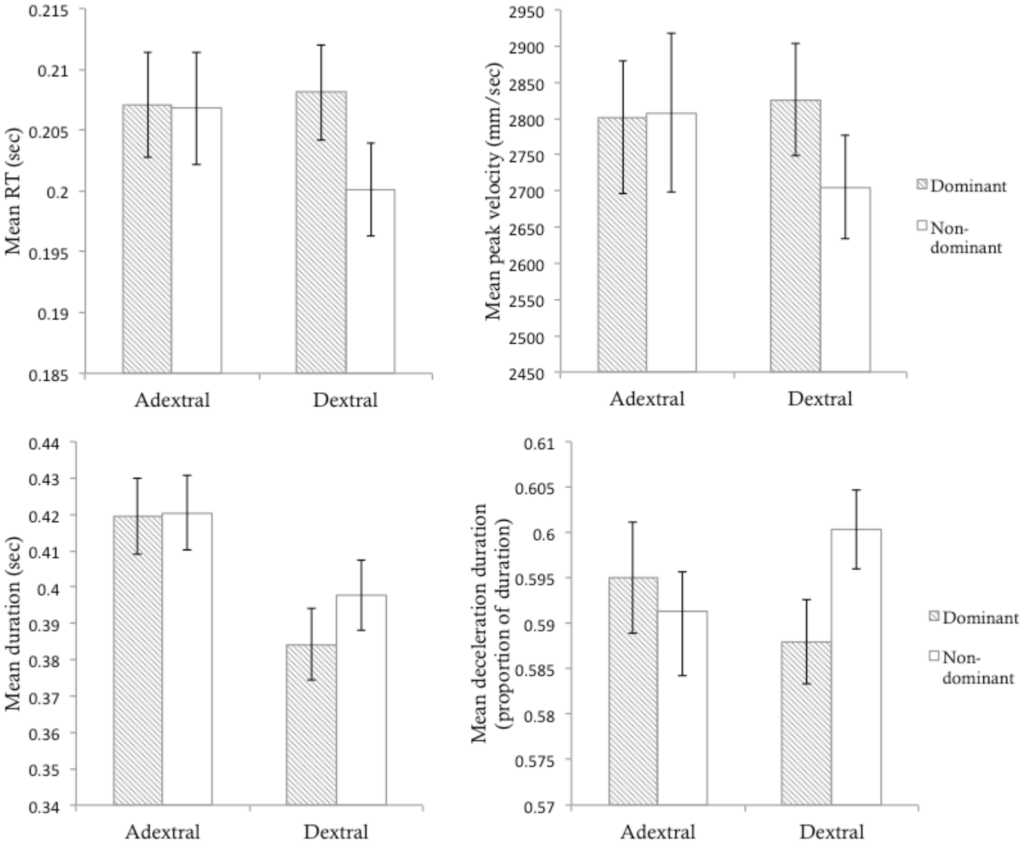


Figure 2.7 – Mean scores for the dominant and non dominant hand of each group for the four dependent variables. The data follows a similar pattern to that reported by Goodale (1990); see figure 2.1, pg 26. Error bars represent +/- 1 standard error of the mean.

2.3.2.2 Reaction time ANOVA

A significant main effect of hand was found favouring the non dominant hand (*F*(1, 100)=14.29, *p*<.001, ηp^2=.13). The interaction between group and hand was also significant (*F*(1, 100)=12.71, *p*=.001, ηp^2=.11). This interaction was driven by the dominant hand of the dextral group showing significantly lower RTs than the non-dominant hand (*t*(50)=6.21, *p*<.001), as there was no difference between the hands in the adextral group (see the top left panel of figure 2.7).

2.3.2.3 Peak velocity ANOVA

A significant main effect of hand was found favouring the dominant hand (*F*(1, 100)=7.87, *p*<.01, ηp^2=.07). The interaction between group and hand was also significant (*F*(1, 100)=9.85, *p*=.002, ηp^2=.09). This interaction was driven by the dominant hand of the dextral group showing significantly higher PVs than the non-dominant hand (*t*(50)=5.80, *p*<.001), as there was no difference between the hands in the adextral group (see the top right panel of figure 2.7).

2.3.2.4 Duration ANOVA

A significant main effect of hand was found favouring the dominant hand (*F*(1, 100)=24.42, *p*<.001, ηp^2=.20). The interaction between group and hand was also significant (*F*(1, 100)=19.31, *p*<.001, ηp^2=.16). This interaction was driven by the dominant hand of the dextral group showing significantly lower durations than the non-dominant hand (*t*(50)=8.15, *p*<.001). There was no difference between the hands in the adextral group (see the bottom left panel of figure 2.7).

2.3.2.5 Deceleration duration ANOVA

No significant main effect of hand was found (*F*(1, 100)=3.37, *p*=.07), but the interaction between group and hand was significant (*F*(1, 100)=11.84, *p*=.001, ηp^2=.11). This interaction was driven by the dominant hand of the dextral group showing significantly lower deceleration durations than the non-dominant hand (*t*(50)=4.19, *p*<.001), and no significant difference between the hands in the adextral group (see the bottom right panel of figure 2.7). Unlike in Goodale (1990), where deceleration duration was calculated as ‘duration – time to peak velocity’, the current deceleration duration measure is calculated as a proportion of the overall duration.

2.3.3 Proportion analyses

Although measures of central tendency can be useful, for the purposes of this thesis it was important to investigate these dependent measures’ potential relationship to brain asymmetry. Therefore analyses of any differences in the prevalence of manual asymmetries between dextrals and adextrals were carried out. For the purposes of these analyses ‘hand’ is reported as right or left, as opposed to dominant or non-dominant. If the pattern of typical manual asymmetries is related to 'typical' cortical organisation of functions, then it is more relevant whether the hand used is the left or right, than the dominant or non dominant.

In the dextral group 78.4% of the sample had an RT advantage with their left hand, an asymmetry present in only 51.0% of the adextrals (see figure 2.8). For peak velocity, 76.5% of the dextral sample had a higher peak velocity with their right hand, as did 43.1% of the adextrals (i.e. more adextrals had a higher peak velocity with their left hand). A right hand advantage in duration was present in 86.3% of the dextrals, and 51.0% of the adextrals. Finally, 68.6% of dextrals and 54.9% of the adextrals had a deceleration duration advantage with the right hand.

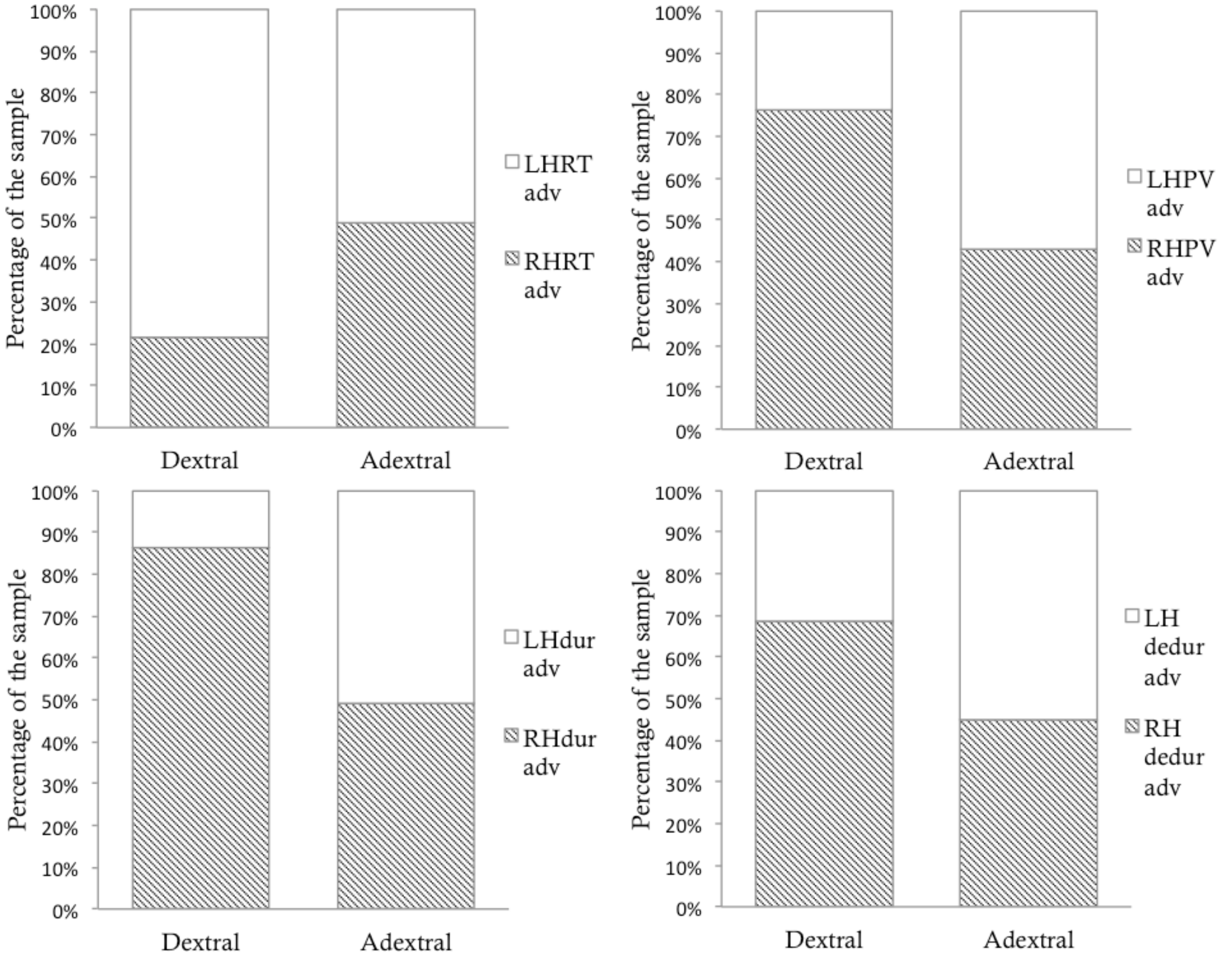


Figure 2.8 – Stacked bar charts displaying the percentage of each sample with a left or right asymmetry in each of the four dependent measures. The top left panel contains RT advantages, the top right panel contains PV advantage, the bottom left panel contains duration advantages, and the bottom right panel contains deceleration duration advantages. Shaded areas indicate the % of that sample with a right hand advantage for that measure.

Four z-tests were carried out to statistically compare the percentages of each sample displaying the above manual asymmetries. The percentage of the sample showing a shorter RT with their left hand was significantly higher in dextrals (+27%) than adextrals (*z*=2.78, *p*<.01), with 95% confidence intervals suggesting the real difference in percentage between the groups is between 23 and 36%. The percentage of the sample with a higher peak velocity with their right hand was also significantly higher in dextrals (+33%) than adextrals (*z*=3.59, *p*<.001), with 95% CIs of 13% and 26%. The prevalence of shorter movement durations with the right hand was also statistically higher (+35%) in the dextrals (*z*=3.58, *p*<.001), with 95% CIs of 31% and 44%. No significant difference was found in the prevalence of a right hand deceleration duration between dextral and adextral samples (*z*=1.43, *p*>.05).

It was possible to break the dextral and adextral samples down further into two groups each based on two additional behavioural asymmetries that were recorded. With samples of this size, an interesting covariate can be examined for the first time. Carey and others have suggested that foot dominance and eye dominance are weakly related to cerebral asymmetries (Annett, 1967; McManus, 1999; Carey, 2001; Carey et al., 2001). If these suggestions are accurate, groups of consistently sided people should be, on average, the most (all right) and the least (all left) lateralised for language.

Eye and foot dominance were recorded from 97 of our 102 participants (48 dextrals, 49 adextrals). Writing hand was used to define four hand/eye/foot preference groups; right handed, right eyed and right footed ("RRR": *n*=28), right handed and left eye or footedness ("R_Mixed": *n*=20), left handed and right eye/footed ("L_Mixed": *n*=30), and left handed, left eyed and left footed ("LLL": *n*=19). The percentages of these samples displaying the patterns that may relate to 'typical' cerebral dominance were investigated, to provide further evidence as to whether these manual asymmetries in reaching are related to cerebral asymmetries (as suggested by the hand/eye/foot congruency, or lack thereof). As demonstrated in figure 2.9, prevalence of all 'typical' manual asymmetries decreased as left-sidedness increased. Even within handedness groups, the prevalence of 'typicality' has a marked decrease. Incidence of a right hand deceleration duration advantage shows the least depreciation across the groups, corresponding to the null result of the z-test comparing this feature between dextrals and adextrals.

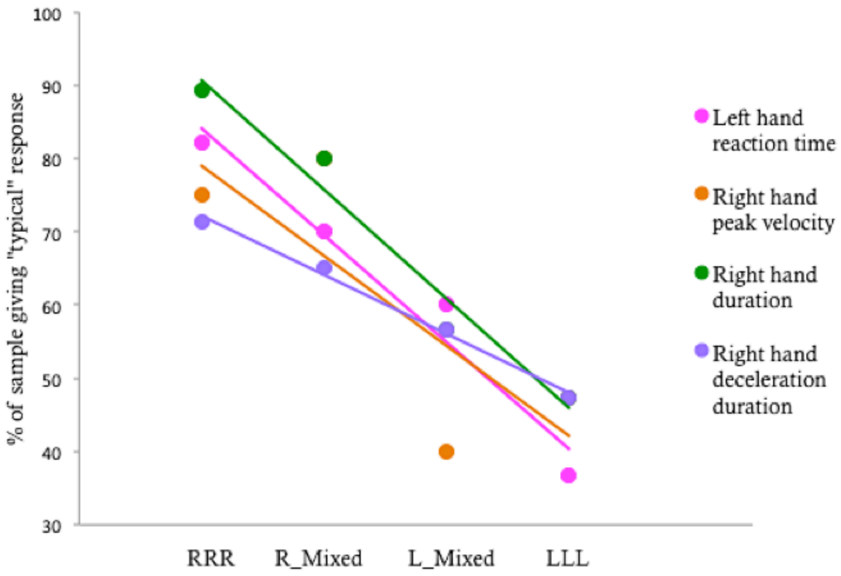


Figure 2.9 – Prevalence of 'typical' manual asymmetries as a function of left-sidedness. The percentage of each sample showing the typical manual asymmetry is plotted on the *y*-axis, with each of the four groups labelled on the *x*-axis.

2.3.4 Post hoc tests – magnitude of asymmetry

It is striking that the adextrals are near 50:50 for right and left hand advantages across all dependent measures (except arguably peak velocity). What the reported analyses do not illustrate is whether adextral participants are less asymmetric than dextral participants. Therefore additional independent samples *t*-tests were run on hand difference scores, but participants were split into groups based on having the same hand advantage for any given measure. For example, dextrals and adextrals with a left hand RT advantage were compared, separately to dextrals and adextrals with a right hand RT advantage. If these t-tests are not significant, then the magnitude of the asymmetry in the dependent measure is the same for dextrals and adextrals. Significant differences indicate that dextrals and adextrals with the same asymmetry have differing magnitudes of that asymmetry. If the adextrals have significantly smaller difference scores than the dextrals for any of these tests, it would implicate a more symmetrical response pattern within adextral participants.

Dextrals with a left hand RT advantage (n=40) displayed a 12 msec advantage on average, whereas adextrals with a left hand RT advantage (n=26) had a 10 msec advantage. This difference was not statistically significant ($t(64)=1.45$, $p>.05$). There was also no significant difference found between dextrals and adextrals with a right hand RT advantage (*t*(34)=1.70, *p*>.05). Dextrals (*n*=11) had a 6 msec advantage whilst adextrals (*n*=25) had a 10 msec advantage.

In terms of peak velocity no significant difference was found between those with a right hand peak velocity advantage (*t*(59)=0.59, *p*>.05). Dextrals had a 178.72 mm/sec advantage (*n*=39), whereas adextrals (*n*=22) had a 205.20 mm/sec advantage. When comparing those with a left hand peak velocity advantage however, adextrals (*n*=29) had a significantly larger advantage (143.77 mm/sec) than dextrals (*n*=12; 67.64 mm/sec); *t*(39)=2.09, *p*<.05.

No significant difference was found between duration advantage of dextrals (*n*=44; 16 msec) and adextrals (*n*=26; 13 msec) with a right hand duration advantage (*t*(68)=1.48, *p*>.05). A significant difference in advantage between dextrals (*n*=7; 4 msec) and adextrals (*n*=25; 15 msec) with left hand duration advantages was present (*t*(30)=2.75, *p*=.01). Of course the number of dextrals with a left hand duration advantage is smaller than desirable for statistical comparisons.

Finally, no significant difference was found between dextrals (*n*=35; 2.4%) and adextrals (*n*=28; 2.1%) in terms of right hand deceleration duration advantage (*t*(61)=0.59, *p*>.05). Likewise there was no difference between dextrals (*n*=16; 1.3%) and adextrals (*n*=23; 1.8%) in terms of magnitude of left hand deceleration advantages (*t*(37)=1.20, *p*>.05).

2.4 Discussion

The results of the MANOVA analysis suggest that a combination of these four dependent measures does differentiate the handedness groups. Dominant hand duration may be the most relevant dependent measure. The separate ANOVAs reported for RT, peak velocity, duration, and deceleration duration each revealed a significant interaction between hand used (dominant or non-dominant) and handedness group. The dextral sample favoured their dominant hand for all movement parameters except RT, where the non dominant hand was, as usual, faster. Adextrals had no significant differences between the mean movement measures of their dominant and non dominant hands. Finally, z-tests found significant differences between proportions of hand advantages in dextrals and adextrals for every manual asymmetry except deceleration duration. The dextral sample had a right hand advantage for all dependent variables except RT, where most had a faster left hand. The adextral sample, however, were roughly 50:50 in terms of left or right hand advantage across movement measures.

The averaged results from our dextral and adextral samples largely replicate those of Goodale (1990), except our dextrals had the more commonly reported non-dominant hand advantage in RT. Another notable difference is that the participants in Goodale (1990) have much slower RTs (~300 msec slower) than those reported in the present dataset. Movement durations are also much slower (~200 msec) in the Goodale (1990) sample. Since the current task was much more demanding (in terms of localisation, attention, and physically moving further distances) than that in Goodale (1990), this finding is probably the result of our emphasis on the importance of speed to our participants. Participants may be tempted to label their non dominant hand their 'bad' hand, and therefore initiate slower movements with that hand. If they are encouraged to move as quickly as possible, the resulting ballistic movements are less likely to be affected by top-down decision making about which hand should be faster. This explanation may account for the lack of a left hand RT advantage in the dextral sample from Goodale (1990).

The dextral right hand advantage in peak velocity, duration and deceleration duration appears to be fairly reliable across these two studies, as well as others (Fisk & Goodale, 1985; Carson et al., 1993; Elliott, Chua, & Pollock, 1994; Carnahan, 1998). Likewise, the lack of asymmetry in adextral samples on these measures is also consistent across these two studies.

In terms of the proportion data, the pattern of asymmetry in dextrals supports our hypotheses for all movement measures. Nevertheless, the lack of asymmetry in adextrals, as assessed by proportions, goes against predictions. It was anticipated that if these asymmetries were related to cerebral organisation, >50% of adextrals would present with asymmetries in the same direction as the majority of dextrals, but just that the proportion would be smaller than that of the dextrals. As only ~50% of the adextral participants show the same asymmetries as dextrals, one possibility is that manual asymmetries are not related to cerebral asymmetries. There is further evidence from our results, however, that does not support this conclusion.

Firstly, if the motor asymmetries favouring the right hand in dextral samples were due to 'practice' effects with the dominant hand rather than functional brain asymmetries, a full reversal of these effects in adextrals would be expected (at least in so far as many years of handwriting and tool-related activities are similar in dextrals and adextrals). Reversal of typical asymmetries is clearly not the case in our sample, where the adextral group are split 50:50 in all asymmetries. Additionally, when participants were split into four groups according to their eye and foot preference as well as handedness, prevalence of the typical response pattern decreased in a linear fashion from the most right-sided group to the most left-sided group. These data are particularly convincing as these groups were defined by eye and foot preferences, which have no *prima facie* connection to asymmetries in hand movements. Some researchers have suggested that footedness is a better predictor of some lateralised functions than handedness (Elias, Bryden, & Bulman-Fleming, 1998). Strauss and Wada (1983) recorded eye and foot dominance in 73 patients who underwent the Wada test. Their data also suggested that a combination of hand/foot preference provides more useful information regarding cerebral speech dominance than handedness alone, but eye preference was of little predictive value. Therefore, our hand/eye/foot group data add to the evidence that manual asymmetries are related to brain organisation.

The magnitude of asymmetries in dextrals and adextrals were also compared. Although reporting the proportional data allowed explanation of the adextrals' symmetrical results at the group averaged level, it was still unclear whether the adextrals were less asymmetrical than dextrals generally. For example, were these 50:50 proportions due to most adextrals being roughly equal with both hands, and half happen to have a very small left hand advantage and the other half a subtle right hand advantage? Or do the 50% of adextrals with a left hand advantage for example, have as large an advantage as dextrals with the same asymmetry? Independent-samples t-tests indicated that the only significant differences are between dextrals and adextrals (grouped by hand advantage direction) with a left hand peak velocity advantage (larger in the adextrals), and dextrals and adextrals with a larger left hand duration advantage (larger in the adextrals). The mean scores suggest that the dextrals in these two groups have very slight asymmetries, whereas the adextrals in these groups are strongly left-sided. On all other measures, dextrals and adextrals had equivalent magnitude of asymmetry. Literature such as Goodale (1990) and Boulinguex, Velay, and Nougier (2001b) claims that adextrals have less pronounced lateralisation than dextrals, but it is not clear whether this assertion is about individual adextrals, or adextrals as a group. The data from the current investigation suggests that individual adextrals are just as asymmetrical as dextrals, although it should be acknowledged that subgrouping of this sort may reduce power to detect significant differences.

The 50:50 left/right advantage split for all measures (except arguably peak velocity) from the adextral sample warrants further investigation. The use of a dichotomous split as 'left' or 'right' advantage regardless of the magnitude of the advantage may contribute to this finding. Additional data is currently being collected on a similar experiment (with reduced trial numbers and target locations). Once enough data has been accumulated investigating the *distributions* of the left/right hand differences in dextrals and adextrals could help demonstrate the symmetry in the adextral sample more convincingly. For example, if the distribution had a mean of zero, that would be a very different distribution to that of the dextral asymmetries (which we expect to be extremely skewed).

Part of the motivation for collecting such a large number of trials from such large dextral and adextral samples was to allow for estimates of how many trials and participants are necessary for studies investigating manual asymmetries. This analysis is on going; nevertheless primary analyses of hand asymmetry across trials suggest that 120 trials per hand (rather than the 240 collected in the current study) would result in equivalent hand advantage classification in over 95% of dextrals and 90% of adextrals. In fact, classification of asymmetries in just one block of 40 trials per hand was concurrent with hand advantage after 240 trials in over 87% of dextrals and 79% of adextrals.

These analyses were possible due to the balanced-design, which controlled for target order. Each hand reached to each target in each block, therefore effects related to target distances and hemispace (Carey, Hargreaves, & Goodale, 1996) are completely controlled for. Due to this feature, it is possible to compare RT/peak velocity/duration/ deceleration duration between the hands in their respective first blocks. Therefore we can calculate hand differences in block one and block two together, and so on until all six 'block pairs' have been included. This cumulative style of analysis allows for calculation of how many blocks were necessary before the participant's hand asymmetry was largely similar to the final asymmetry recorded after all 480 trials.

To assess how many participants are necessary for these sorts of experiments an approach such as that used with simulated data to create figure 2.2 (pg 28) may be appropriate. In this instance, multiple random samples of different participant *n*s would be taken from the real participant data. Then the prevalence of the result found in this large-scale study would be assessed across the differing group sizes. Such an analysis is long overdue. Even in studies using dextrals only, sample sizes are often *n*=10 or less. Only manual asymmetries studies from our lab have sample sizes that are routinely greater than 20. In a recent analysis, Carey et al. (2015) suggest sample sizes of 26 or more are needed to be certain of left hand RT advantages in dextrals.

In summary, all asymmetries were found in the predicted direction in dextrals but not adextrals, for both averaged data and proportions. However, a majority of adextrals did not give reversed response patterns to dextrals, and analyses of the magnitude of manual asymmetries as well as the modulation of these effects by hand/foot/eye groups suggest that asymmetries in these four measures of speed are related to cerebral organisation of functions.

Chapter 3 – Potential electrophysiological markers of face processing asymmetry and language lateralisation

3.1 Introduction

ERPs are an index of brain electrical activity measured from electrodes set on the scalp. Continuous EEG is recorded whilst a stimulus is presented to the participant. The EEG is broken down into epochs that are time-locked to stimulus onset, and the brain waveforms that appear in this epoch are the ERPs (Rugg & Coles, 1995). Presenting any visual stimulus to a participant results in a P1-N1-P2 complex; an initial increase in waveform amplitude, followed by a decrease, and a further increase (Luck & Kappenman, 2011). Different categories of visual stimuli can manipulate the amplitude of these components, and these changes are used as a quantitative measure of functional activity (Donchin, Ritter, & McCallum, 1978).

The N170 component is a variant of the N1, which may be particularly responsive to face stimuli. This component is categorised as the maximal negative dip within a timeframe of ~130-210 msec post-stimulus (Bentin, et al., 1996; Botzel et al., 1995; Rossion et al., 2000). It peaks in occipito-temporal electrode sites at around 170 msec on average, following the presentation of a stimulus, hence its label (Bentin et al., 1996). The component tends to be larger in response to faces (when compared to a control stimulus) in both hemispheres, but is often largest over right scalp sites (Bentin et al., 1996; Rossion et al., 1999). Electrophysiologists who study the face N170 are usually uninterested in the asymmetry in this particular feature (with most experiments instead concerned with the N170's "face selectivity"; see section 1.4 of the general introductory chapter), however, for my purposes this asymmetry is the appealing aspect of the N170.

Considering what we know about the lateralisation of face processing functions, a rightward asymmetry in a measure that is related to face perception could be a useful marker of a participant's cerebral organisation. In fact, attempts have been made at source analysis of the N170 and results point towards the posterior superior temporal sulcus (Batty & Taylor, 2003; Itier & Taylor, 2004, Nguyen & Cunnington, 2014), an area the human neuroimaging and primate single-cell recording literatures suggest is involved in face and body processing (see Allison, Puce & McCarthy, 2000, for a review). If the N170 amplitude is a marker of cerebral asymmetries, we would expect not only a larger N170 over right scalp sites in group-averaged waveforms, but also at the individual level. A majority of participants could follow this pattern, and the number of participants showing this effect should interact with handedness, given that more adextrals will have atypical cerebral organisation.

It is difficult, however, to find estimates for **how often** a rightward asymmetry in N170 amplitude occurs. To gain some insight into how often a lateralised N170 component is reported, I searched for papers investigating N170s in response to face stimuli, and have summarised those that provide details concerning the lateralisation of the component in table 3.1. Of the 32 papers inspected, 21 reported the laterality of the largest N170 component. In these 21 papers, 15 found a larger N170 amplitude over right scalp sites than left, with the remaining studies finding no effect of hemisphere, as opposed to a larger N170 over left scalp sites. Therefore this rightward asymmetry in the N170 response to faces appears to be fairly robust, evident in ~70% of the papers in table 3.1.

In addition to face stimuli, some scientists have made claims of a *leftward* asymmetry in N170 amplitude following *word* stimuli (Rossion, Joyce, Cottrell, & Tarr, 2003; Maurer, Bradeis, & McCandliss, 2005; Simon, Petit, Bernard, & Rebai, 2007; Maurer, Zevin, & McCandliss, 2008; Maurer, Rossion, & McCandliss, 2008). As with face N170 studies, I have compiled a table summarising N170 papers using words/language as stimuli that provide laterality data at the group level – see table 3.2. In these 11 papers, all report larger N170 amplitudes over left scalp sites. As we would perhaps expect stronger lateralisation of language functions than face perception processes, this result is fairly convincing evidence that this pattern of lateralisation is related to functional hemispheric asymmetries in processing these different stimulus categories.

A handful of studies have analysed N170 amplitude variances to both face and word stimuli in the same people (Rossion, Joyce, Cottrell, & Tarr, 2003; Joyce and Rossion, 2005; Maurer, Rossion, & McCandliss, 2008; Mercure, Dick, Halit, Kaufman, & Johnson, 2008; Mercure, Cohen Kadosh, & Johnson, 2011; Dundas, Plaut, & Behrmann, 2014: see tables 3.1/3.2 for details). The first of these studies involved 15 right-handed participants viewing images of faces, words and cars. Average N170s from this study are displayed in figure 3.1. It is clear that the N170 following face presentation has a more negative amplitude over right scalp sites than left. Likewise, the N170 following the presentation of word stimuli elicits a more negative N170 over left scalp sites than right.

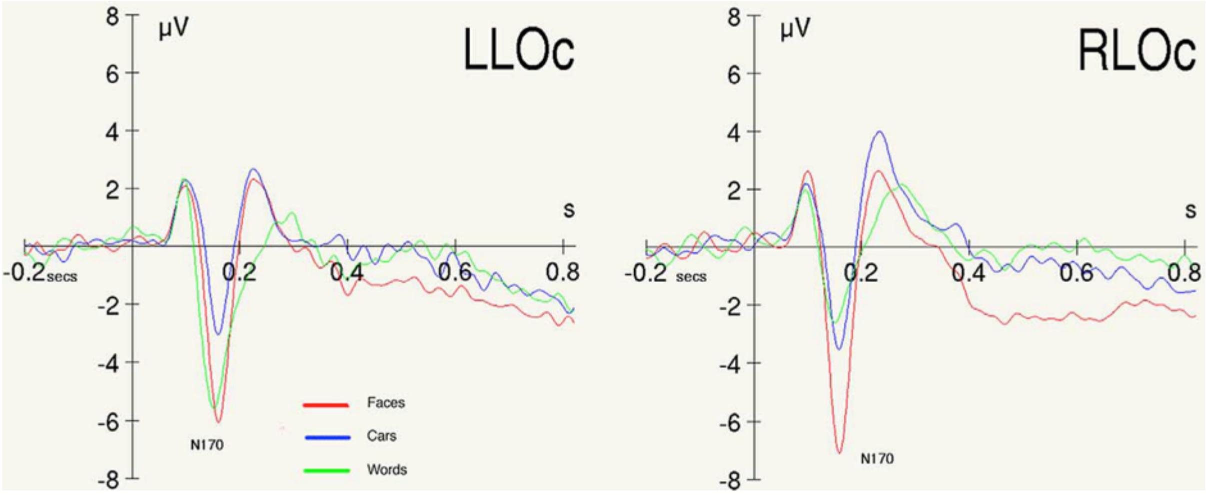


Figure 3.1 – The N170 response to all three categories at left and right occipito-temporal electrode sites (Rossion, Joyce, Cottrell, & Tarr, 2003). Note the difference between hemispheres for the N170 for faces (right > left), and the N170 for words (left > right).

In this group's two later papers, this effect is replicated (see table 3.1 for details) and the authors conclude that this asymmetry must be related to hemispheric dominance for face and language processing. As summarised in table 3.2, the other three studies who recorded responses to both faces and words found mixed results for N170 lateralisation in response to face stimuli, but all studies reported a strong left lateralisation in response for words.

Of the papers summarised in tables 3.1 and 3.2, only four included adextral participants (Rossion et al., 1999; Batty & Taylor, 2003; Goffaux, Gauthier & Rossion, 2003; Itier & Taylor, 2004). Even so, these sample sizes are extremely small (a problem discussed in the introduction of the previous chapter: see Chapter 2, page 28), *n* ranging from two to four participants. In all four of these studies, the adextral data is analysed with the dextral data, under the assumption that the adextrals will mostly respond as do dextrals. Whilst this assumption will be typically correct, a larger sample of adextrals would provide a good opportunity to link these skull asymmetries to underlying cerebral dominance.

Author(s)	Date	Task	#Dex	#Adex	Finding re lateralisation
Bentin, Allison, Puce, Perez & McCarthy	1996	Number of participants unknown. Multiple experiments involving passive viewing of various stimulus categories (e.g. faces, scrambled faces, inverted faces, cars, scrambled cars, inverted cars).	NR	NR	A more negative N170 to faces found at the right scalp site than at the left (not statistically significant in each study, but present numerically for all).
Linkenkaer-Hansen, Palva, Sams, Hietanen, Aronen & Ilmoniemi	1998	9 subjects passively viewed images of upright and inverted faces with varied degradation. Whole scalp MEG and EEG recorded.	9	0	7/9 participants had no asymmetry in N170 amplitudes for each stimulus category; of the two remaining one had strongest activity on the right, and one on the left.
Rossion, Delvenne, Debatisse, Goffaux, Bruyer, Crommelinck, & Guerit	1999	14 subjects viewed drawings of faces and their inversions, two per trial, and made a same-different identity judgement.	11	3	Larger inversion effect over right hemisphere than left (which strengthened when only right-handed subjects were included in the analysis).
Campanella, Hanoteau, Depy, Rossion, Bruyer, Crommelinck, & Guerit	2000	12 participants took part in a matching task with three different pairings of face stimuli: morphed faces with the same identity, two faces with different identities, and two identical morphed faces.	12	0	No main effect of lateralisation, but differences in the N170 between different stimulus pairs was found at the right scalp site but not the left.
Rossion, Joyce, Carttrell, & Tarr	2003	15 participants viewed images of faces, cars, or words, and made a relevant keypress response to each presentation depending on whether the image was upright or inverted.	NR	NR	More negative N170 over right scalp sites for faces, and left scalp sites for words
Batty & Taylor	2003	26 participants viewed faces and non-facial stimuli (cares, planes, butterflies), and gave a keypress response to non-facial stimuli.	22	4	No hemisphere effects on N170 amplitude or latency.
Goffaux, Gauthier & Rossion	2003	13 participants gave keypress responses to upright or inverted images of cars and faces processed with broad-pass or high/low pass filters.	11	2	The N170 for faces was largest on the right for broad-pass and low spatial frequency conditions.

Itier & Taylor	2004	16 participants viewed images of faces, inverted faces, textures, mushrooms, flowers, houses, lions, tools and road signs, making a keypress response to a target checkerboard stimulus.	13	3	A larger N170 amplitude over right than left at posterior parietal electrodes for faces and inverted faces.
Joyce & Rossion	2005	16 participants viewed upright and inverted images of faces, cars and words, responding to inversion with a keypress.	16	0	The N170 for faces was larger on the right, whilst the N170 for words was larger on the left.
Blau, Maurer, Tottenham, & McCandliss	2007	26 participants viewed faces followed by a line drawing and auditory word, with the task to learn associations between the line drawing and the word (faces varied in emotion).	26*	0	A larger N170 response to fearful than neutral faces. No effect of hemisphere.
Gajewski, Schlegel, & Stoerig	2008	28 participants split into two groups: half participants viewed stimuli upright, other half inverted. Stimuli were greyscale photos of faces and doors. Respond to faces with one keypress and doors with another.	28	0	N170 amplitude larger at right scalp site (T6).
Maurer, Rossion, & McCandliss	2008	18 participants responded to occasional inversions whilst viewing faces and words. Stimuli were presented either in blocks of faces or words OR faces and words interleaved.	18	0	Larger N170 over left scalp sites for words; larger N170 over right scalp sites for faces (only in a condition when faces and word stimuli were interleaved)
Mercure, Dick, Halit, Kaufman, & Johnson[3]	2008	45 participants tested in three experiments (n=13, 19, 13) performing a one-back task viewing faces, words and abstract patterns (varying in spatial frequency and size).	45	0	A left-lateralised N170 for words was found in all experiments, compared to a right-lateralised N170 for faces in one experiment, and no lateralisation of the N170 in the remaining two experiments.
Japee, Crocker, Carver, Pessoa & Ungerleider	2009	31 (4 excluded) participants had to categorise the emotion of a target face after being shown a neutral mask. (MEG)	NR	NR	Stronger N170 over right scalp sites.
Moulson, Fox, Zeanah, & Nelson	2009	125 children split up based on status (in care, foster care, never institutionalised).	NR	NR	Never-institutionalised group showed a larger amp N170 on the right hem. Institutionalised group showed no lateralisation.

Caharel, d'Arripe, Ramon, Jacques, & Rossion	2009	20 participants viewed faces (two per trial; same and different identities) and performed a matching task with a keypress response.	20	0	Larger N170 in the right hemisphere; and a significantly larger N170 to different identities in the right hemisphere but not left.
Daniel & Bentin	2010	16 subjects (aged 70-90; 16 young controls aged 19-33) carried out an oddball target detection, different categories of stimuli (watches, faces, flowers) – button press when flower on screen.	NR	NR	N170 amplitude larger in old group, and on right hem sites in the young group – no hem difference in the old group.
Martens, Leuthold, & Scweinberger	2010	20 participants responded to a set of faces giving a response with one hand to familiar faces and the other hand to unfamiliar faces (counter-balanced).	20	0	N170 peak amplitude was larger over the right than the left parietotemporal electrode.
Gajewski & Stoerig	2011	28 participants split into two groups: half viewed stimuli upright, other half inverted. Stimuli were images of human faces, monkey faces, dog faces and doors. Respond to faces and doors with separate keypresses.	28	0	No effect of hemisphere. N170 amplitude more pronounced for human faces vs other faces and doors.
Mercure, Cohen Kadosh, & Johnson[3]	2011	18 participants viewed pictures of faces, cars, words, and non-words - pressing a button whenever a target image (butterfly) was presented.	NR	NR	Larger N170 over left scalp sites than right for word stimuli, no significant difference between left and right for faces stimuli.
Dundas, Plaut, & Behrmann[3]	2014	17 adults and 17 children completed a VHF tasks (same/different judgement) with both face and word stimuli.	34	0	More negative N170 over the left scalp than right for words; no difference in amplitude between scalp sites for faces.

Table 3.1 – A brief description of studies that reported lateralisation of the N170 component in response to face stimuli.

In 15/21 studies a stronger N170 or an N170 related effect over right scalp sites and not left occurred. It is relevant that none of the remaining studies find a larger N170 over left scalp sites; they find bilateral amplitudes.

[1] **NR** = Not reported.

[2] The researchers state the participants had "predominant right-handedness" as opposed to classifying them by, or reporting, their preferred writing hand – it is possible there are some adextrals in the sample.

[3] These papers include face and word stimuli in the same participants. Whilst they do not report individualised data, 4/6 find a larger N170 for faces over right scalp sites, and all find a larger N170 for words over left scalp sites, which is encouraging for our purposes.

Author(s)	Date	Task	#Dextrals	#Adextrals	Finding re lateralisation
Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier	1999	24 participants completed a mental oddball task (counted number of target stimuli) whilst viewing different categories of word stimuli (words/pseudowords/nonwords/symbol strings).	24	0	Larger N170 over left scalp sites for orthographic stimuli, but larger over right for nonorthographic stimuli.
Rossion, Joyce, Carttrell, & Tarr	2003	15 participants viewed images of faces, cars, or words, and made a relevant keypress response to each presentation depending on whether the image was upright or inverted.	NR[1]	NR	More negative N170 over right scalp sites for faces, and left scalp sites for words
Maurer, Brandeis, & McCandliss	2005	10 participants were shown words, pseudowords and symbol-strings, and were instructed to respond when they detected an immediate repetition.	10	0	Larger N170 for words than for pseudowords, “especially at the left hemisphere channels”. N170 for words less than 1μV different L vs R.
Rossion & Joyce	2005	16 participants viewed upright and inverted images of faces, cars and words, responding to inversion with a keypress.	16	0	The N170 for faces was larger on the right, whilst the N170 for words was larger on the left.
Simon, Petit, Bernard, & Rebai	2007	10 participants completed a lexical decision task viewing frequent/infrequent words and pseudowords.	10	0	Larger N170 amplitude over left scalp sites for frequent than infrequent and pseudowords.
Huber, Tian, Curran, O’Reilly, & Woroch	2008	31 participants in Exp 1 and 30 in Exp 2. Participants performed forced-choice perceptual identification (word stimuli).	61	0	Bigger N170 over left occipital sites in Exp 1, but not Exp 2.
Maurer, Rossion, & McCandliss	2008	18 participants responded to occasional inversions whilst viewing faces and words. Stimuli were presented either in blocks of faces or words OR faces and words interleaved.	18	0	Larger N170 over left scalp sites for words; larger N170 over right scalp sites for faces (only in a condition when faces and word stimuli were interleaved)

Mercure, Dick, Halit, Kaufman, & Johnson	2008	45 participants tested in three experiments (*n*=13, 19, 13) performing a one-back task viewing faces, words and abstract patterns (varying in spatial frequency and size).	45	0	A left-lateralised N170 for words was found in all experiments, compared to in response to faces where a right-lateralised N170 was found in one experiment, but no lateralisation of the in the remaining two experiments.
Lin, Chen, Zhao, Li, He & Weng	2011	14 participants viewed real and pseudo Chinese characters, and structurally matched but unpronounceable stimuli.	14	0	Real and pseudocharacters produced larger N170s over left scalp sites.
Mercure, Cohen Kadosh, & Johnson	2011	18 participants viewed pictures of faces, cars, words, and non-words - pressing a button whenever a target image (butterfly) was presented.	NR	NR	Larger N170 over left scalp sites than right for word stimuli, no significant difference between left and right for faces stimuli.
Dundas, Plaut, & Behrmann	2014	17 adults and 17 children completed a VHF tasks (same/different judgement) with both face and word stimuli.	34	0	More negative N170 over the left scalp than right for words; no difference in amplitude between scalp sites for faces.

Table 3.2 – A brief description of studies that reported lateralisation of the N170 component in response to word stimuli.

All 11 studies report a stronger N170 or an N170 related effect over left scalp sites.

[1] **NR** = Not reported.

The best data for evaluating the potential predictive power of lateralised N170s in individual people would be provided by the proportions of dextrals in a sample who had numerically more negative N170s over one side of the skull or the other. Despite finding studies in which the asymmetry of the N170 is discussed, reports of the percentage of the sample that show the effect are almost noon-existant, or rare to say the least. Only one study I found gave individual participant data, only because the results did *not* show an average lateralised N170 (Linkenkaer-Hansen, Palva, Sams, Hietanen, Aronen & Ilmoniemi, 1999). It is, therefore, hard to estimate the success of the N170 as a predictor in individuals.

To assess the suitability of a lateralised N170 to faces or words as useful markers of cerebral organisation, it would be useful to know how frequent a lateralised bias is in individual participants. If these biases are related to cerebral asymmetries in functional processes, we would expect the asymmetries to be reduced in a sample of adextrals. Rossion and colleagues acknowledge that differences in the lateralisation of these waveforms in dextral and non-dextral groups could help confirm that these skull asymmetries really are related to cerebral asymmetries. Unfortunately they tend to test rather small numbers of adextrals, and then do not report the data separately for dextrals and adextrals (probably because the groups do not differ).

In this investigation, my colleagues and I set out to test a sample of participants on an ERP paradigm involving both face and word stimuli. It was assumed that all our dextral participants would have conventional cerebral lateralisation.

Experiment one of this chapter was an initial feasibility study that included six dextrals and one adextral, and an oddball paradigm with two conditions involving face and word stimuli. Experiment two was a larger scale investigation with some methodological improvements, and a subset of participants with known brain lateralisation from fMRI verbal fluency and face localiser tasks (full fMRI methods covered in Chapter 6). If the lateralisation of the more negative N170 amplitude is a product of an individual's cerebral organisation of language or face processing, then we would predict that in individuals with conventional brain organisation, participants would have a larger N170 amplitude to faces over right scalp sites, and to words over left scalp sites.

3.2 Method

3.2.1 Participants

Participants were seven students from Bangor University School of Psychology, six dextrals (mean WHQ score = 28), and one adextral (WHQ score = -25, female, age 20). The dextral group contained three females and had an age range of 21-52 (mean = 28.6).

3.2.2 Stimuli and materials

The face condition stimuli were 64 faces from the Endl face database (Endl et al., 1998). These faces were presented greyscale on a grey screen background. Similarly 64 five and six letter words were taken from the MRC psycholinguistic database (Cotlheart, 1981) and were matched for frequency. These word stimuli were written in white in a black box, and were presented on a grey screen background. Faces were 300 x 400 px (9.2 x 12° of visual angle) and words were 400 x 100 px (12 x 3.1°). The experiment was developed in Presentation® software (Version 0.70, www.neurobs.com), and was presented on a 23" LCD LED backlit monitor via a PC.

3.2.3 Procedure and design

Participants were positioned in a comfortable chair 50 cm from the PC monitor in a dimly lit room. Each block of 64 trials began with a fixation cross preceding the presentation of a target face/word for 5 seconds. Subjects would begin the trials with a key press when they were ready. Each trial involved a fixation point for 300 msec, followed by the presentation of a stimulus for 300msec. Participants would then give one of two button press responses; "Z" or "M". These keys were assigned to distractor faces/words or target faces/words, counterbalanced across participants. The fixation-cross remained on the screen throughout and participants were instructed to remain fixated during stimulus presentation. Four blocks were undertaken, totalling 384 trials each for the face and word conditions, comprising 336 distractor trials and 48 target face trials. The face and word experiments were not interleaved, and the order in which participants took part in these tasks was counterbalanced.

3.2.4 EEG Recording Methods

Electroencephalogram (EEG) was recorded continuously from 64 scalp positions according to a 10-20 system from Ag/AgCl electrodes mounted in an elastic cap.

Recordings were referenced against Cz as the initial common reference and digitised with a frequency of 1 kHz. The band-pass was set to 0.01-200 Hz. Horizontal and vertical electrooculograms (EOG) were also recorded. Electrode impedences were kept below 5kΩ.

Offline filtering used a low pass filter at 35 Hz and a slope of 48 dB/octave. The EEG was segmented into 1700 msec epochs, starting 200 msec before stimulus presentation. All epochs were then averaged into ERPs separately for both the faces and words conditions across each channel. Average waveforms were then created over preselected right and left scalp sites separately, comprising: PO7, PO9, P7, P9 and T7 for the left sites, and PO8, PO10, P8, P10, and T8 for the right sites (commonly used in N170 studies – see Dundas et al., 2014; Rossion et al., 2003). A grand average waveform for all the dextral participants was also calculated.

3.2.5 Data analysis

As this was a feasibility study, we were interested in the proportions of our sample showing a more negative N170 amplitude for face or word stimuli over the right or left scalp sites. Therefore, analyses will be largely descriptive, comparing the left and right N170 amplitudes, anticipating a more negative N170 for words over the left scalp sites, and for faces over the right scalp sites.

3.3 Results

Average waveforms for right and left scalp sites from three example participants are displayed in figures 3.2 – 3.4. In response to faces, two out of six dextrals presented with a more negative N170 over the right scalp sites, three displayed a more negative N170 over the left scalp sites, and the remaining participant showed no clear asymmetry in N170 amplitude. In response to word stimuli, two of the six dextrals showed a more negative N170 over left scalp sites, two showed a more negative N170 over right scalp sites, and the remaining two participants showed no visible asymmetry between scalp sites. The adextral participant (see figure 3.4) had a larger N170 over the left scalp sites in response to both stimulus types.

Grand averages were calculated for both face and word data (see figure 3.5), displaying a larger N170 over right scalp sites overall for both stimulus types. As our fundamental hypothesis that the vast majority of our participants would show the pattern of a larger N170 over the right sites for faces and the left site for words, no further statistical analyses were carried out.

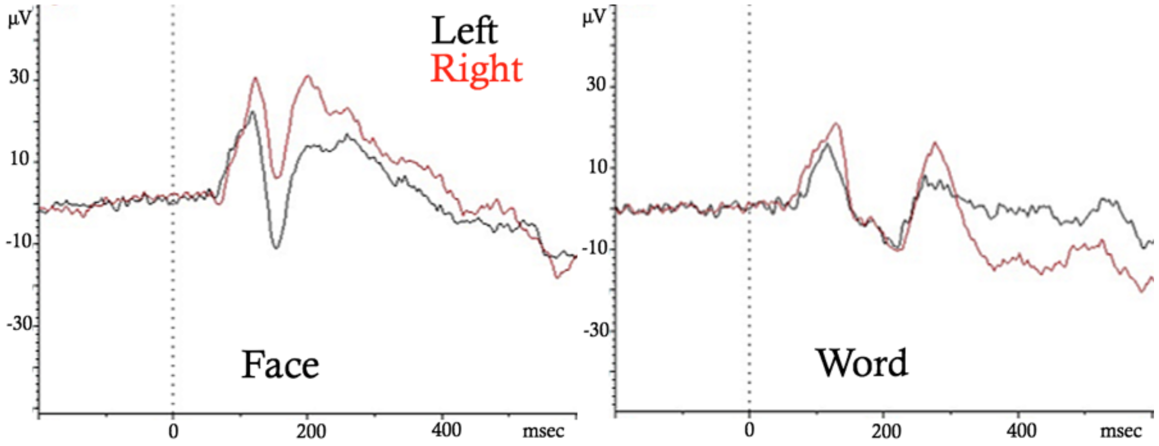


Figure 3.2 – Averaged waveforms from left and right scalp sites in one male dextral subject. Graphs display amplitude (μV) as a function of time (msec) – as in figures 3.3, 3.4 and 3.5. This participant had a marked asymmetry in N170 amplitude in response to faces but not words.

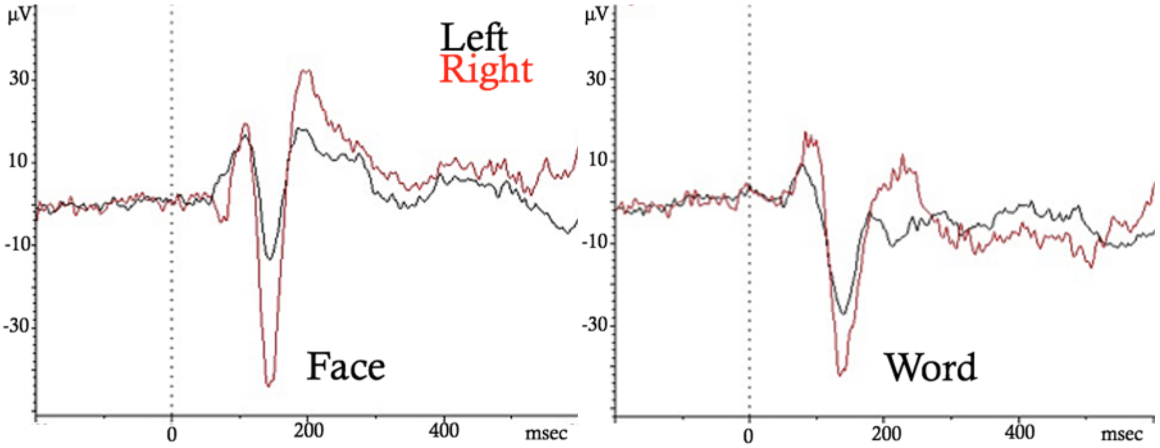


Figure 3.3 – Averaged waveforms from left and right scalp sites in one female dextral subject. In this participant, both face and word N170s are larger over right scalp sites.

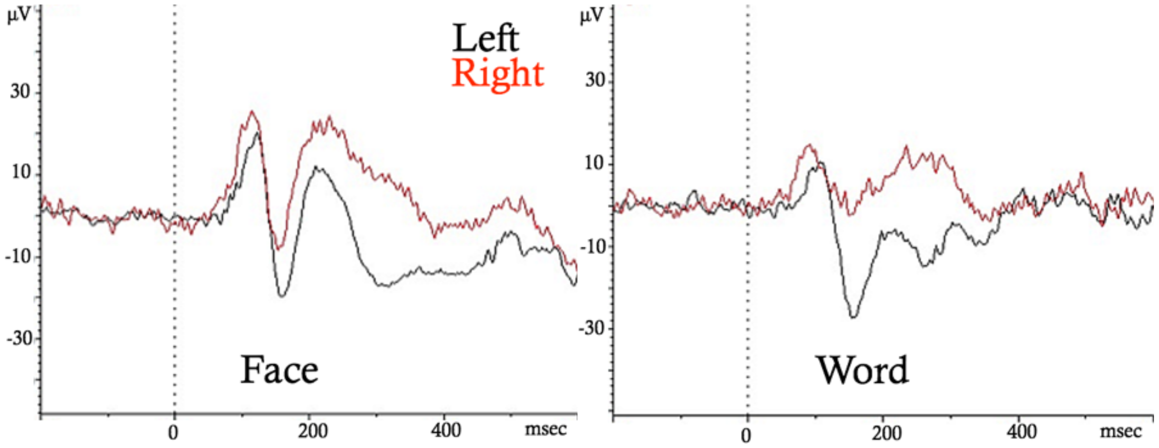


Figure 3.4 – Averaged waveforms from left and right scalp sites in one female adextral subject. In this participant, both face and word N170s are larger over left scalp sites.

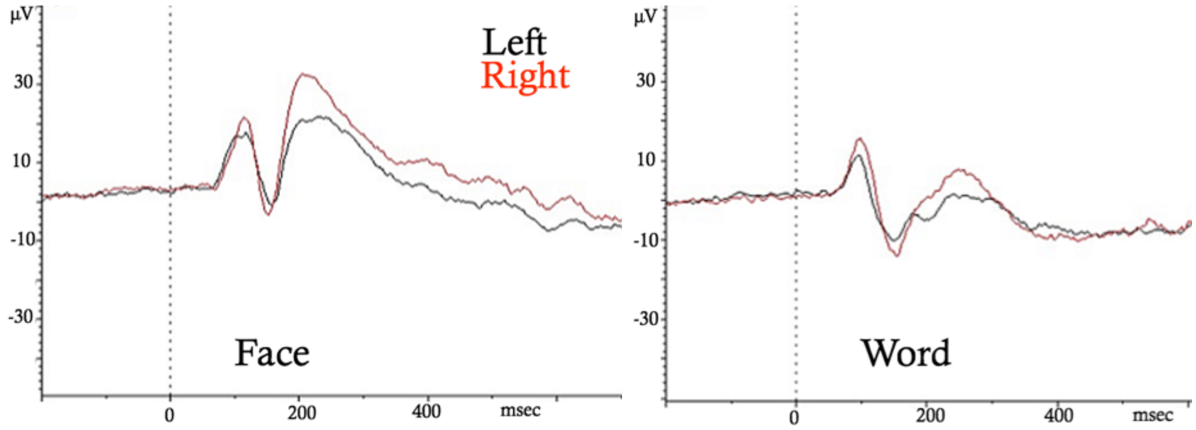


Figure 3.5 – Averaged waveforms from left and right scalp sites across all subjects. A slight, non-significant difference in N170 amplitude favours the right hemisphere for both face and word stimuli.

3.4 Interim discussion

The variability of participants' N170 asymmetry for the two tasks devised herein was sufficiently large that we concluded that this particular paradigm would not prove to be an effect prescreen for cerebral lateralisation for face processing or language functions. In fact, we discontinued this study because we did not find asymmetries in individual participants following the pattern of typical lateralisation, that we would expect to be consistent in some of our dextral subjects at least. Previous reports of a right lateralised N170 elicited from face stimuli, however, suggest that there is some relationship between this waveform and lateralisation of functions.

My second supervisor (Prof Guillaume Thierry) suggested that target-non target judgements might not have required enough depth of processing of the word and face stimuli, such that they might both require 'pattern matching' mechanisms employing the right hemisphere. Prof Thierry suggests this process accounts for the more negative N170 over the right scalp sites in the average waveforms for both face and word conditions.

Additionally, in some of his own published works attempting to artificially manipulate the N170 using non-face stimuli, Prof. Thierry found evidence that the P1 component is potentially more sensitive to faces than the N170 (Thierry et al., 2007a; Thierry et al., 2007b; Dering, Martin, Moro, Pegna & Thierry, 2011). In figure 3.5, the P1 is the initial positive component peaking around 120msec. Like the N170, in our averaged datasets, the P1 has a larger amplitude over the right scalp sites in both conditions. Nevertheless we decided it was worth examining in a second, larger experiment with the following improvements.

A noun/verb judgment and a male/female judgement task were employed, in the hope that this paradigm would increase depth of processing of the stimuli, and therefore result in more lateralised responses. Some a priori hypotheses were also made about the P1 waveform. Given its sensitivity to face stimuli compared with other stimulus categories, it is predicted that this waveform will behave similarly to the N170. Therefore a larger amplitude of the P1 is expected in response to faces over right scalp sites, and to words over left scalp sites.

3.5 Modified task paradigm to further investigate the potential for N170 amplitudes as indicators of hemispheric specialisation

3.5.1 Method

3.5.1.1 Participants

Participants were 34 students from Bangor University, and were divided into two groups based on hand-writing hand and WHQ score. The dextral group contained 22 participants (14 females) with an age range of 20-28 year (mean = 23.19), and a mean WHQ score of +29.05; whereas the adextral group *n*=10 (7 females) with an age range of 19-30 years (mean = 23.36), and a mean WHQ score of –18.09.

An additional two adextrals were tested after taking part in the neuroimaging project detailed in Chapter 5. These participants were selected for having atypical language representation (i.e. right hemisphere dominance) in response to a fMRI verbal fluency paradigm. These participants are investigated separately in section 3.4.2. Subsequently, eight other participants from this experiment also took part in the neuroimaging experiment (two dextrals, six adextrals), and their data is examined more closely in section 3.4.2.

3.5.1.2 Apparatus and stimuli

Stimuli were presented on a 23” AOC PC monitor. The face condition stimuli were 144 faces (72 male and 72 female) from the KDEF face database (Lundqvist, Flykt, & Ohman, 1998). These faces were cropped uniformly into 425 x 300 px ovals (10.7 x 7.6°), and presented in greyscale on a black background. Half of the faces were male and half were female. Similarly 144 words were used from the MRC psycholinguistic database (Coltheart, 1981; http://www.psych.rl.ac.uk/). Finding words that are exclusively nouns or verbs in English was surprisingly difficult, giving that many words (e.g. "watch", "water") can serve as either nouns or verbs. We controlled for this as best we could, using concrete nouns, but we would assume that as long as the participant is trying to do the task, they would be processing the word linguistically, regardless of its classification. Words were written in white on a black background 400 x 100 px (10 x 2.5°) rectangular background. Both tasks were written and presented in E-Prime® version 1.0 (Psychology Software Tools, Inc.).

3.5.1.3 Procedure

Participants were positioned in a comfortable chair 60cm from an LCD monitor in a dimly lit room. Each trial began with a fixation cross for 1000 msec, and the presentation of a stimulus for 200 msec. The word task involved the brief presentation of single words at fixation, after which the participant had to categorise the word as a noun or verb using the keys A or L in the 1000 msec inter-trial interval. Similarly in the face task, face stimuli were briefly presented centrally at fixation, and participants had to categorise the face as male or female, again using A or L. Response keys were counterbalanced across participants. Each task contained two blocks of unique stimuli (144 trials), and participants completed two runs of each task, resulting in 288 trials of each condition.

3.5.1.4 EEG recording methods and analysis

Electroencephalogram (EEG) was recorded continuously from 128 scalp positions (according to a 10-20 system) from BioSemi active electrodes mounted in an elastic cap. In accordance with typical BioSemi set-up, recordings were referenced against CMS as the initial common reference and digitised with a frequency of 2048 Hz. Individual ERPs would be re-referenced to the average reference during data processing. The EEG were filtered online between 0.01-400Hz, and offline low pass at 30 Hz. Horizontal and vertical electrooculograms (EOG) were also recorded, and ocular-correction ICA was used to remove artefacts relating to eye movements. Electrode offsets were kept below 50 µV in all cases, corresponding to typical impedance measures of signal quality.

The EEG was segmented into 1000 msec epochs, starting 100 msec before stimulus presentation. All epochs were then averaged into ERPs for both the faces and words conditions across each channel. Averages were created of the waveforms at preselected scalp sites in lateral occipitotemporal regions. These electrodes were A9-A12 and D30-32 over left skull and B6-B12 over right skull (corresponding to the area covered by P5/P7/P9/PO7/PO9, and P6/P8/P10/PO8/PO10 commonly used in N170 studies, see Dundas et al., 2014; Rossion et al., 2003), resulting in average waveforms from seven left and seven right scalp sites. The P1 measurement was taken as the peak positive amplitude between 70 and 140msec, and the N170 measurement was the peak negative amplitude between 140 and 210msec (Rossion et al., 2003; Thierry et al., 2007a). Grand averages were also calculated separately for the dextral and adextral groups (but did not include the two participants of known atypical language lateralisation).

Again, a larger proportion of the participants to have rightward biases in P1 and N170 amplitude to faces, and leftward biases in amplitudes in response to words was expected. If these waveforms are related to cerebral organisation of face processing and language functions, more reversed responses (i.e. left bias for faces or right bias for words) in the adextral group than the dextral group were expected (but our small sample of adextrals makes it difficult to infer information about the likely proportions of this group). These data were analysed largely descriptively. The number of participants with the responses hypothesised to relate to typical cerebral organisation is reported, and as are any asymmetries in the group averaged data for each sample.

3.6 Results

3.6.1 Proportions and central tendency

Initially, simply how many of each sample showed larger N170 amplitudes over the left or right scalp sites for each task was examined. In response to the face stimuli, 17/22 (77.27%) of the dextral sample had a numerically larger N170 over right scalp sites, as did 3/10 adextrals. In the word task, however, only 11/22 dextrals showed a larger N170 over left scalp sites, yet 7/10 adextrals showed this response. The averaged N170 data revealed that N170 amplitudes to faces were numerically larger over right scalp sites than left in the dextrals, but the opposite was true in the adextrals. In response to word stimuli, dextrals and adextrals showed a larger N170 over left scalp sites, albeit this difference being particularly small in the dextrals – see figure 3.6.

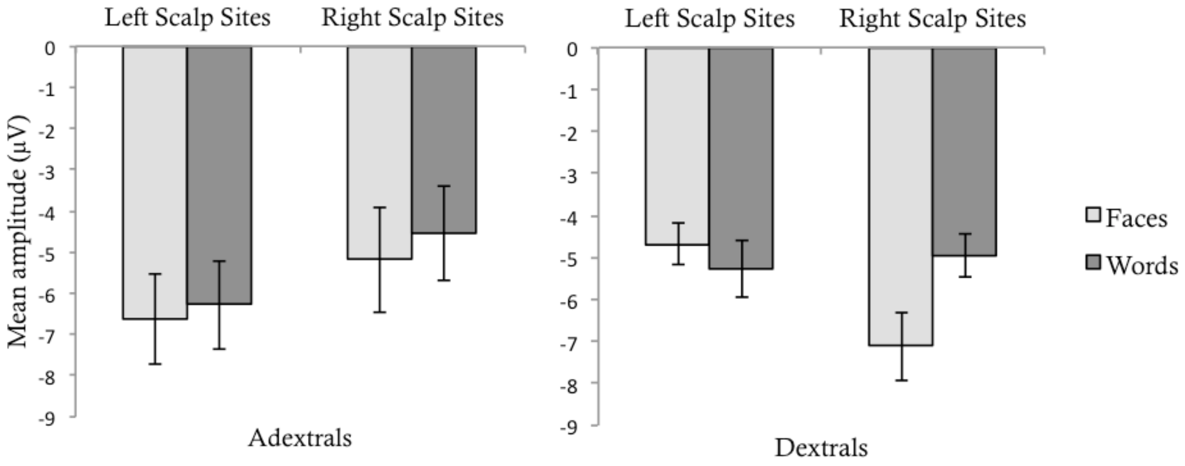


Figure 3.6 – Mean peak N170 amplitudes to face and word stimuli over left and right scalp sites plotted separately for dextrals (*n*=22) and adextrals (*n*=10). Only the dextral group show the commonly reported rightward asymmetry in the N170 to faces. Error bars = +/- 1 SEM.

The initial inspection of P1 amplitudes revealed that 14/22 (63.64%) of the dextral sample had larger P1 amplitudes over right scalp sites in response to face stimuli,

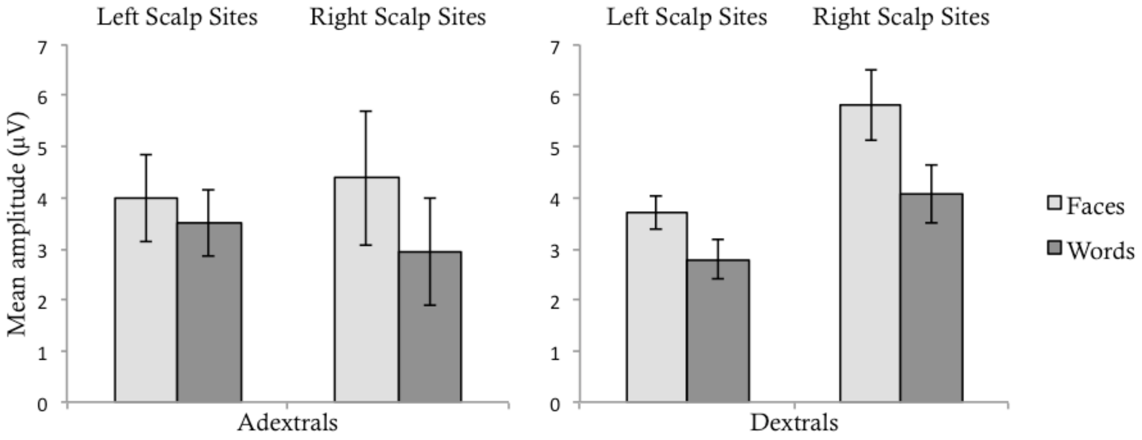


Figure 3.7– Mean peak P1 amplitudes to face and word stimuli over left and right scalp sites plotted separately for dextrals and adextrals. Error bars = +/- 1 SEM.

as did 5/10 adextrals. In the word task, only 8/22 dextrals had larger P1 amplitudes over left scalp sites in response to words, as did 7/10 adextrals. The averaged data shows higher mean P1 amplitudes over right scalp sites for faces in both groups, whereas in response to words the groups differ; dextrals having a larger mean P1 amplitude over right scalp sites, and adextrals showing the reverse response (see figure 3.7).

To compare the peak amplitudes statistically four 2x2 (scalp site x group) ANOVAs were run, one for each waveform and each task. A significant interaction between scalp site and group was found in the face N170 data ($F(1)=8.67$, $p<.01$,

ηp^2=.22, obs power=.81), with post-hoc t-tests demonstrating significantly higher N170 amplitudes over right scalp sites in dextrals (*t*(21)=2.85, *p*=.01), but over left scalp sites in adextrals (*t*(9)=2.89, *p*<.02). No other scalp site x group ANOVAs found any statistically significant differences.

Although no group differences were statistically significant in these analyses of group data, there could be statistically significant differences between the proportion of each sample showing an effect. We used z-tests to compare the numbers of dextrals and adextrals showing rightward biases in N170 and P1 amplitudes in response to faces, and leftward biases in response to words, although we interpret these data with extreme caution due to the small sample size of adextrals. There were no significant differences between dextrals and adextrals on any of the measures except in the N170 data in response to faces (*z*=2.67, *p*<.01).

3.6.2 Participants with known cerebral dominance

As mentioned in the participants section, two adextrals with known right hemispheric dominance for language were included after taking part in an fMRI project (see Chapter 5). This project involved using a verbal fluency task and a face localiser task to determine individual's cerebral asymmetry for language and face processing. One of these participants has reversal of both language and typical face processing dominance; the other has right hemisphere dominance for both functions. Despite their differing face lateralisation on fMRI measures, both these participants had a larger N170 for faces over right scalp sites, and a larger P1 over left scalp sites. In terms of word stimuli one participant had a larger N170 over right scalp sites, but both had a larger P1 over left scalp sites (see figure 3.8 for individual waveforms from the participant with atypical language and face lateralisation).

Of the dextral participants included in the above analysis, two took part in the fMRI project to be presented in Chapter 5. Both these individuals were typically organised with language dominance lateralised to the left hemisphere and face perception to the right. In the current experiment, however, one of these participants showed larger N170s to both faces and words over left scalp sites, and the other had larger N170s over right scalp sites for both stimulus types (see figure 3.9 for individual waveforms).

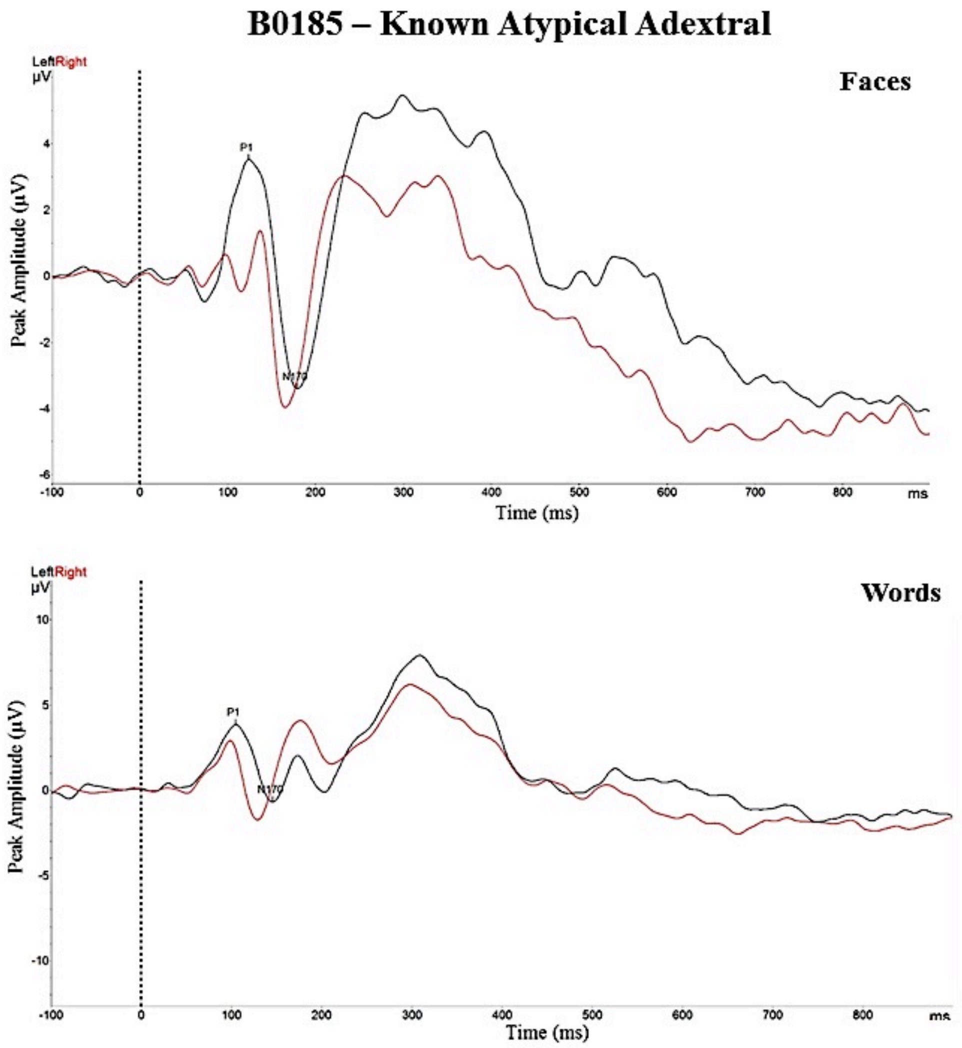


Figure 3.8 – Average waveforms in response to faces and words over left and right scalp sites from a adextral participant who shows the reverse of typical cerebral asymmetries as measured by fMRI localiser tasks. This participant has a rightward bias in N170 amplitude for both faces as well as words, results which again, are not concordant with the fMRI data.

In terms of the face task, two out six adextrals show concordance between their N170 data and their fMRI data, whereas four show concordance between their P1 asymmetry and fMRI data. In response to words, four out of six show agreement between N170 and fMRI asymmetry, and between P1 and fMRI, however, these are not the same four participants (two overlap). See figure 3.10 for waveforms from an adextral participant we know has typical cerebral organisation. Four waveform measures (word/face N170/P1) are available for each of ten fMRI participants. Table 3.3 contains fMRI LI measures for each participant and the congruency of each ERP waveform. The waveforms agree with the imaging data in 50% of cases.

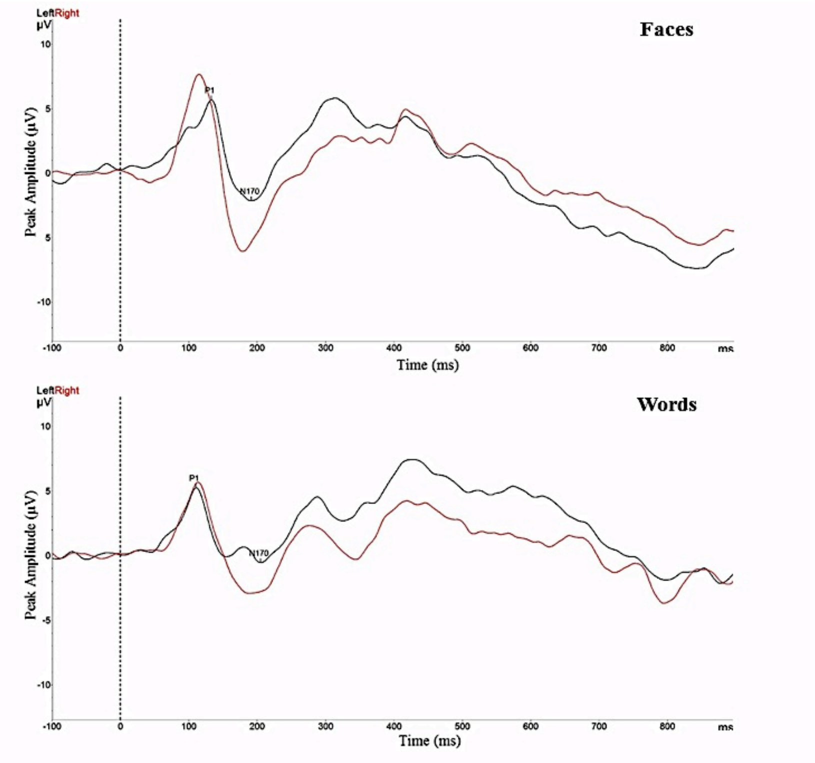


Figure 3.9 – Average waveforms in response to faces and words over left and right scalp sites, from a dextral participant who has typical cerebral asymmetries as measured by fMRI localiser tasks. This participant has a rightward bias in N170 amplitude for both faces and words, results which are not concordant with the fMRI data.

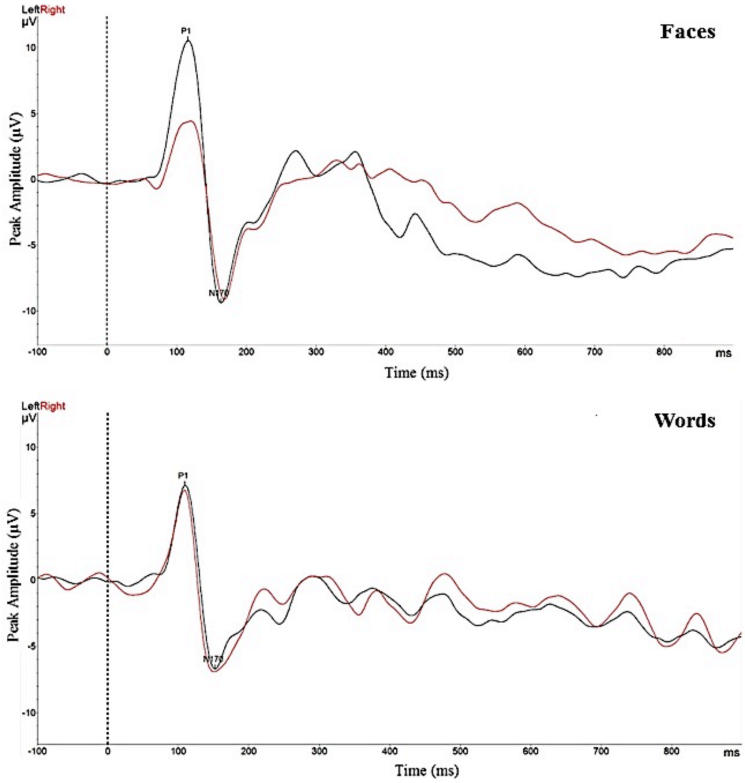


Figure 3.10 – Average waveforms in response to faces and words over right and left scalp sites from an adextral participant who has typical cerebral asymmetries as measured by fMRI localiser tasks. The differences between the N170s across the left and right scalp sites are negligible in this participant, but numerically the N170 amplitudes give the reverse finding to the fMRI data.

Participant#	LanguageLI	Face LI	N170Words	N170Faces	P1 Words	P1 Faces
B0130	.87	-.68	🟥	🟩	🟥	🟩
B0174	.69	-.68	🟩	🟥	🟥	🟥
B0069	.41	.18	🟩	🟩	🟥	🟩
B0325	.43	-.53	🟥	🟥	🟩	🟥
B0331	.73	.18	🟥	🟩	🟩	🟥
B0358	.79	-.10	🟩	🟥	🟩	🟩
B0360	.35	-.49	🟩	🟥	🟥	🟩
B0380	.59	.46	🟩	🟥	🟩	🟩
B0183	-.72	-.48	🟥	🟩	🟥	🟥
B0185	-.58	.71	🟩	🟥	🟥	🟩

Table 3.3 – Congruency of individual participant LIs from neuroimaging measures of language and face processing with ERP lateralisation. A positive LI indicates left hemisphere dominance. Red squares show waveforms that do not agree with the imaging data and green squares show agreement.

3.7 Discussion

These two studies were designed to evaluate the potential usefulness of electrophysiological measures for prediction of cerebral dominance in individual people. There is some suggestion in the data of the second, larger study for potential usefulness of the N170 response to face stimuli. The dextral sample displayed a statistically significant mean difference in N170 amplitude favouring the right scalp sites for faces, supporting previous findings (Bentin et al., 1996; Rossion et al., 1999). More interestingly for our purposes, a substantial majority of the sample (77.3%) showed this effect at the individual level. As proposed in the introduction, the proportion of a dextral sample expected to have right lateralised face processing functions is less confidently estimated than the proportion with left lateralised language functions. Therefore, ~80% could be seen as an encouraging success rate. Only 3/10 adextrals showed a rightward asymmetry in N170 amplitude for faces, which is the opposite proportion from what we would predict, but this sample is of course too small to infer anything generalizable from this proportion. It is worth commenting that the second study may not have substantially improved upon the first in terms of the face task, as a large proportion showing a rightward N170 for faces may have been reached if testing had continued.

For the language task the second study does not appear to improve dramatically on the first; neither study was successful in producing leftward asymmetries in N170s to words, opposing what has been reported previously (Bentin et al., 1999; Rossion, Joyce, Cottrell, & Tarr, 2003; Simon, Petit, Bernard, & Rebai, 2007). At the individual level, half our dextral participants showed a numerically larger N170 over right scalp sites. Interestingly 7/10 adextrals had a leftward bias for words, but this sample is too small to infer anything from this proportion. In those studies where both faces and words were included as stimuli, it was the rightward face response that was less frequent than the leftward word response (Rossion, Joyce, Cottrell, & Tarr, 2003; Joyce and Rossion, 2005; Maurer, Rossion, & McCandliss, 2008; Mercure, Dick, Halit, Kaufman, & Johnson, 2008; Mercure, Cohen Kadosh, & Johnson, 2011; Dundas, Plaut, & Behrmann, 2014).

The P1 data from experiment two is even less convincing. Whilst a majority of dextrals (63.6%) still show a rightward asymmetry in response to faces, the mean difference between scalp sites is not significant. Less than half of this sample show a leftward bias in P1 amplitude to words. In the adextrals, half show a rightward bias in N170 amplitude to faces, and as in the N170 data, 7/10 show a leftward bias for words. Interestingly the seven participants showing a leftward bias in the N170 word data are not the same seven participants showing this bias in P1 amplitude.

When we take into account the participants for whom we have fMRI measures, overall the ERP measures are extremely variable at the individual level. Many of these participants do not show concordance between their fMRI laterality for faces/words, and the N170 or P1 lateralisations. For the purposes of this thesis, this finding is the nail in the coffin. The aim of this body of work is to find tasks that tap into cerebral asymmetries that can aid prediction of lateralisation of functions at the individual level. Whilst we expect and accept measurement noise, a task that cannot classify even typically lateralised, dextral participants is not especially desirable.

Of course we must acknowledge our small sample of adextrals. Even without fMRI estimates, running this paradigm with a larger number of dextral and adextral participants could be useful, as perhaps there are patterns in the data that we do not have sufficient power to analyse. For example, extremely left-sided adextrals (e.g. Knecht et al., 2000) may be more likely to show peak N170s at the reversed scalp sites in response to face or word stimuli, or the lateralisation of the N170 could correlate with measures such as eye-dominance, foot preference, and WHQ score. Although if robust lateralisation of these waveforms is not present in dextrals, it is unlikely that these measures would improve outcomes.

Data collection from more individuals who had taken part in our fMRI paradigm could also have been useful to estimate how often the N170 marker fails at predicting the known laterality of a participant. Ideally, when including participants from the fMRI experiment, we could have preselected individuals with extremely lateralised fMRI data; perhaps a 'stronger' lateralisation would provide more signal reaching the scalp electrode sites. We did, however, include some extremely left lateralised for language participants (for example, an LI of +.87, i.e. 87% more activation in the left hemisphere than the right on our language task) that had right lateralised N170s and P1s to words. Likewise, a participant with an LI of -.68 for face perception had left lateralised N170s and P1s to faces. Therefore strength of lateralisation, at least as measured by our fMRI paradigms, does not result in more concordant ERP data.

After analysing this dataset, we decided that the ERP data did not seem a worthwhile enough predictor of brain asymmetry for us to continue down this avenue of research. Although EEG is relatively inexpensive in terms of running costs per participant, it is moderately expensive in terms of participant and experimenter time. Experimenters have to make choices about how best to spend their and their participants' time; half an hour of capping, an hour of data collection, post-collection tidy up cap cleaning etc, data processing (1 hour per person), compared with behavioural measures of asymmetry that take minutes (a dichotic listening test, for example). Therefore we set out to collect data on easier to implement behavioural tests, based on the indirect measures discussed in section 1.4 of Chapter 1 (pg 13), that we could test a larger sample of adextrals on more quickly.

Chapter 4 – Behavioural indicators of functional asymmetries

4.1 Introduction

Many neuropsychologists have employed measures of perceptual asymmetry, such as dichotic listening and VHF tasks, as indirect measures of cerebral asymmetries (e.g. Bryden, 1965, 1973; Kimura, 1967; Hilliard, 1973; Blumstein, Goodglass, & Tartter, 1975; Levy & Reid, 1978; Hugdahl & Franzon, 1985; Dagenbach, 1986; Hugdahl & Anderson, 1986; Franzon & Hugdahl, 1987; Mattingley, Bradshaw, Nettleton, & Bradshaw, 1994; Nicholls, Bradshaw, & Mattingley, 1999, etc). Despite the inexpensive and relatively brief delivery time of these behavioural tests, researchers often only used one of these measures with a set of participants. Of those who did include multiple tests, most only compared two measures: language-related dichotic listening and VHF tasks (Bryden, 1967, 1973; Hines & Satz, 1974; Fennell, Bowers & Satz, 1977a, 1977b; Dagenbach, 1986).

It is likely that the lack of research including more than one indirect measure is due to several of these studies finding no positive correlation between the language related dichotic and VHF tasks (Zurif & Bryden, 1969; Fennell, Bowers, & Satz, 1977a; Smith & Moscovitch, 1979). However, the constantly reported common finding is a right biased result in response to language stimuli. Therefore, regardless of poor inter-correlations, it is difficult to conclude that these tests are therefore unrelated to language asymmetry. One way to test if these experiments relate to cerebral asymmetry is to include adextrals in the sample; assuming fewer of them have typical cerebral dominance, the RVF or REA should be present, but reduced in this group.

In studies analysing adextral data on indirect perceptual tests, this is exactly the reported effect (e.g. Curry, 1967; Hines & Satz, 1974; Cowell, & Hugdahl, 2000; Foundas, Corey, Hurley, & Heilman, 2006). These researchers often imply that mean differences are due to a larger proportion of the adextral group showing the reversed side bias (McManus, 1983), but neglect to investigate these proportions, or report them. However, as ~70% of the adextral sample should have the same brain organisation as dextrals (although see Chapter 2 pg 28 for a discussion about issues with this assumption in small *n* adextral samples), the difference between the mean dextral and adextral scores are occasionally not significantly different (Zurif & Bryden, 1969; Brysbaert, 1994). Unfortunately, this pattern of results has been considered as evidence that either these tests are not strongly tied to hemispheric dominance of functions, or, that right and left handers do not have differing cerebral organisation (Zurif & Bryden, 1969; Brysbaert, 1994). The latter, to many, seems unlikely, given other sources of evidence (Carey & Johnstone, 2014). Nevertheless, if a mean difference between dextrals and adextrals is not found, it is still possible that a larger number of dextrals showed the response relating to typical cerebral organisation, than adextrals.

Although the literature surrounding these indirect tests is vast, it is not standard practice in this research to discuss the proportions of large dextral or adextral samples showing typical and atypical responses. Earlier studies of this kind report the proportions of dextral or adextral groups that exhibited one asymmetry or the other (e.g. Bryden, 1965; Curry, 1967; Hugdahl & Franzon, 1985; Hugdahl & Andersson, 1986). Unfortunately this practice has become less common as experimental psychologists have increasingly focussed on inferential statistics. Knowing more about these proportions would help estimate the potential usefulness of an indirect test as a tool for predicting cerebral asymmetries. For example, assuming the incidences of typical and atypical language organisation provided by Rasmussen and Milner (1977), a perfect predictor of language asymmetry would elicit a certain response in ~96% of dextrals and ~70% of adextrals. Therefore if the results of a dichotic listening paradigm yielded a majority of both handedness groups showing a REA, and the prevalence was higher in the dextral group, we might conclude that task is tapping into language asymmetry. This logic for investigating proportions to aid prediction of typical or atypical cortical organisation is the key theme of this chapter, as all tasks herein were analysed from this standpoint.

It would be useful to collect data on multiple behavioural perceptual tests within the same people. As mentioned earlier, some experimenters have attempted this approach (Bryden, 1967, 1973; Hines & Satz, 1974; Bowers & Satz, 1977a, 1977b; Dagenbach, 1986) and largely find that VHF and DL measures do not correlate as highly as expected, or in some cases, at all. These findings led to conclusions that there is a dissociation between auditory and visual language processing. Most studies of this kind were performed at a time before technological advances allowed for careful control over stimuli, and, more crucially, the ability to scan participants with fMRI protocols to determine individual laterality (to be investigated in Chapter 5) to relate to any possible perceptual or behavioural measures of interest. Such an approach would not only help establish which tests result in proportions approximating population estimates of brain asymmetry, but could also provide the opportunity to assess whether a combination of multiple weak predictors could form a single, more useful, predictive variable.

4.1.1 CV dichotic listening

The starting point for the development of the test battery presented in this chapter was a consonant-vowel (CV) dichotic listening paradigm (Hugdahl & Anderson, 1984; Hugdahl, 2003; Hugdahl et al., 2009; Hugdahl & Westerhausen, 2010) kindly shared with us by the Bergen DL laboratory (http://fmri.uib.no). This task involves the simultaneous presentation of two different consonant-vowel syllables to the left and right ear, the idea being that which stimulus (left or right) the participant reports could be indicative of underlying language dominance in the contralateral hemisphere (Kimura, 1967). If this task could aid prediction of language dominance, its short administration time is extremely attractive.

As the potential usefulness of quick behavioural predictors such as CV dichotic became apparent, other short indirect measures were added to our testing sessions. The final battery involved a further five tasks; a VHF Stroop task and the octave illusion (supposedly related to left hemispheric processing), and a greyscales task, an in-house face recognition test, and an in-house dichotic listening task based on the Efron & Yund (1974) tone task (favouring right hemisphere-related functions).

4.1.2 Lateralised Stroop task

Dyer (1973) reported that when presenting Stroop words in a VHF task, participants would have delayed vocal reaction time (VRT) and/or make more errors when the incongruent colour word was presented in the visual field projecting to the language dominant hemisphere. Hugdahl and Franzon (1985) investigated this phenomenon in 20 dextral and 10 adextral male subjects. The adextrals were preselected for having a LEA on a CV dichotic listening paradigm, providing sufficient evidence to expect atypical organisation in at least some of the adextral group. In the dextral population all but three subjects made more errors in the RVF than in the left, although there was no effect of VHF on VRT. In the adextral group, seven out of 10 made more errors in the LVF, and there was a significantly slower mean VRT in the LVF than the right. As these adextrals were preselected for a measure related to right-hemisphere language dominance, the present study aims to investigate proportions of a random sample of adextrals showing these effects, for easier comparison to large group Wada test estimates.

4.1.3 The octave illusion

A further indirect measure that has been associated with left hemisphere processes is the auditory octave illusion (Deutsch, 1974). This illusion involves a sequence of tones, alternating in pitch between 400 Hz and 800 Hz, that are presented in equal amplitude to both ears simultaneously. However, when one ear receives the 400 Hz tone, the other receives the 800 Hz tone (see figure 4.1). A commonly resulting percept is that all the higher tones are presenting to one ear, and the lower tones to the other (Deutsch, 1974; 1978; 1980). This illusion perception varied across handedness groups; most dextral participants (25/31; 81%) reported hearing the high tones in the right ear, whereas adextrals (*n*=17) did not show a group level asymmetry. Only six adextrals gave the typical dextral response, seven gave the reverse of this response, and four had no strong asymmetry.

To investigate this difference in asymmetry further, Deutsch (1983) compared percept of the octave illusion as a function handedness and familial sinistrality. Of the dextrals with no familial sinistrality (*n*=86) 87.2% gave a right ear response, whereas in the dextrals with an adextral parent or sibling (*n*=54) this right ear response decreased to

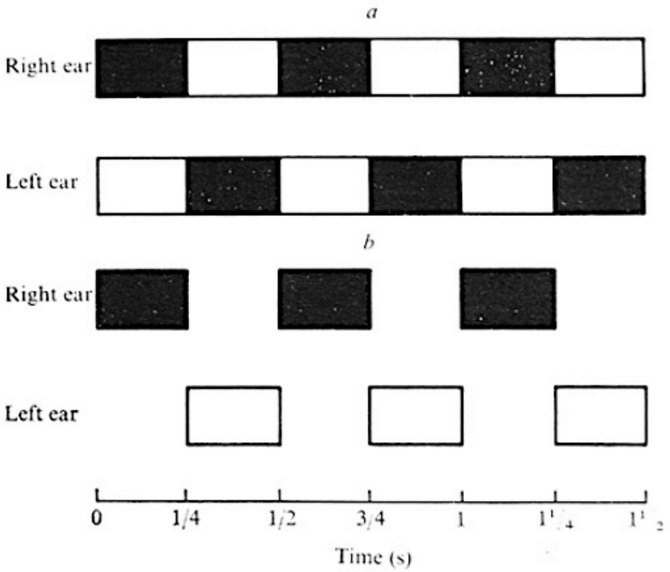


Figure 4.1 – A representation of the octave illusion (Deutsch, 1974). The dark boxes represent the 800 Hz tones and the light boxes the 400 Hz tones. The top panel *a* shows a representation of the actual stimulus configuration, and the bottom panel *b* indicates the most commonly obtained illusory percept.

72.2% of the sample. Only 55.6% of the adextrals with no familial sinistrality (*n*=9) provided this right ear response, decreasing to 45.4% in adextrals with an adextral parent or sibling (*n*=22). Therefore modulation of potential genetic factors relating to hand preference, as well as hand preference itself, appears to affect individual participant's perception of the octave illusion stimulus.

Whilst the mechanism behind this illusion remains unclear, Deutsch (1980) suggests that the perception of the octave illusion could be dependent upon pathways conveying information from the dominant side of auditory space (described as the side contralateral to the language dominant hemisphere), and that the strength or asymmetry of these pathways would be decreased in adextral subjects.

4.1.4 The greyscales task

As well as these left hemisphere measures, tasks relating to right-hemisphere related asymmetries were included in the present test battery. Not only would such tests allow for potential assessment of theories of complementary hemispheric specialisation, but they may also capture some of the unexplained variance in responses to the left-hemisphere related measures.

Nicholls and colleagues (1999) tested free-viewing perceptual asymmetries in 24 healthy dextral participants with the greyscales task, in which participants were presented with two left-right mirror-reversed brightness gradients (see figure 4.2). They were asked to select which stimulus is darker overall. Participants had a tendency to select the stimulus that was darkest on the left (68% of the trials in group averaged data), and response times were faster for left responses than for right. Mattingley et al. (2004)

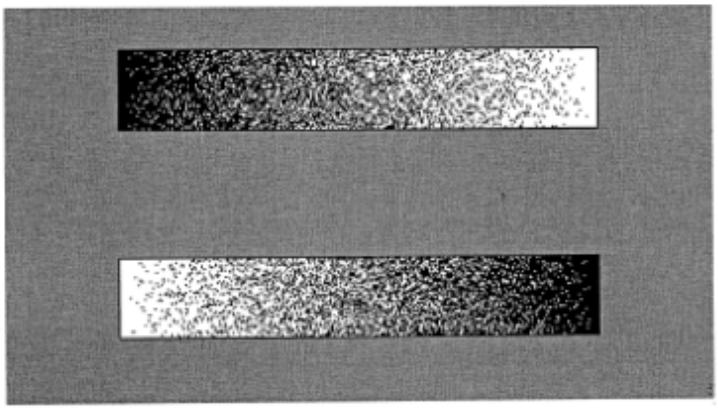


Figure 4.2 – An example of the greyscales stimuli as used by Nicholls et al. (1999). Although the light/dark information in the two 'bars' is identical (but reversed), most participants experience the top bar as slightly darker.

administered this task to three participant groups; patients with damage to the left hemisphere (*n*=20), damage to the right hemisphere (*n*=20), and right-handed healthy controls (*n*=20). Left hemisphere patients showed extreme biases towards the bar darkest on the left, right hemisphere patients showed extreme biases to the bar darkest on the right, and controls demonstrated a small but significant leftward bias.

These sets of results suggest that side biases in responses to the greyscales task may be indicative of a subtle (and perhaps attentional) asymmetry favouring the right hemisphere. To our knowledge there has been no analysis of adextral performance on the greyscales task. If this leftward bias were related to a right hemispheric asymmetry, less adextrals than dextrals should respond in this fashion.

4.1.5 VHF face recognition task

A more obvious right-hemisphere asymmetry is face perception. Multiple VHF studies have shown a LVF advantage in response to face stimuli (e.g. Geffen, Bradshaw, & Wallace, 1971; Marcel & Rajan, 1975; Klein, Moscovitch, & Vigna, 1976; Leehey & Cahn, 1979). For example, Hilliard (1973) conducted a study in which unfamiliar faces were presented to the RVF or LVF of 20 dextral subjects. Following this initial presentation, a centrally presented comparison face was displayed, and participants had to judge whether it was the same face as in the visual-field presentation or not. Participants were significantly better at recognising faces from the LVF than from the RVF. We aimed to conduct a similar task, but opted for bilateral presentation, as a series of studies by Boles (1987; 1990; 1994) showed that VHF differences were larger and more reliable when stimuli are presented in a simultaneous bilateral fashion, compared to single visual field presentation (discussed in Hunter & Brysbaert, 2008).

4.1.6 Efron dichotic listening

A right-hemisphere-related auditory dichotic listening task was also employed in the current study. Although the literature on CV dichotic paradigms far outweighs that of tasks involving non-verbal stimuli, there are studies that have found a significant LEA in response to dichotic presentation of tone stimuli (Curry 1967; King & Kimura, 1972; Carmon & Nachshon, 1973).

Efron and Yund (1974) described a task where subjects were presented with two tone bursts of 1500 Hz and 1900 Hz. In one ear the 1500 Hz tone would present first, followed by the 1900 Hz tone, whilst the other ear received the reverse order of the same two tones. When asked to describe whether the second tone was higher or lower in pitch than the first, all participants reported the presentation pattern of the left ear. However this experiment was conducted with a very small sample size (*n*=5). The authors concluded that this result related to a right-hemispheric specialisation for processing nonlinguistic sounds.

To test this hypothesis, Efron and Yund (1976) included a sample of six adextral and 24 dextral participants in a further study utilising this task design. Of the dextral participants, only seven displayed the atypical REA, whereas in the limited adextral sample three participants had a REA.

Gregory (1982) assessed this task in a larger number of participants, and with improved stimuli. In this experiment 75% of participants showed this left ear advantage, but there was no difference in proportion between dextral and adextral participants. There were some methodological issues with this study however, in that participants were allowed to listen to the tone combination "as many times as they wished until they could make a decision as to which was higher in pitch" (page 90). Therefore it is unknown how many trials which participants needed. For example, 7% of the sample could not come to a decision and were recorded as having no clear dominance, but it is unknown if they had a LEA on trial one, then listened again and had a REA, or if they had NEA within trial.

In this chapter, the aims and hypotheses for each neuropsychological test are the same. It was predicted that if any given task is a good predictor of cerebral asymmetry, the proportions of participants giving the typical response (that is, the direction that corresponds to 'typical' cortical organisation) would be the majority in both dextral and adextral samples. However, the proportion of the adextral sample giving this typical response would be significantly less than that of the dextrals, as assessed by a z-test. Due to this difference in proportion, it was also anticipated that most tasks would elicit a mean response that is biased in the same direction in both dextrals and adextrals (e.g. REA, LVF advantage, etc), and that magnitude of the side bias will be greater in the dextrals, making them more 'asymmetrical' as a group.

4.2 Methods

4.2.1 Participants

Participant demographics for all tasks in this chapter are displayed in table 4.1 below. All participants were students and staff at Bangor University recruited through email campaigns and online university advertisements.

Task	Group	Sex	Age	WHQ
CV Dichotic	Dextral	M=60 F=72	24.05	+27.05
	Adextral	M=66 F=87	24.67	-18.20
Lateralised Stroop	Dextral	M=28 F=36	26.2	+28
	Adextral	M=20 F=33	24.8	-11
Octave illusion	Dextral	M=46 F=57	24.82	+27.24
	Adextral	M=48 F=60	25.33	-17.80
Greyscales	Dextral	M=34 F=41	26.10	27.92
	Adextral	M=45 F=57	25.54	-16.73
VHF face recognition	Dextral	M=23 F=31	26.82	+28.02
	Adextral	M=31 F=31	27.32	-16.74
Efron Dichotic	Dextral	M=46 F=56	24.26	+27.20
	Adextral	M=49 F=61	25.26	-17.90

Table 4.1 – Participant demographics for each study in this chapter. Group means are displayed in the age and WHQ columns. It is important to note that several participants took part in all studies.

4.2.2 Apparatus and materials

All stimuli were presented using EPrime 2.0 software (Psychology Software Tools, Pittsburgh, PA) running on a PC. The Stroop task required the measurement of vocal reaction time (VRT), which was recorded through a voice key comprising a 20mm diameter microphone connected to a sound relay-detector and timer. A trigger to start the timer was sent from the presentation PC at stimulus onset, and the voice key sent a trigger back to the recording PC upon voice detection. The Stroop and greyscales tasks involved stimulus presentation on our bespoke glass table using a short-throw projector (for a detailed description of these apparatus see Chapter 2). The VHF face recognition task was presented on a 24” 60 Hz monitor. The remaining three experiments in this chapter involved auditory stimuli, which were delivered through a pair of Beyerdynamic

DT770 PRO 80 OHM headphones. Care was taken to ensure the two channels were matched for sound pressure level (SPL) using a decibel meter. Outputs were fixed at 80 dB (balanced at +/- 0.1 dB).

4.2.3 Stimuli and procedures

4.2.3.1 CV dichotic listening

Participants were given a set of headphones and listened to one pair of syllable per trial. They were instructed to report verbally after each presentation, which of six options (Pa, Ta, Ga, Ka, Da, and Ba) they heard. The experimenter would enter this response using a keypress, initiating the next trial. Participants were warned that they may hear more one stimulus or more than one, and were instructed to report the syllable they heard first or "most clearly". These instructions are standard procedure in the current CV dichotic listening literature (e.g. Hjelmervik et al., 2012; Kompus et al., 2012). Additional instructions were given to the participants that they should try not to 'listen' to one ear or the other, and that they should try and centre their attention. Participants were asked to point to a sheet containing a table of the syllables as they responded, as this may help minimise accidental attentional drift. Participants were encouraged to respond quickly but there was no time limitation on how quickly they could respond.

Three blocks of 36 trials were completed per participant, with self-paced inter-block breaks. The first block contained a mixture of all possible syllable combinations, whereas the second and third block only contained stimuli matched for voice onset time. The second block contained those with a long voice onset time (Pa Ta Ka), and the third contained only the short voice onset time syllables (Ba Da Ga). The stimuli were .wav files consisting of pairs of syllables where one was delivered to the left-channel, the other to the right. There was a soundfile of each possible combination of these syllables, including same-same pairs (which accounted for 18 of the trials and were not included in the analysis). The syllables were temporally synchronised to have the same onset time in the left and right channel, and had a mean duration of 400 msec.

4.2.3.2 Lateralised Stroop task

Participants stood centred at the middle of the presentation table. A fixation cross was presented at the start of each trial and participants were instructed that it was essential they maintain fixation. Stroop word stimuli appeared at a rate of one per trial either centrally over the fixation cross, or at 7.58° lateral to fixation in either visual field (assuming a viewing distance of 55 cm). The stimulus was presented for 200 msec before offset, at which point the program waited for the participant's response via the voice key, and the experimenter's input ("R" on the keyboard for "red", "B" for "blue", etc). Congruent trials were presented in 20% of trials, and 20% of trials were central presentations (randomised to ensure these were not the same 20%).

The coloured words presented were "red", "blue", "green" and "white". This final “colour” is an unusual choice, however, due to technical limitations of our projector, it was extremely difficult for participants to distinguish between yellow and green (colours that were used in the Hugdahl and Franzon studies this task is derived from). Therefore we replaced yellow with white, which seemed easier to detect (discussed later in this chapter). A total of 100 trials were presented in two blocks of 50, with a participant-paced rest break in between them. The experimenter manually triggered every trial, so it was possible for a mid-block break when requested.

4.2.3.3 The octave illusion

Participants were given a set of headphones and instructed that they would hear a "complex series of tones" and that their task was to decide which ear was receiving "more high tones". This is a modification of the original task in that our design only allowed a two forced-choice response, whereas traditionally more complex responses including the tones being higher in one ear and then the other, or no difference between the ears were accepted and recorded (Deutsch, 1974). It was not made clear to participants that the two ears were experiencing the same, jittered stimuli. We asked participants to respond as soon as they had an answer, either verbally or by pointing to the ear that they felt presented more high tones.

The stimulus was a one minute long .wav file of the Octave illusion obtained with permission from Diana Deutsch's UCSD webpage (http://deutsch.ucsd.edu/psychology/pages.php?i=202). This soundfile contained a sequence of sine wave tones with frequencies alternating between 400 Hz and 800 Hz and durations of 250 msec (see figure 4.1, page 72). The sequence presented over both headphone channels simultaneously, however the presentation of the high/low tones were staggered so that when one ear was presented the 400 Hz tone, the other received the 800 Hz tone.

4.2.3.4 The greyscales task

Participants were stood centred at the glass-topped lab table. Each trial consisted of the presentation of a pair of greyscale bars (under free-viewing conditions), which remained on screen until the participant responded, by verbally stating which bar, top or bottom, appeared darker to them. The experimenter would input the response using a keypress. The acquisition of a response would trigger the following trial. There were 40 trials in total. Participants were instructed to respond as quickly as possible, and were reminded of this throughout.

Stimuli consisted of 40 .jpeg files of two left-right mirror reversed brightness gradients (or "greyscales") presented on a white background. One end of each bar was white, the other was black, and in between shading transitioned from black to white. The bars were presented on top of one another. The length of the greyscales, and whether the left/right darkest bar was presented in the top or bottom location varied from trial to trial. The stimuli were kindly provided by Prof. Nicholls (Flinders University: http://www.flinders.edu.au/sabs/psychology/research/labs/brain-and-cognition-laboratory/the-greyscales-task.cfm).

4.2.3.5 VHF face recognition task

Participants were seated at the computer and positioned in a headrest 50 cm away from and centred to the monitor. Each trial began with a central fixation cross followed by the bilateral presentation of two greyscale face stimuli for 160 msec, followed by two masks for 50 msec. The presentation duration of these stimuli was hard to decide upon, due to the wide variation in the literature (42-66 msec – Hilliard, 1973; 59 msec – Yovel, Tambini, & Brandman, 2008; and 100 msec – Turkewitz & Ross, 1983). In an initial pilot phase with eight subjects, participants could not perform above chance in either visual field at any of these stimulus durations. One hundred and sixty msec was the shortest duration time at which pilot participants performed above chance. Participants were instructed to fixate throughout this presentation. After stimulus offset two faces would appear above and below fixation, for an unlimited period of time (during which participants' eyes were free to move), and participants had to report which face had been in the previous pair via a keypress response. Only one of these faces would have presented in the original pair. The keypress response would initiate a variable 200/400/600 msec delay followed by the next trial.

There were two blocks of 48 trials. Faces appearing in each trial together were matched for gender and noticeable features (contrast, hair, dark eyebrows, etc). The same set of faces was used in each block (but with no repeats within block), so that faces that had appeared in the left visual field would also appear on the right. Trial order was randomised. Stimuli were 144 greyscale faces cropped into 300 x 424 px ovals (9 x 12.6° of visual angle).

4.2.3.6 Efron dichotic listening

This task was adapted from Gregory (1982). Participants were seated at the computer, and were instructed that they would be presented with two sounds per trial, and that their task was to identify whether the second sound was higher or lower in pitch than the first (responding with one of two key presses). It was not made clear to participants that the two ears were experiencing different stimuli; they were only told to judge the pitch difference between the "first sound" and the "second sound". A response triggered a 1000 msec delay followed by the next trial. Participants were asked to be as quick and as accurate as they could with their responses. Each of the experimental soundfiles described below presented five times, with the filler trials presenting three times each. This resulted in one block of 36 trials.

The stimuli were .wav files each consisting of two pairs of tones. Two initial tones presented simultaneously in each channel, as did a further second pair of tones. The tones had a duration of 320 msec (with a 20 msec rise and decay time), with a 500 msec silence presented in between the tones (Gregory, 1982). The four frequencies used were 1450 Hz, 1550 Hz, 1650 Hz, and 1750 Hz; created using Audacity® audio editing software (Mazzoni & Dannenberg, 2002). Frequencies were paired only with the closest alternative stimulus (i.e. combinations of 1450 Hz and 1750 Hz were not present). There was a .wav file of each combination of the above frequencies, resulting in six soundfiles. Additionally two "filler" files were created where the left and right channels experienced identical stimuli presentation (a pairing of 1450 Hz and 1550 Hz, and another of 1750 Hz and 1650 Hz).

4.2.4 Analysis and Design

Results for these tasks are reported in separate sections. Results from many of these experiments are expressed as a laterality index (LI). LIs were calculated using the following traditional formula:

$$\text{Laterality Index} = \left(\frac{RVF-LVF}{RVF+LVF}\right)100$$

In our calculation, a negative score indicates a leftward perceptual bias, and a positive score a rightward bias. These sides refer to the percept, rather than the associated hemisphere. Using CV dichotic as an example, a score of +100 would indicate that the participant was 100% more likely to report the syllable that was presented to the right ear (with -100 suggesting the reverse – 100% more likely to report the left ear syllable). However in our lateralised Stroop task and VHF face recognition task, raw measures were used, as accuracy was more relevant (unlike the other tasks where forced-choice decisions are based on percept and are never 'incorrect').

It was anticipated that a majority of both groups would present with the predicted direction-specific response, with that majority being smaller in the adextral group. Therefore each results section includes a *z*-test to calculate whether the percentages of dextral and adextral samples showing a particular effect were significantly different to one another (i.e. if the adextral proportion is significantly smaller). An analysis of group differences (dextrals vs adextrals) in the dependent measure is also included, using an independent-samples t-test (excluding the octave illusion where participants' responses are dichotomous). The expectation was that dextrals would have stronger averaged asymmetries than adextrals, given the anticipated differences in proportions. As the hypotheses for all these measures are directional, all statistical comparisons reported are one-tailed.

4.3 Results

4.3.1 CV dichotic listening

We predicted a higher (and therefore more rightward) LI score for the dextrals than the adextrals, and also more of the dextral sample to display a REA. There was a significant difference in the predicted direction ($t(283) = 1.81$, $p<.04$, 1-tailed), with dextrals (M=23.8, SD=23.1) having a higher average LI than adextrals (M=18.3, SD=27.5). The proportions of each sample showing a LEA (atypical) or REA (typical) can be seen in figure 4.3. A *z*-test found the proportion of participants with an REA in the dextral sample to be higher (+7%; 95% CIs 2-12%) than that of the adextrals (*z*=1.65, p<.05, 1-tailed).

Raw accuracy scores from the left and right ear were also analysed. It has been argued that this comparison is more informative than the use of LIs alone, as it indicates which ear shows the advantage/disadvantage, rather than just the difference between them (Hugdahl, personal communication 18th December 2015). Mean left ear accuracy scores were 29.9% (*SD*=9.2%) in dextrals, and 32.5% (*SD*=11.1%) in adextrals, which was significantly different measured by a *t*-test (*t*(283)=2.07, *p*<.04). Right ear accuracy was 49.5% (*SD*=11.7%) in dextrals and 47.6% (*SD*=12.7%) in adextrals, and this difference was not significantly different (*t*(283)=1.28, *p*=.20). Therefore, it is an increased accuracy in left ear responses that drives the difference between the two groups on this measure.

4.3.2 Lateralised Stroop task

For this experiment difference scores between RVF and LVF VRT and accuracy were both analysed separately. It was predicted that there would be more errors and/or slower VRT in the RVF in both groups, and this response would be more frequent in the dextral sample.

Only correct trials were used for VRT analysis, and a difference score was calculated as LVF – RVF VRT. No significant difference was found between the groups for VRT difference (*t*(160)=1.43, *p*=.15). Dextrals had a mean VRT of 687.6 msec (*SD*=131.4) in the LVF and 691.1 msec (*SD*=128.6) in the RVF; adextrals had a mean VRT of 699.9 msec (*SD*=101.0) in the LVF and 691.9 msec (*SD*=106.1) in the RVF. Bonferroni-corrected pairwise comparisons (corrected for three tests) indicated that VRTs in the central space (*M*=724.1 msec) were significantly slower than VRTs in both the LVF (*M*=693.7 msec; *t*(160)=4.81, *p*<.001) or the RVF (*M*=691.5 msec; *t*(160)=5.51, *p*<.001), but that these were not significantly different to each other. The percentage of each sample displaying slower VRTs in each visual field is displayed in figure 4.1. The proportion of the dextral sample showing slower VRT in the RVF was significantly higher (+16%; 95% CIs 9-23%) than that of the adextrals (*z*=3.44, *p*<.001, 1-tailed; see figure 4.3).

Our participants were essentially at ceiling in terms of Stroop accuracy, and in general very few errors were recorded. An accuracy difference score was calculated as the proportion of correct trials in the LVF minus the RVF. Despite the accuracies difference by <2%, a significant difference in this score was found between dextrals and adextrals (*t*(160)=2.54, *p*=.01). Dextrals had a mean accuracy of 0.96 (*SD*=0.04) in the LVF and 0.95 (*SD*=0.05) in the RVF, whereas adextrals had a mean accuracy of 0.96 (*SD*=0.05) in the LVF and 0.97 (*SD*=0.05) in the RVF. A subset of 33.5% of participants had equal accuracy in the left and right visual fields (in this case usually this was through making zero errors). Of the remaining participants who displayed a numerical difference, the percentage of each sample performing worse in the RVF was significantly higher (+23%; 95% CIs 16-29%) in the dextral group (*z*=3.36, *p*<.001, 1-tailed; see figure 4.3 for percentages).

4.3.3 The octave illusion

As the nature of this measure is that it is dichotomous, no inferential statistics can be carried out on group averages. It was expected that a majority of both groups would give a right ear response, but with a decreased frequency in the adextral sample. The percentage of each sample reporting the right ear was 64.7% of dextrals and 54.1% of adextrals, see figure 4.3. A *z*-test found that the proportion of dextrals with a right ear response was significantly higher (+10%; 95% CIs 4-17%) than the adextral sample (*z*=1.65, p<.05, 1-tailed).

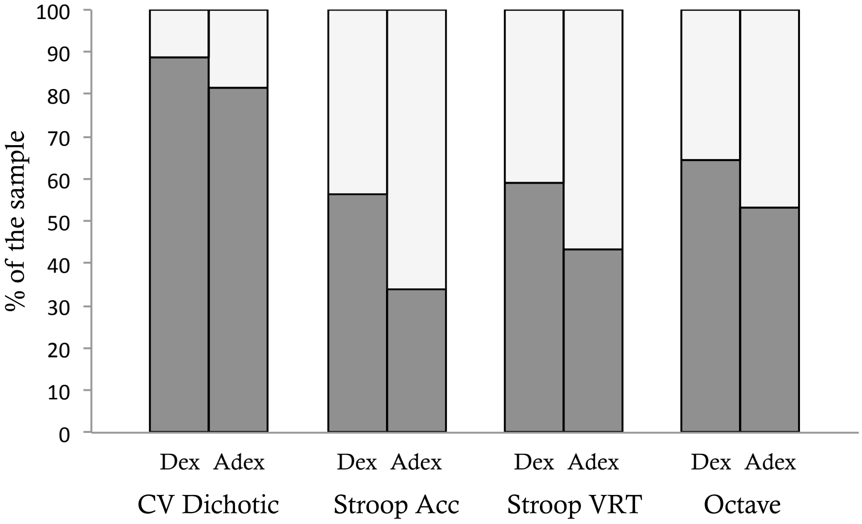


Figure 4.3 – Percentages of each sample showing typical responses on the left-hemisphere related tasks. Dark grey indicates the ‘typical’ response, whereas light grey shows the ‘atypical’ proportion. The percentages for each task in this figure are significantly different between dextrals and adextrals.

4.3.4 Greyscales

It was anticipated that most participants in both groups would make choices corresponding to the bars that were darkest on the left being darkest overall (producing a negative LI), but that this response would be more frequent in the dextral sample. No significant difference in mean LI (-22.3 [*SD*=36.5] and -23.5 [*SD*=39.0] for dextrals and adextrals respectively) was found between groups (*t*(175)=0.20, *p*<.05). The same percentage of each sample showed no directional difference (and therefore an LI of 0); 4.1% of dextrals and 4.1% of adextrals. Only those showing a numerical difference between left and right biased were included in proportional analyses. There was no significant difference between the proportion of the dextral (+7%; 95% CIs 1-13%) and adextral samples showing a leftward bias (*z*=0.91, *p*>.05; see figure 4.4).

4.3.5 VHF face recognition task

In this task it was predicted that most participants would report more of the faces presented in the LVF, and that this pattern would be stronger or more prevalent in the dextral sample. Accuracy difference scores were calculated as proportion of correct trials in the LVF – RVF, so that a negative score indicated a LVF advantage. Both dextral and adextral groups showed on average a slight RVF advantage which was not different between groups (*t*(114)=0.33, *p*>.05). Dextrals had a mean proportion of correct trials of 0.61 (*SD*=0.08) in the LVF and 0.62 (*SD*=0.09) in the RVF, and adextrals scored 0.61 (*SD*=0.09) in the LVF and 0.63 (*SD*=0.10) in the RVF. Five adextral participants had no difference between the VHFs, and were not included in the proportional analysis. The proportion of dextrals with a LVF advantage was significantly higher (+11%; 95% CIs 5-18%) than that of the adextrals (*z*=1.35, *p*>.05; see figure 4.4), but both samples had a smaller proportion with a LVF advantage than a RVF advantage, against our hypothesis.

4.3.6 Efron dichotic

It was anticipated that most participants would have a LEA, and therefore a negative LI. The incidence of LEA was expected to be higher in the dextral sample. No significant difference in LI was found between dextrals (*M*=-15.7, *SD*=37.0) and adextrals (*M*=-8.6, *SD*=34.0); *t*(209) = 1.45, *p*>.05. NEA was reported in 4.0% of the dextrals and 8.4% of the adextrals. More of the adextral sample showed a LEA than the dextral sample, therefore *z*-test was not carried out (see figure 4.3 for proportions).

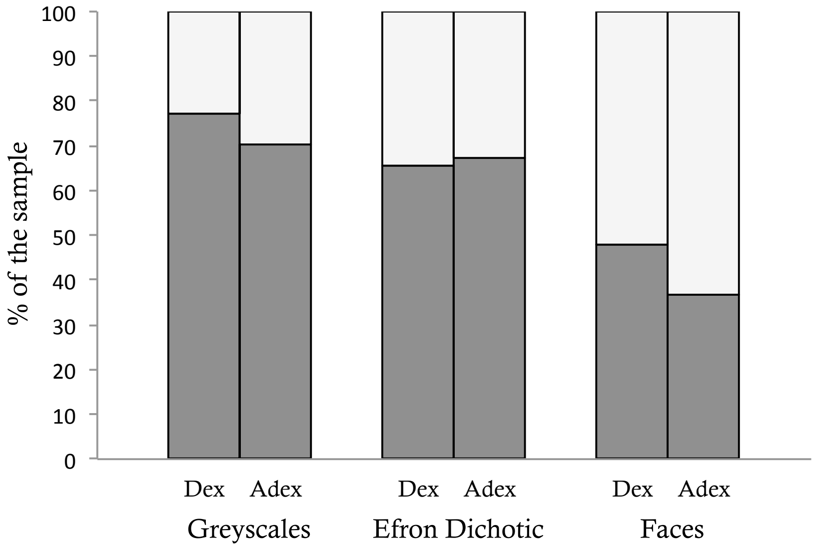


Figure 4.4 – Percentages of each sample showing typical responses on the right-hemisphere related tasks. Dark grey indicates the 'typical' response, whereas light grey shows the 'atypical' proportion. A significant difference was present between the dextral and adextral samples on the VHF face recognition task only.

4.3.7 Cross-task analysis

Proportions across task are displayed above on two separate figures; figure 4.3 for tasks relating to typically left hemisphere functions and figure 4.4 for tasks relating to typically right hemisphere functions. Bivariate correlations were run between all measures to assess if being strongly lateralised on one task would be related to strong lateralisation on another measure, and also if left versus right hemisphere related tasks were correlated. These tests were one-tailed due to strong directional predictions that scores from tests that investigate functions from the same hemisphere should be positively correlated, and comparisons across tests relating to different hemispheres should be negatively correlated. Only CV dichotic and Efron dichotic, and of course the two Stroop measures (accuracy and VRT) were significantly correlated (r=.13, p<.03, and r=.19, p<.01 respectively). However, the directional prediction between scores on CV dichotic and Efron dichotic would be a negative correlation, however, so the correlation between these measures was not interpreted. A matrix scatterplot displaying all relationships between all measures can be seen in figure 4.5.

Some score comparisons, such as between Stroop accuracy and the greyscales task, appeared more related in one handedness group than the other. We ran correlations between all the measures again for the two handedness groups separately, and found that only a negative correlation between Stroop accuracy and greyscales (r=-.25, p<.03) was present in the dextral sample. In the adextral group a significant correlation was found

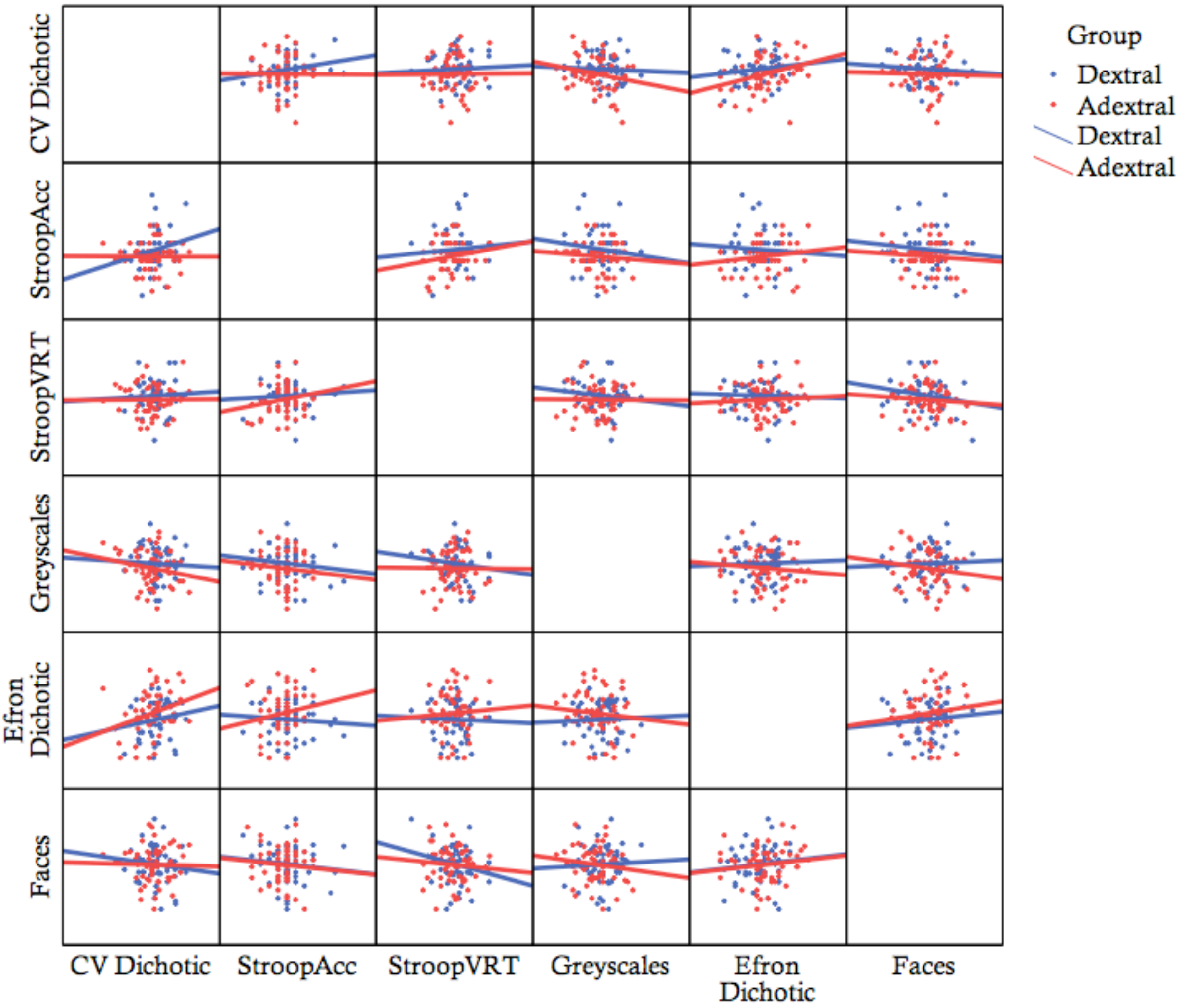


Figure 4.5 – A matrix scatterplot of dextral and adextral scores taken from six measures described in this chapter. In the top three rows, the "left hemisphere related" tasks, the dextral regression line was predicted to be above the adextral one, indicating a stronger rightward asymmetry. In the bottom three rows the opposite was expected, indicating a stronger leftward asymmetry. The slopes of the regression lines were anticipated to be in the same direction for both handedness groups; positive across correlations of tasks relating to the same hemisphere, and negative in comparisons across tests relating to different hemispheres. Significant correlations were present only between the two Stroop measures. When calculated separately for handedness group this correlation was only significant in adextrals, and a significant relationship between greyscales and Stroop accuracy was present in the dextrals. As the octave illusion task involved a two-forced choice paradigm, its data is not displayed.

between Stroop accuracy and VRT (*r*=.27, *p*<.01). A significant correlation was also found between CV dichotic and Efron dichotic (*r*=.20, *p*<.02), but again, in the unpredicted positive direction.

There is evidence provided by Knecht et al. (2000) that strength of sidedness on a handedness questionnaire could be indicative of brain asymmetry, with his data suggesting the incidence of right brain dominance for language increases to 27% in those who are strongly left handed. If these tasks really relate to cerebral asymmetries of functions, the proportion of the sample showing the 'typical' response should decrease, as strength of left-sidedness increased. Therefore the participants were split into five groups based on their WHQ score (which ranges from -30 to +30). These bins were selected in such a way that largely comparable sample sizes of participants were present in each WHQ group, resulting in the following subgroups: strongly right (greater than or equal to +28), weakly right (from +20 to +27 inclusive), mixed (between +/-19), weakly left (from -20 to -27 inclusive), and strongly left (less than or equal to -27). As the largest dataset was from the CV dichotic listening paradigm, these bins were based upon this sample. For this specific test, group numbers were strong right (*n*=66), weak right (*n*=38), mixed (*n*=60), weak left (*n*=36) and strong left (*n*=45), whereas for the VHF face task (with the smallest sample size) they were strong right (*n*=29), weak right (*n*=13), mixed (*n*=22), weak left (*n*=4) and strong left (*n*=21).

Figure 4.6 and table 4.2 show that the expected decrease in prevalence of 'typical' responses (as strength of left sidedness increases) occurs in all tasks except for greyscales, which has a fairly flat function. CV dichotic listening scores appear to be the most affected by handedness group.

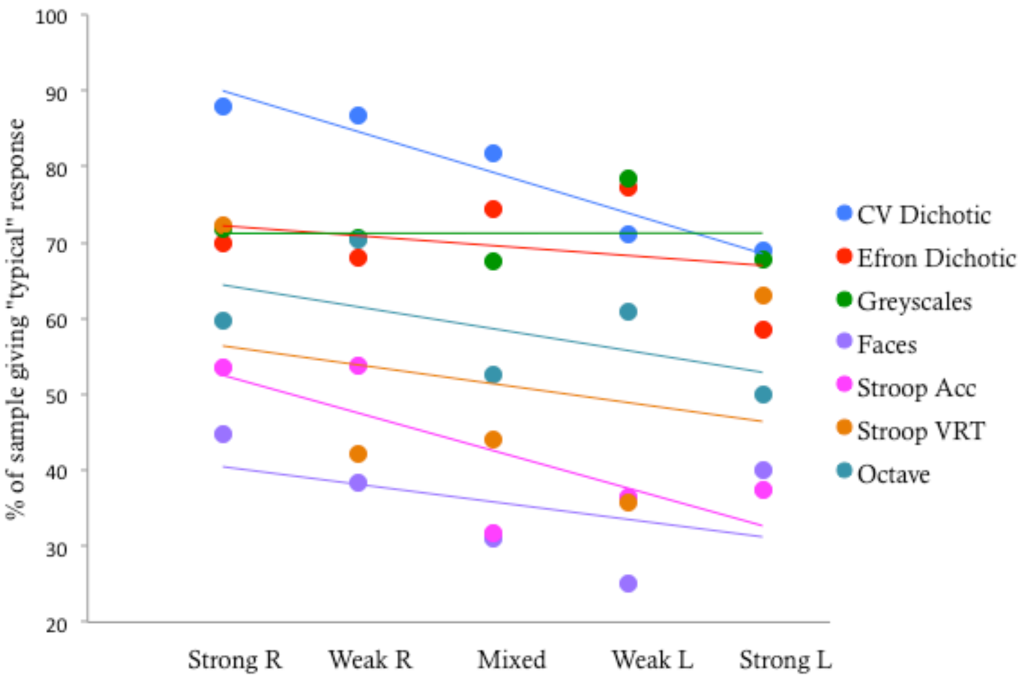


Figure 4.6 – The percentage of each WHQ group displaying typical behavioural responses associated with typical brain organisation. A negative slope indicates a decrease in prevalence of the 'typical' response as left-sidedness increases.

Task	Regression slope
CV Dichotic	$y = 95.39 - \mathbf{5.37} * x$
Efron Dichotic	$y = 73.55 - \mathbf{1.31} * x$
Greyscales	$y = 71.23 + \mathbf{0.01} * x$
Faces	$y = 42.80 - \mathbf{2.31} * x$
Stroop accuracy	$y = 57.51 - \mathbf{4.96} * x$
Stroop VRT	$y = 58.90 - \mathbf{2.49} * x$
Octave illusion	$y = 67.32 - \mathbf{2.88} * x$

Table 4.2 – The equation for each slope in figure 4.6, showing the relationship between the prevalence of the typical response and strength of handedness. The beta weights (the constants x is multiplied by) are bolded; a higher beta weight for any given test indicates that handedness group more strongly affects prevalence of the typical response of that test. In this case, incidence of the typical response on CV dichotic is most strongly related to handedness group.

A factor commonly discussed in laterality research is sex, which is seen as a modulator of hemispheric asymmetry (reviewed in Sommer, 2010). Sex is not a particularly helpful predictor of functional organisation (except in that males are more likely to be left handed, and therefore more likely to have atypical lateralisation). Roughly equal numbers of males and females were recruited in each handedness sample, but to check if sex explains any of the variance in the outcome measures, independent samples t-tests were run between males and females on the CV dichotic listening task and the Stroop task. These two tasks were chosen as they were the most lateralised amongst the six behavioural measures. There was no significant difference between left ear scores ($t(283)=0.60$, $p=.55$) or right ear scores ($t(283)=0.98$, $p=.33$) of males/females on the CV dichotic listening task. Likewise, no significant difference was found between RT difference scores ($t(160)=0.30$, $p=.77$) or accuracy difference scores ($t(160)=0.87$, $p=.39$) between males/females in the lateralised Stroop task.

4.4 Discussion

Significant mean differences were found between dextrals and adextrals in Stroop accuracy score and CV dichotic LI. In terms of proportions, significantly more dextrals gave typical responses in both Stroop measures, CV dichotic listening, and the octave illusion. No significant differences in proportion between the handedness groups were found for the greyscales task. More adextrals than dextrals gave an LEA in the Efron dichotic task, and less than half of both samples had a LVF advantage in the VHF face recognition task. It is interesting that none of the right-hemisphere related task data followed predictions, whereas all of the left-hemisphere related tasks did. These results could be explained by the argument that it is possible language is the most lateralised cerebral asymmetry (Toga & Thompson, 2003). It could be that asymmetrical biases relating to this function are present even in noisy and indirect behavioural measures, due to its strong lateralisation.

The functions underlying the greyscales and Efron dichotic tasks may be less asymmetric at either (or both) the individual or population level, however, we know that face processing asymmetry is fairly right lateralised (Kanwisher, McDermott, & Chun, 1997; Yovel, Tambini & Brandman, 2008). Badzakova-Trajkov, Häberling, Roberts, and Corballis (2010) measured both language and face lateralisation using fMRI measures in dextral and adextral participants. In their large sample of left-handed participants (*n*=48) they found that 81.3% were left hemisphere dominant for language (compared to 95.3% of dextrals), and 72.7% were right hemisphere dominant for faces (compared to 94.3% of dextrals). Furthermore, behavioural VHF tasks have shown to be sensitive to this asymmetry (Geffen, Bradshaw, & Wallace, 1971; Marcel & Rajan, 1975; Klein, Hilliard, 1973; Moscovitch, & Vigna, 1976; Leehey & Cahn, 1979; Yovel, Tambini & Brandman, 2008). The chimeric face task literature, albeit a different sort of test to ours, repeatedly reports robust detection of a leftward bias in participants' responses (e.g. Luh, Rueckert, & Levy, 1991; David, 1989; Burt & Perrett, 1997; Brady et al., 2005; Butler & Harvey, 2005; Ferber & Murray, 2005; Rueckert, 2005; Bourne, 2008). Therefore, we suspect a fault in our design, rather than a lack of rightward face processing asymmetry in our sample.

When reviewing the face VHF literature, studies have used huge variations of design features such as the size of stimuli, presentation duration, colour versus greyscale, and so on (Geffen, Bradshaw, & Wallace, 1971; Rizzolatti, Umiltit, & Berlucchi, 1971; Hilliard, 1973; Klein, Moscovitch, & Vigna, 1976; Broman, 1978). Stimulus presentation duration was of particular concern in the design of this study (briefly mentioned in section 4.2.3.5 above). The VHF face recognition task was the second version attempted, after an initial test was run using uncropped and less well-matched faces (those that appeared within the same trial were matched only for gender). This earlier version also included stimulus presentation on the lab table rather than at a fixed distance on a computer monitor. In this initial experiment faces were presented for 340 msec, and only 5/14 dextrals and 16/31 adextrals showed a LVF bias. As well as less constrained viewing conditions than traditional tachistoscopic studies, we also felt that the long stimulus duration may have enabled eye-movements into either visual field (participant accuracy was higher than we expected in both visual fields).

Therefore the current version of this task utilised a better-controlled set up, including a chin rest and fixed viewing distance from vertically presented stimuli on a monitor (echoing tachistoscopic presentation), but also decreased stimulus duration to 160 msec. Although studies report durations as short as 42-66 msec (Hilliard, 1973), 59 msec (Yovel, Tambini, & Brandman, 2008) and 100 msec (Turkewitz & Ross, 1983), in an initial pilot phase, participants could not perform above chance in either visual field at these stimulus durations. The 160 msec duration time employed in the final version of this task was essentially the shortest duration time allowing for pilot participants to perform above chance.

Whilst the face stimuli in this experiment were relatively well matched for contrast information, dominant features (such as dark eyebrows), overall face shape and gender, as well as being uniformly cropped, it is still possible that some faces were easier to identify than others. In an attempt to account for this possibility, the design was balanced so that every face presenting in every location, i.e. once each in the left and right visual field in the test phase, and on the top and bottom as a target or a foil in the response phase. It is possible, however, that there are still some ‘bad items’ present that all participants attend to more so in one visual field than the other. An item analysis could be run to assess this issue, but for the purposes of this thesis, a task where the results depend on subtle differences that can be driven by slight features of a stimulus is largely undesirable.

Unfortunately the Efron dichotic data replicates the findings of Gregory (1982), in that there was no difference in the prevalence of the left ear advantage between dextrals and adextrals. The data in figure 4.6 suggests that prevalence of the typical response decreases as left-sidedness increases; however, the individual data points show that this negative slope is largely driven by the strong left group (*n*=32), and that the weak left and the mixed group (*n*=25 and *n*=41 respectively) actually had a slight increase in prevalence relative to the strong right group (*n*=55). Therefore it is likely that this task is not tapping into a cerebral asymmetry that is different between dextrals and adextrals. Gregory (1982) suggests that his results may reflect involvement of the right hemisphere, but claims that there is a lack of evidence to suggest that ear dominance for pitch discrimination is due to asymmetries in the cortex rather than in auditory nerve pathways. For our purposes, if a task cannot successfully differentiate between a random sample of dextral and adextral subjects, it is unlikely to aid our prediction of cortical organisation at an individual participant level.

Efron himself suggests that this particular task (and many others) are not necessarily the best evidence for underlying cerebral asymmetries. He stated that changing the difference between the two tones used changes ear dominance in individuals, therefore this is not an appropriate test of underlying cerebral asymmetry for pure tones (Efron, 1990). For our purposes, even if the tone pairing was a specific one, what was relevant was whether the task differentiated dextral and adextral subjects, which it did not. Nevertheless, for another tone task, the octave illusion, there is a significant difference in magnitude of asymmetry between dextrals an adextrals, albeit in this case one that favours the right ear.

The data from the greyscales task suggests it may also be less helpful in aiding prediction of cerebral asymmetry, despite patient data from this task strongly suggesting the leftward bias is related to brain organisation (Mattingley et al., 2004). Indeed, the task is very lateralised in both the dextral and adextral groups. The main methodological limitation of the greyscales task is that the manipulation can be noticeable for participants, at unpredictable phases of testing. For example, after some number of trials participants may notice that they are always reporting the bar that is darkest on one side or the other. The participant becoming consciously aware of this response bias could instigate always choosing the gradient that is darkest on the side that they have been biased to, or switching their response bias. Either of these outcomes would cause measurement noise. However, participants were not interviewed about their strategies. Perhaps, counter intuitively, fewer trials may have reduced this measurement error.

Including some “filler” trials with a real, but slight, difference between the overall darkness of the two bars may have been more likely to keep participants attending to dark versus light rather than left versus right. Another modification could be to edit the colour profiles of the ‘greyscales’ to include green to white/blue to white/red to white variants, where the participant would report which bar was “more green” for example, based on a pre-stimulus instructional slide before every trial. Under these conditions we would hope that the distraction of the varying colours would prevent the participants becoming too conscious of the mirror symmetry inherent in the test stimuli.

Although all three left-hemisphere related tasks led to significantly different proportions of ‘typically responding’ dextral and adextral subjects, the Stroop test results have not supported our hypotheses. We predicted that a majority of adextrals would make more errors or be slower to respond in the RVF relative to the LVF, but that this majority would be smaller than that of the dextrals with the same response bias. The majority of adextral participants, however, had worse accuracy and slower VRT in the LVF relative to the RVF. This disadvantage for adextrals in the LVF replicates the effect found by Hugdahl and Franzon (1985), however, they had preselected adextrals who were left eared on a CV dichotic listening task. In a sample such as theirs we might expect a higher proportion of atypically lateralised adextrals, and therefore atypical responses on the task would be predicted, but ours was a random sample of adextrals. Only two thirds of our sample actually had any difference in accuracy between their visual fields as many participants did not make any errors. Hugdahl and Franzon (1985) found that only 2/20 dextrals (and no adextrals) made no errors. Of those who did make errors, however, the number of participants making only three errors or less was 5/18 dextrals and 7/10 adextrals, so the number of errors recorded from their participants was also low. It could be that the low error numbers in the present study could be due to experimenters not pushing participants to go quickly.

Aside from asking participants to respond “as quickly and as accurately as possible” fast VRTs was not reinforced. As both accuracy and VRT were recorded, it was assumed that if a participant were extremely accurate a VRT asymmetry would be present, and likewise if someone was fast, there would be differences in accuracy for the two VHFs. Franzon and Hugdahl (1987) conducted a follow up study where they claimed that participants who were instructed to take as much time as required to respond accurately had not only slower VRTs overall, but also a bigger VRT decrease in the RVF, when compared with a group instructed to respond as rapidly as possible regardless of accuracy. This second group also made more errors overall, and the increase in errors in the RVF was larger than for the group instructed to be as accurate as possible. In our dextral sample, mean VRT was roughly 50 msec slower than in Hugdahl and Franzon’s (1985), and our mean adextral VRT was ~100 msec slower than their mean adextral VRT. Therefore it is possible that we have a higher frequency of zero errors than in their samples due to our participants' slower VRTs, from a lack of pressure to respond quickly.

The current study includes 'non-Stroop errors' (i.e. a response that was neither the colour of the word or the word itself) in the accuracy scores. Although the colour (and word) 'yellow' was replaced with 'white' (due to difficulties distinguishing yellow and green in a pilot phase), some participants struggled to identify white versus green. To avoid this problem in our lab in future perhaps only the three easily identifiable stimuli should be used. A better quality project might also go some way to improving this experiment. Under these improved conditions, as well as instructing participants to respond as quickly as possible, it is anticipated participants would make more errors.

The CV dichotic listening task was able to differentiate dextral and adextral subjects both in terms of group averages and proportions. A majority of both groups displayed a right ear advantage, which has been hypothesised to be related to left hemisphere language lateralisation (Kimura, 1961; Krashen, 1976; Hugdahl & Andersson, 1984). Although the proportional difference is small, a significantly larger majority of dextrals (86.4%) displayed this right ear advantage than adextrals (81.6%). Therefore an individual's score on this task could be indicative of potential language lateralisation. CV dichotic at least reflects more similar proportions to prevalence of leftwards language lateralisation than preferred handwriting hand.

The proportion of adextral participants with a right ear advantage was 81.6%; about 12% higher than the ~70% we assume are left lateralised for language (Rasmussen & Milner, 1977). In a task that results in a directional response such as this one, it is unclear how the ~15% of bilateral adextrals would respond. Under our task conditions it is possible to score a LI of zero, but no participant did. Zatorre (1989) found that almost all participants in left and right hemisphere language groups had right or left ear advantages respectively, whereas the bilateral group showed almost no difference between the ears on average, but individuals fell equally above and below the zero mark. If this were the case in our participants, it would be sensible to report higher numbers of right and left ear advantages than the Wada test proportions from Rasmussen and Milner (1977): ~77.5% and ~22.5% respectively. In our dextrals, however, the proportion displaying a right ear advantage (86.4%) is lower than the ~96% we would expect. We would also anticipate no bilateral subgroup in the dextral sample, therefore the above explanation cannot account for this dissociation.

An alternative explanation is that due to measurement noise, some participants show ear advantages that are not indicative of their hemispheric asymmetry for language. Behavioural tests such as those in this chapter are subject to external influences. Participant biases in attention direction are a problem for all indirect tests, but this issue has been extensively discussed in the dichotic listening literature. This focus has led to a version of the task in which, after the traditional 'non-forced attention' trials, participants are instructed to attend to the left and right ears separately (Bryden, Munhall, & Allard, 1983; Hugdahl & Anderson, 1986). Under these conditions most participants are able to strengthen their non-forced/natural ear advantage when forced to attend to it, as well as reverse their ear advantage when attending to their non-dominant ear (Asbjornsen & Hugdahl, 1995). Some researchers take this result to mean that ear dominance cannot be entirely indicative of hemispheric asymmetry (Hiscock & Kinsbourne, 1995), whereas others see it as a way to calculate a more precise ear asymmetry (Hugdahl & Andersson, 1986).

For our purposes it is of some concern that participants may manipulate their results by selectively attending to one side, despite being instructed not to do so. If several participants did deviate from instruction, however, significantly different proportions of right ear dominance between dextrals and adextrals were present in the predicted direction regardless. In an independent study not included in this thesis, a variant of the selective-attention paradigm was carried out with a small subset of 20 dextral and 20 adextral participants, and found that in the forced left block only 13 of 33 subjects who had a right ear advantage in the non-forced condition, could reverse their response to a left ear advantage. Of the remaining seven participants with a left ear advantage under non-forced conditions, three reversed to having a right ear advantage. We concluded that participants generally struggled to entirely reverse their ear advantages, even when instructed to direct their attention to their 'non dominant' ear. This result, alongside the forced-attention paradigm taking three times longer to administer, led to us continuing with the non-forced paradigm. Even if the measure taken from dichotic listening is related to a non-language attention property that is simply highly correlated with language, it is still useful for us in the exact same way that any of these behavioural measures would be. If the results relate to language lateralisation either directly, or through language's correlation with another process, it could improve prediction of hemispheric dominance for language. A next step would be to test participants with known language lateralisation with these tests to investigate their sensitivity to functional asymmetries. Data from an initial attempt to do this with individuals classified by fMRI measures are presented in the following chapter.

Chapter 5 – fMRI of language, face, and body processing, and evaluating predictors of brain asymmetry

5.1 Introduction

fMRI has become the leading methodology in cognitive neuroscience research. Previously, neuropsychologists relied heavily upon patients with focal lesions in order to make inferences about functional organisation, however, this once inaccessible and rare technology is now open to most university researchers, and allows for the non-invasive study of more readily-available neurologically-intact participants. Key functions such as language and face perception processes have been investigated with fMRI, establishing now commonly recognised neural networks and locations for these functions. In the present context, however, progress in imaging research related to understanding cerebral asymmetries in individuals has been relatively sparse.

There have attempts to evaluate fMRI's ability to determine hemispheric dominance for functions in individuals (Rutten, Ramsey, van Rijen, Alpherts, & van Vellen, 2002; Spreer et al., 2002). Largely this literature involves analysing concordance between fMRI data and data from the Wada test (e.g. Binder et al., 1996; Sabsevitz et al., 2003; Janecek et al., 2013). For example, Spreer et al. (2002) tested the reliability of hemispheric language dominance determined by fMRI against evaluation using the Wada test in 22 patients with epilepsy (18 right handers). Thirteen patients were tested on the Wada test bilaterally whilst 9 only had unilateral evaluation. It was found that laterality indices were consistent with Wada test results in all patients, including three patients with "reversed" right-hemisphere language dominance, and one with bilateral language representation (using an a priori bilateral boundary of an LI between +/-0.2). There are several papers making these comparisons (Binder et al., 1996; Sabsevitz et al., 2003; Benke et al., 2006; Binder, Swanson, Hammeke, & Sabsevitz, 2008; Janecek et al., 2013), and all provide evidence for the use of fMRI as a possible replacement for the Wada test. For analysing healthy populations, where Wada testing is not possible, fMRI is the current gold standard in determining laterality of language functions.

There are many papers of this type, but for our purposes they have some limitations. Whilst they do often provide the proportions of individuals who are left/right/bilateral (although, as I will discuss later in this introduction, there are real issues surrounding a priori definition of 'bilateral' activation in fMRI), they often have small numbers of adextrals, almost all of these participants have brain damage from drug-resistant epilepsy. These studies vary greatly in their methods of left and right hemisphere comparisons. Some use specific language area ROIs developed within each participant (Rutten, Ramsey, van Rijen, Alpherts, & van Vellen, 2002; Spreer et al., 2002), some use ROIs developed in healthy controls (Desmond et al., 1995), some use whole hemisphere comparisons (Binder, Swanson, Hammeke, & Sabsevitz, 2008), whilst others simply visually inspect the individual activation maps (Benke et al., 2006). And finally, although they do all tend to employ block design language localisers, these too come in various forms.

The fMRI subtractive block design, favoured in function localisers, is where the stimulus (or various stimuli) of interest and a control stimulus are presented to the participant, and the BOLD activity to the control stimulus is subtracted from that of the stimulus of interest (a process first described in rat studies [see Ogawa, Lee, Nayak, & Glynn, 1990; Ogawa, Lee, Kay, & Tank, 1990] then carried out with humans by the same research group – see Ogawa, Tank, Menon, Ellermann, Kim, Merkle, et al., 1992). This is known as the subtraction method, and is necessary because blood flow in the brain is of course constantly fluctuating for a variety of reasons. Therefore a subtraction contrast controls for activity that is unrelated to the relevant stimulus by removing it with the control stimulus. Identifying an appropriate control condition is crucial to achieving an accurate representation of activation for the function under investigation, and in the neuroimaging of language these controls are far from standardised.

Binder's group compared five different auditory paradigms commonly used to map speech comprehension systems (Binder, Swanson, Hammeke, & Sabsevitz, 2008). They argued that there was no clear agreement in the literature on which procedure produced the strongest activation overall, which is best for detecting regions of interest, or which is associated with the largest degree of lateralisation. Their results suggested that tasks that required an active role for the participant in the language condition produced more activation than passive listening protocols, a semantic decision vs tone decision (high or low) task produced the most activation in the left hemisphere, and the protocols with an active control condition resulted in stronger left lateralisation of activation than those using passive rest as a control condition. However, it is arguable that a pitch discrimination task is not a suitable control condition when assessing language laterality. It is not a less 'relevant' version of the active stimulus, but rather a task assessing a different function altogether; one that is often suggested to be right lateralised (Joseph, 1988; Johnsrude, Penhune, & Zatorre, 2000; Hyde, Peretz, & Zatorre, 2008).

In Spreer et al. (2002), the language task employed was a subtest of the Wilde Intelligence Test (Jäger & Althoff, 1994) where participants had to identify a pair of synonyms from a list of five words. The control task, however, was a colour-matching task, where participants had to select one of four coloured squares that was the closest to a target colour. Whilst I have found no fMRI experiments investigating activation asymmetry for a colour-matching task, there is evidence from tachistoscopic studies, as well as split-brain and unilateral lesion patients, that this kind of colour detection or image-matching task is more demanding upon the right hemisphere than the left (Pennal, 1977; Warrington & Taylor, 1978; Levy & Trevarthen, 1981). The concern here is that these sorts of baselines could increase the number of left lateralised subjects reported, due to increased baseline activity in the right hemisphere, rather than increased activity to the language task in the left hemisphere.

These research groups are focussed on comparing outcomes from the Wada test with fMRI protocols. There are many other researchers interested in specific linguistic processes and the anatomy of the language network, who tend to focus on activations to specific linguistic features in specific brain regions (Burton, Small, & Blumstein, 2000; Price, 2000, 2010; Gandour et al., 2003; Scott & Johnsrude, 2003; Karuza, Newport, Aslin, Starling, Tivarus, & Bavelier, 2013; McGettigan, Eisner, Agnew, Manly, Wisbey, & Scott, 2013). Therefore, for much of the neuroimaging of language literature, the largely leftward lateralisation of these functions is commonly reported but not of particular interest. For the purposes of this thesis, analyses of exclusively language-related regions and processes are not of high importance. Priorities for this research are that the contrast is robust enough to produce substantial activations in individual participants, and that these are lateralised in at least some dextrals/adextrals. Therefore I will focus on the literature where the researchers had similar aims to ours; classifying individual participants in healthy populations as typically or atypically lateralised.

Hunter and Brysbaert (2008) conducted a study assessing how useful VHF measures are in measuring cerebral dominance. Twenty-six left-handed subjects took part in a word and picture naming VHF task, and based on the results ten were selected for a fMRI task. Six of these participants had a strong RVF advantage in the behavioural component, two had no clear VHF difference, and two had a clear LVF advantage. The aim of the fMRI component was to determine individuals' actual hemispheric asymmetries. Participants carried out a silent word generation task in which 10 single letters were presented for 18 secs each, and participants had to think of as many words as possible beginning with that letter (in neuropsychology this task is typically referred to as 'single letter fluency'). The control condition involved the display of the nonsense string "dada" for 18 secs whilst participants repeated this mentally throughout the presentation, and both activation and control blocks were interleaved with 18 sec rest periods (a modified version of the fluency task used by Stephan Knecht in both fMRI and fTDS studies; Knecht et al., 2000; 2001; 2003). To quantify individual participants' lateralisation, Hunter and Brysbaert (2008) calculated a LI. Using predefined regions of interest in the left and right inferior frontal cortex (meant to include Broca's area and its homologous region in the other hemisphere), they calculated LIs as the number of activated voxels in the left ROI minus the number of activated voxels in the right ROI, over the sum of the two, so that a positive LI meant left hemisphere dominance. Their results showed that all six subjects with a RVF advantage in the VHF task had left hemisphere language dominance (LIs ranging from +0.60 to +1.00). Of the two participants with a clear LVF advantage, both were right hemisphere language dominant (LIs of -0.66 and -0.97). The remaining subjects who had no clear side bias in the VHF task had LIs of +0.37 and -0.19, falling within the +/-0.40 range that Hunter and Bryrbaert (2008) specified for bilateral language. They conclude, rather modestly given their incredible results, that VHF could therefore be a useful way to estimate hemispheric asymmetries.

Nevertheless there are some methodological issues with this study. The authors do not assess the data in a threshold-independent manner. When using the subtraction method researchers usually set a statistical threshold of $p<.05$; therefore "activation" is any voxels surviving the $p<.05$ comparison from the relevant task to the control. Any decrease of this threshold will increase the number of active voxels, and vice versa. Therefore, when comparing left activations with right, the method by which researchers quantify "activation", and the threshold at which they make this comparison, can drastically affect LIs. Hunter and Brysbaert (2008) acknowledge this limitation, but state that their method of calculating LIs produces values that are not statistically different to LIs calculated with other methods (but they do not provide a source for this claim). They also argue that LIs calculated in this manner correlate well with those from Wada and fTDS measures (Chlebus et al., 2007; Jansen et al., 2004), and claim that regardless of the cut-off values chosen, their strongly left/right lateralised participants remained so (this point suggests a number of thresholds were used, but the number and range of these thresholds were not provided). Finally, they specify a boundary between LIs of +/-0.40 to classify individuals as bilateral. This seems rather overly cautious; a positive or negative LI of 0.40 indicates a 40% increase in activity in one hemisphere over the other, which seems a substantial difference. They provide no justification for choosing this particular cut off. In spite of these caveats, it is clear from the data and activation maps provided in the paper, that this task enabled categorisation of participants at the individual level.

Subsequent papers investigating language lateralisation at the individual level have employed this silent verbal fluency paradigm (Abbott, Waites, Lillywhite, & Jackson, 2010; Badzakova-Trajkov, Häberling, Roberts, & Corballis, 2010; Van der Haegen et al., 2011; Powell, Kemp, & Garcia-Finana, 2012). All of these experiments produce fairly robust responses in the left hemisphere of the majority of the sample. For example, Van der Haegen et al. (2011) prescreened a total of 250 adextral students (182 females, mean age 19.9 years) with picture/word naming VHF tasks (adapted from Hunter & Brysbaert, 2008; with the improvement of monitoring eye-movements). Twenty participants showing a LVF advantage of at least 10 msec took part in the fMRI verbal fluency task. Additional subjects included 14 with a clear RVF advantage in both tasks, and 16 with mixed responses, totalling 50 subjects. These 50 subjects carried out a very similar silent word generation task to that used by Hunter & Brysbaert (2008). Notable differences are a reduced stimulus presentation time of 15 secs, and a new method for calculating LIs from the fMRI data.

In order to avoid using a particular statistical threshold to calculate the difference in activation between the two hemispheres, Van der Haegen et al. (2011) used a toolbox developed by Wilke and Lidzba (2007; the LI-Toolbox), which employs bootstrapping methods to calculate a threshold-independent LI, which is less influenced by outliers or data sparsity (see section 6.2.5 of this chapter for a detailed description of this method). Largely this study is an improvement upon Hunter and Brysbaert (2008), however, a more restricted ROI was employed (Broca's area/BA 44 and 45 only), and an even more stringent bilateral criterion of +/-0.60 is specified, with no justification for the increase from +/-0.40 or of why such a stringent criteria is necessary[5]. Thirty-four of the participants included had concordant VHF and fMRI LIs, with 15 participants displaying right hemisphere language dominance as measured by fMRI and a -0.60 LI cutoff.

This verbal fluency paradigm has enabled other researchers in this field to classify language lateralisation at the individual level, and therefore this method was used in the present thesis for the functional measure of language dominance. Whilst also using the LI-toolbox we would relax the criteria for left/right/bilateral by simply using the zero-crossing as a cut-off, categorising participants dichotomously as having "more left" or "more right" activation (see Carey & Johnstone, 2014 for discussion of some of the advantages of using a dichotomous classification system for cerebral asymmetry). Of course participants falling within, say, +/-0.10 would require cautious interpretation, but as the present study was largely exploratory, and as dichotomous classification has been used with all other measures in this thesis (unless a participant had an LI of 0), the fMRI data is treated in the same way. This verbal fluency paradigm is relatively short for an fMRI testing session, and therefore we decided to conduct a face and body localiser task in the same individuals during the same testing session. This design would allow us to explore questions surrounding causal complementary specialisation. For example, individuals who are atypically lateralised for fluency may also be atypically lateralised in terms of face and body perception.

Task selection was much simpler when reviewing the face fMRI literature. As summarised in the general introductory chapter, "face localiser" tasks have been used to elicit face-related brain activity, which appears to be more commonly lateralised to the right hemisphere (Kanwisher, McDermott, & Chun, 1997; Woodhead, Wise, Sereno, & Leech, 2011). In these studies investigating brain activity in response to faces, the same paradigm is regularly used; simple blocked-design presentation of images of faces, and objects or scenery. The contrast subtraction method is used to take activity related to general object or scene perception away from face-related activity, resulting in the ability to analyse only face specific activations or brain areas (Kanwisher, McDermott, & Chun, 1997; Downing, Jiang, Shuman, & Kanwisher, 2001; Schwarzlose, Baker, & Kanwisher, 2005; Woodhead, Wise, Sereno, & Leech, 2011).

---

[5] In personal communications with Marc Brysbaert (12th September 2014), he informed us that they were conservative with this criterion by design, to ensure that their atypical participants were really atypical.

In reading this literature what becomes apparent is that over time, employing several alternate stimulus types that are contrasted against faces became rarer, with current studies usually only taking measures from between two and five stimulus categories (O'Neil, Hutchison, McLean, & Kohler, 2014; Jiang, Badler, Righi, & Rossion, 2015; Zachariou, Safiullah, & Ungerleider, 2015). Some researchers include a "body" stimulus category, allowing for a measure of body specific activation to be obtained as well as face processing activity (Downing, Jiang, Shuman, & Kanwisher, 2001; Willems, Peelen, & Hagoort, 2010; Woodhead, Wise, Sereno, & Leech, 2011).

The extrastriate body area (EBA) is a region of functional activation that occurs in response to visual presentations of bodies or body parts (Downing, Jiang, Shuman, & Kanwisher, 2001). In all 19 subjects from the original paper detailing the EBA's response profile, most body-related activity was lateralised to the right lateral occipitotemporal cortex (Downing, Jiang, Shuman, & Kanwisher, 2001). Although authors in these fields commonly report right hemisphere activations, this finding is simply an additional detail when describing the location of the region.

When compared to language, there has been less research in these domains relating to handedness, and the studies that do exist have even smaller participant numbers. For instance, Bukowski, Dricot, Hanseeuw, and Rossion (2013) investigated lateralisation of face processing in 11 left handers using an fMRI face localiser paradigm. They analysed activations in five areas related to face perception: the FFA, the occipital face area (OFA), the posterior superior temporal sulcus (pSTS), the amygdala, and the parieto-occipital junction. They found that in the averaged activation map, 62% of the statistically significant activation was present in the right hemisphere. For the ROI analyses, all regions were more lateralised to the right hemisphere, except the FFA, which had only 37% of its activation in the right hemisphere. They state that a "substantial proportion" of their subjects have a larger FFA in the left hemisphere – see figure 5.1 where data from dextrals analysed in a separate paper are provided for comparison (Rossion, Hanseeuw, & Dricot, 2012).

It is refreshing to see data from individual subjects being reported, and the authors provide degree of handedness (indicating six of the participants were strongly left-sided). However, this is too small a sample to really provide evidence for any arguments about proportions; the left lateralised FFA result is down to four participants, compared with two right lateralised and five bilateral (defined as having 55% or less

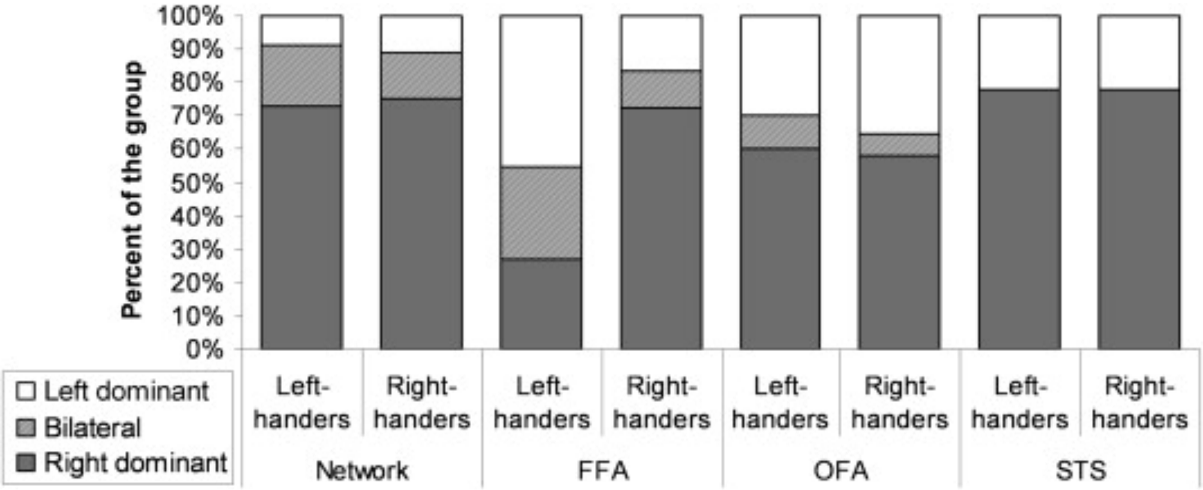


Figure 5.1 – Proportions of the left-handed participants with more right, left, or bilateral activations in different regions in the face perception network (taken from Bukowski, Dricot, Hanseeuw, & Rossion, 2013). "Network" refers to data from the FFA, OFA, pSTS, the amygdala, and the parieto-occipital junction.

active voxels in either hemisphere – again justification for this particular cut off is sparse). A real concern with these analyses is that the regions of interest have been defined in their dextral sample, and are then used for the analysis of adextral subject data, potentially 'missing' activity that may occur in a slightly different region in adextrals. Finally, this study is also subject to suboptimal hemispheric comparison due to traditional thresholding methods.

Willems, Peelen, and Hagoort (2010) set out to assess whether handedness has an effect on the lateralisation of both face and body processing networks. Their study included both dextral and adextral participants (16 in each group) carrying out a face/body localiser. Analysis of the activations, averaged across handedness group, found that the FFA and EBA were right lateralised in right handers, but not in left handers. Unfortunately the authors do not provide individual participant data, but we can see from the averaged data (see figure 5.2) that left handers had slightly more activation in the left FFA than the right (although this difference was not statistically significant). In the EBA, however, there is more activity in the right hemisphere than the left for both handedness groups, but the difference between the hemispheres in the left handers, again, fails to reach statistical significance. Without data on the proportions we can only speculate, but it is likely that in the left-handed group there is a minority subgroup of participants showing a reversed response. This parallels arguments made

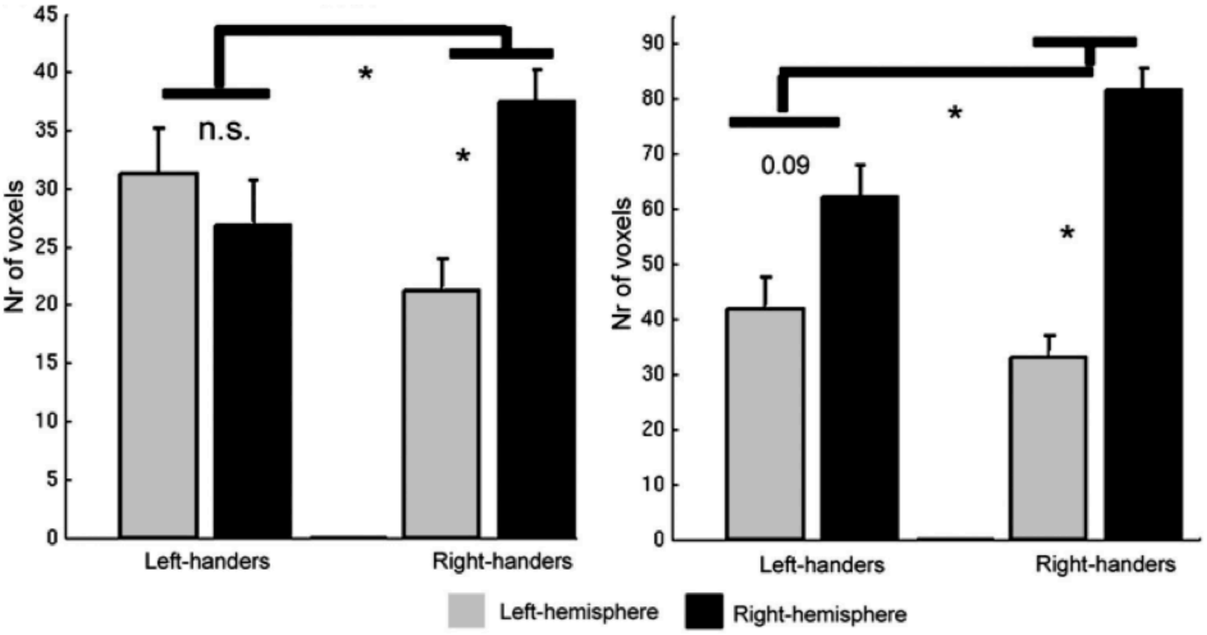


Figure 5.2 – Averaged activation data from left- and right-handers taken from right and left FFA and EBA (taken from Willems, Peelen, & Hagoort, 2010). The FFA data is presented in the left panel, and EBA in the right. Although the difference in OFA activity between hemispheres in the left handers did not reach statistical significance, there was a substantially bigger rightward bias in the OFA than the FFA.

previously regarding behavioural data, where the left handed group response looks like the right handed group response, but with decreased magnitude of asymmetry.

Both the above studies suggest the FFA is at least not as consistently right lateralised in adextrals as compared to dextrals. Of the two adextrals in Kanwisher's original FFA study (1997), one has left FFA dominance, and the other has bilateral representation, but with a larger right FFA overall. As discussed in the general introductory chapter, prosopagnosia following unilateral brain damage is more common after right hemisphere insult, but there is no standardised test for face recognition. Therefore there is no large case-series of laterality data, like that available for language (Rasmussen & Milner, 1977), and no established estimates of how often right dominant face perception is found in dextrals.

We were fortunate enough to be sent individualized data from a published dataset that reports average FFA asymmetry in dextrals (Yovel, Tambini, & Brandman, 2008). In a sample of 61 dextrals, they found that 77% of their sample had right hemisphere dominance (Yovel, personal communication 26th January 2015). It would appear that face perception may be less asymmetrical than language, and therefore a decrease of this asymmetry is expected in adextrals also, given that they are 70% left lateralised than speech and language as opposed to 95%. However, it is unknown how often face processing asymmetry in adextrals is like that of dextrals. The studies that have taken handedness into account have not assessed lateralisation with a threshold-independent measure, and test too few participants. Nevertheless, the causal complementary hemispheric specialisation literature could guide estimates. This approach would assume that if language and face/body perception colateralise to opposite hemispheres, in the 96% of dextrals and 70% of adextrals who are left hemisphere dominant for language, a majority should also be right hemisphere dominant for face and body processing functions, and with a similar decrease in bias in the adextrals.

There is very little neuroimaging research tackling questions of complementary specialisation, and studies that do tend to be focussed on language and visuospatial abilities rather than face perception (Ng et al., 2000; Powell, Kemp, Garcia-Finana, 2012; Cai, Van der Haegen, & Brysbaert, 2013). Badzakova-Trajkov, Häberling, Roberts, and Corballis (2010) carried out the only fMRI study that measures both language and face lateralisation measures in the same dextral and adextral participants. In their large sample of left-handed participants (*n*=48) they found that 81.3% were left hemisphere dominant for language (compared to 95.3% of dextrals), and 72.7% were right hemisphere dominant for faces (compared to 94.3% of dextrals). These authors used the LI-toolbox to avoid thresholding confounds, and also used the entire temporal lobes when comparing face related activity, a less stringent ROI than used by Bukowski, Dricot, Hanseeuw, and Rossion (2013) and Willems, Peelen, and Hagoort (2010). The language task employed by Badzakova-Trajkov, Häberling, Roberts, and Corballis (2010) was the same verbal fluency paradigm detailed above, but unusually in their face task they used video clips of people making emotional faces. As there is evidence that emotion processing is dealt with more by the right hemisphere than the left (Blonder, Bowers, & Heilman, 1991; Borod et al., 1998), perhaps this accounts for the increase in right lateralisation of the left handed groups when compared to Bukowski, Dricot, Hanseeuw, and Rossion (2013) and averaged data from Willems, Peelen, and Hagoort (2010).

fMRI data could be used as a criterion for evaluating how well behavioural measures might predict cerebral asymmetry. To make this line of enquiry possible an fMRI method to determine functional asymmetries in individual people must be developed, so that analysis of behavioural data from participants with known cerebral dominance is possible. The data reported in this chapter are just the start of this line of research. In the following experiment we have used fMRI to determine individual participants' functional hemispheric asymmetries in language processing and face/body perception. To do this we employed previously validated paradigms (verbal fluency and a static face/body localiser). The LI-toolbox was used to compare the entire right hemisphere to the left, and categorised participants dichotomously according to more left or more right hemisphere activation. By using no pre-selected ROIs, the least constrained measure of individual lateralisation was obtained.

5.2 Methods

5.2.1 Participants

Participants were all recruited through opportunistic methods including online advertisements, within-university email campaigns, and word-of-mouth. The resulting sample was composed of students or staff of Bangor University, or the spouse/family member/friend of a student/staff member of Bangor University. The resulting sample included 21 dextrals (12 females), and 33 adextrals (18 females). The dextral group had a mean age of 26.5 years and a mean WHQ score of +27.95. The adextrals had a mean age of 24.48 and a mean WHQ of -16.30. Of the 21 dextrals, 11 were right eye dominant and 18 were right footed for kicking. Of the adextrals, 14 were right eyed, and 11 were right footed.

Ideally, an imaging study of this kind would have been run after enough data from the tasks in chapter five had been analysed with multivariate statistical techniques, however, these participants were selected for scanning at a stage when that study had yet to be completed. Periodically the proportions of dextrals and adextrals who showed leftward or rightward biases on the indirect tests were perused descriptively. Consequently our early impressions were that CV dichotic listening, the octave illusion and greyscales were potentially predictive of brain organisation, therefore we scrutinised our dextral and adextral datasets for individuals who had a left ear advantage for CV dichotic listening or the octave illusion, or who showed a rightward bias in the greyscales task. Although we did not have strict recruitment criteria and were happy to include anyone who had taken part in our indirect test battery, the sample is not entirely random, as some preselected individuals are included. We approached 18 participants on the basis of their behavioural data, and nine of those were included in the imaging dataset (8 of whom were adextral).

5.2.2 Verbal fluency task

Both an active and a control condition were used in a blocked design. Fourteen active and 14 control blocks were alternated with 14 rest blocks, each with a duration of 15 secs. In the active blocks participants were presented with a single letter in the middle of the screen for the duration of the block. During this time participants were instructed to silently think of as many words as they could which begin with that letter. A practice phase was run outside the scanner using the letter “D”. In the control blocks participants were shown either the letter string “RARA” or “LALA”, which are not words in English, and were instructed to mentally repeat these non-words for as long as they were presented on the screen. In the 28 rest blocks a fixation cross was presented and participants were instructed to relax. The 14 letters chosen were the letters that begin the most words in English: T, A, S, H, W, I, O, B, M, F, C, L, D, P (as reported in the Natural Language Toolkit 3.0 - http://www.nltk.org/). This task was broken down into two runs, comprising seven active/control/rest blocks per run (twice as many as in Van der Haegen et al., 2011). Two runs were included to obtain a better estimate of an individual’s LI. This duplication of runs also allowed for investigation into a measure of within session “test-retest” reliability. The letters were randomly presented in any order across these two runs.

5.2.3 Four condition face/body localiser

A face/body localiser was employed to identify face and body selective brain areas. The task involved viewing two blocks each of images of faces, bodies, chairs and scenes. Participants also completed a simple one-back task, pressing a button if they saw a consecutive, repeated image. Which hand participants held the button box in was counterbalanced within the dextral and adextral groups. Each block lasted 10 seconds during which 10 images were presented for 500 msec, with a 500 msec interstimulus interval. Participants completed two runs of this task, with two different fixed stimulus orders, which were counterbalanced across participants.

5.2.4 fMRI acquisition

For the verbal fluency task functional images were obtained using a T2*-weighted gradient-echo EPI sequence (TR = 2500 msec, slick thickness = 2.5 mm, 90° flip angle). In the face/body localiser, the EPI sequence was as above but with a TR of 2000 msec.

Initial stimulus onset was synchronised with the scanner pulse for each run. As well as the functional images, high-resolution structural images were acquired.

5.2.5 Design and analysis

All data were analysed with the SPM12 (statistical parametric mapping) software package (http://www.fil.ion.ucl.ac.uk/spm). Images were realigned to the first functional volume to correct for motion artefacts, and were normalised to standard Talairach space using an EPI template. Two adextral participants, one male and one female, were registered to the ICBM template for East Asian brains, whilst all other participants were registered to the European template brain. To reduce any effects of random noise, normalised data were spatially smoothed using a Gaussian kernel of 6 mm. The general linear model was used to map the hemodynamic response curve onto each experimental condition using boxcar regressors. This boxcar function was then fitted to the time series at each voxel resulting in a weighted beta-image. The fitted model was converted to a t-statistic image, comprising the statistical parametric map. As analysis would be carried out using the LI-Toolbox (Wilke & Lidzba, 2007) setting pre-determined statistical thresholds was not necessary.

Analyses of this dataset will be largely descriptive and exploratory. To assess which hemisphere was 'dominant' for the particular stimulus set, the LI-Toolbox plugin for SPM was used (Wilke & Schmithorst, 2006). This toolbox allows for comparison of right and left hemispheres without commonly cited problems with doing so such as complications that arise from statistical outliers, threshold-dependent comparisons, data sparsity and not taking regional variability of activation into account (Wilke & Lidzba, 2007). The result is a more standardised evaluation of laterality effects. The toolbox employs a bootstrapping method whereby 20 equally sized thresholds are calculated between 0 and the maximum t value in the dataset. Then 100 bootstrapped samples (with a resampling ratio of k=0.25) are taken at each threshold in each hemisphere (or ROI if you have chosen this approach). The 10,000 LI combinations are calculated from these samples for all surviving voxels on the left and right, with the usual LI formula, where a positive score indicates more left hemisphere activation, and negative indicates more right. To avoid effects due to statistical outliers only the central 50% of data are kept. A final LI is calculated from all the LIs weighted to their corresponding threshold.

We calculated LIs for each task for the following contrasts: fluency>non-word, faces>scenes, and bodies>chairs. The latter two are typical of the FFA and EBA literature (Downing, Wiggett, & Peelen, 2007; Taylor, Wiggett, & Downing, 2010; Willems, Peelen, & Hagoort, 2010). In these contrasts all activation to the control conditions is subtracted from that to the active conditions, and the LI analysis was carried out on the remaining activation. Not only were LIs calculated for each participant's fluency, face, and body-related activations using this method, but LI estimates for run one versus run two of each of these three stimulus types were also measured. In this dataset each individual's hemispheric asymmetry for fluency, faces, and bodies was investigated. Correlations were also planned to investigate our nod to test-retest reliability, that is, run one versus run two of each task type. Differences in mean LI between handedness groups were also assessed. These analyses involved simple independent samples t-tests.

Finally, as the core aim of this project is to predict cerebral asymmetries using the measures outlined in previous chapters, multiple regression analyses were carried out with the dependent measures being LI for verbal fluency, or face or body localiser response, and the independent measures being our various behavioural measures. The results section in this chapter is descriptive and exploratory. Outcomes are interpreted and discussed in the results section, but these ideas are expanded in the discussion section.

5.3 Results

Before describing the data from each task, it is worth noting here that despite warnings from colleagues and the literature, statistically significant activations for each contrast for every individual were successfully obtained. Whilst fMRI may be more noisy at an individual level than when using group averages, the data certainly appears sensible, and (as is discussed in section 5.3.5), reasonably reliable within individuals.

5.3.1 Activation maps

After processing fMRI data for each individual, and establishing their lateralisation on the language/face/body task, we created average maps for each of three groups: typically lateralised dextrals, typically lateralised adextrals, and atypically organised individuals. We wanted to visually assess any differences in regions or strength of activation between these groups. These maps were corrected for family wise error (FWE) at p=.05, and were extent thresholded to a minimum cluster size of 20 voxels (as is typical in this literature; see Hunter & Brysbaert, 2008). Figures 5.3-5.5 show the averaged activation maps for the verbal fluency task. One dextral's data was excluded from these maps, the only participant with an LI between +/-.10 (-.036, ~4% difference in activation between the hemispheres), her individual activation map can be seen in figure 5.6. With such a small number of atypicals including her data in these maps could hide asymmetric aspects of asymmetry in the participants with clearer right-hemisphere dominance. Her data are not excluded, however, from any statistical analyses in this chapter.

There are not any substantial differences in activation strength or location between the left hemisphere dominant dextrals and adextrals; arguably there is slightly more right hemisphere activation in the typical adextrals than the typical dextrals. In the average of the four atypical adextrals, there is very little left hemisphere activation, in fact there is less left hemisphere activation in this group than there is right hemisphere activation in the typical groups, however, extent thresholding with a smaller sample size could account for this difference.

Figures 5.7-5.10 display the group averaged activations in response to face stimuli for right and left dominant dextrals, and right and left dominant adextrals respectively. These maps were corrected for FWE and extent thresholded as above. Typically lateralised dextrals (figure 5.7) have strikingly asymmetric face-related activity, with typically lateralised adextrals having a small amount of activity in left hemisphere homologues. The atypical participants, across handedness group, have much more bilateral activity.

Figures 5.11-5.14 contain the average activation maps for right and left brain dominant dextrals and adextrals. One dextral's data was excluded from these maps, the only participant with an LI between +/-.10 (+0.037, ~4% difference in activation between hemispheres; figure 5.14 contains his individual activation map). Much more bilateral activation is present in body typically lateralised participants, than in the face typically lateralised participants.

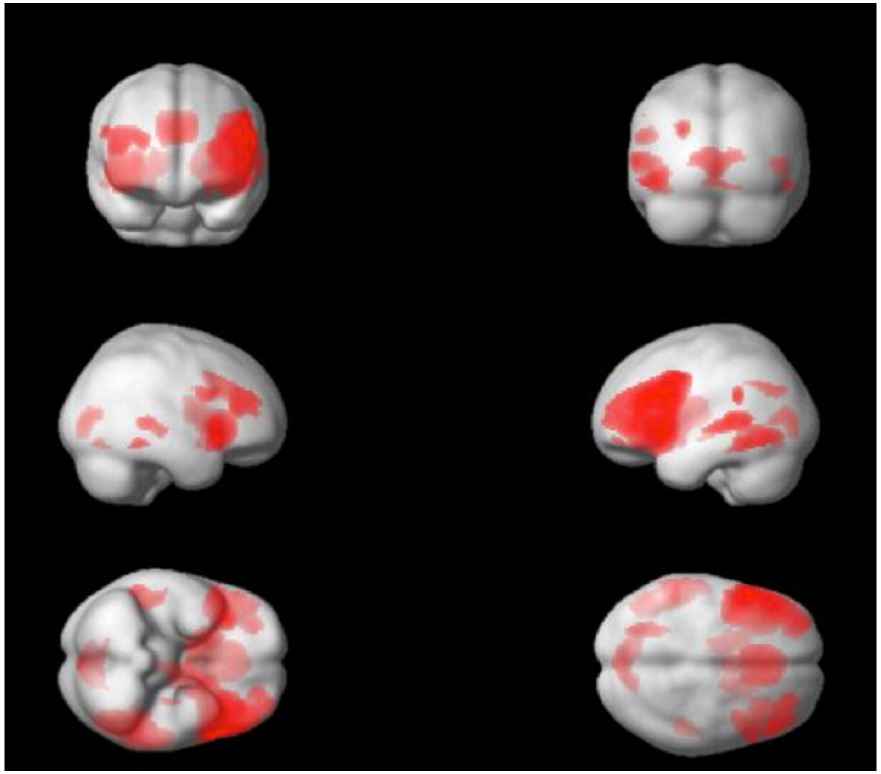


Figure 5.3 – Averaged activation maps from the verbal fluency task for **typically lateralised dextrals** (*n*=20), projected onto a smoothed average brain. These maps were corrected for FWE, and were extent thresholded at a minimum cluster size of 20 voxels. From each view, it is clear to see a higher concentration of activation in frontotemporal regions of the left hemisphere.

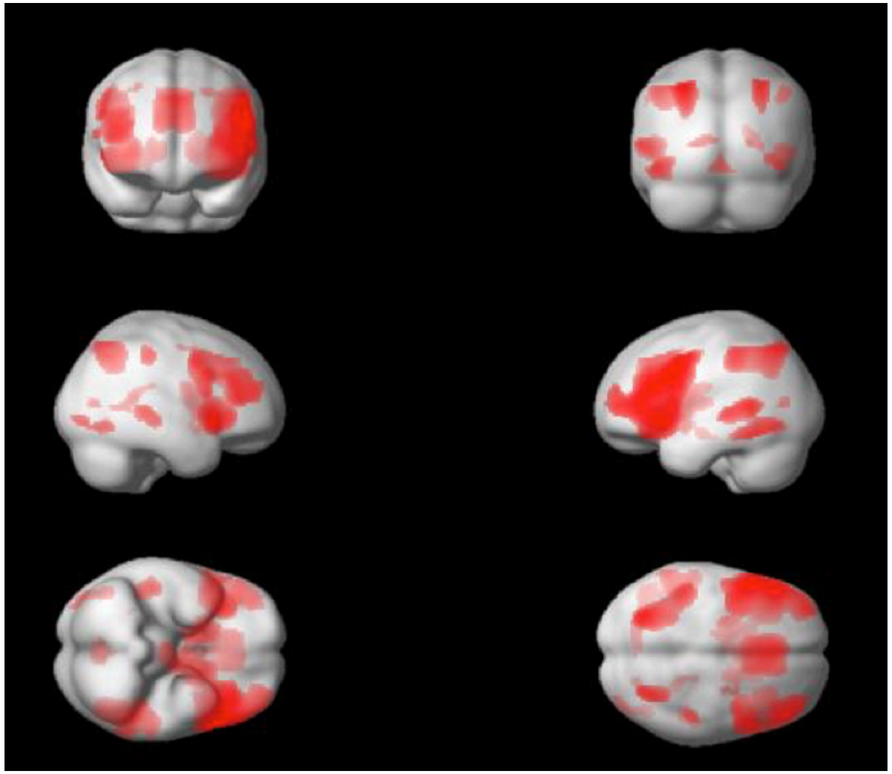


Figure 5.4 – Averaged activation maps from the verbal fluency task for **typically lateralised adextrals** (*n*=29). These maps were corrected as in figure 5.3. From each view, it is clear to see a higher concentration of activation in frontotemporal regions of the left hemisphere. Interestingly, there appears to be slightly more right hemisphere activation than in the typically lateralised dextral average (see figure 5.3).

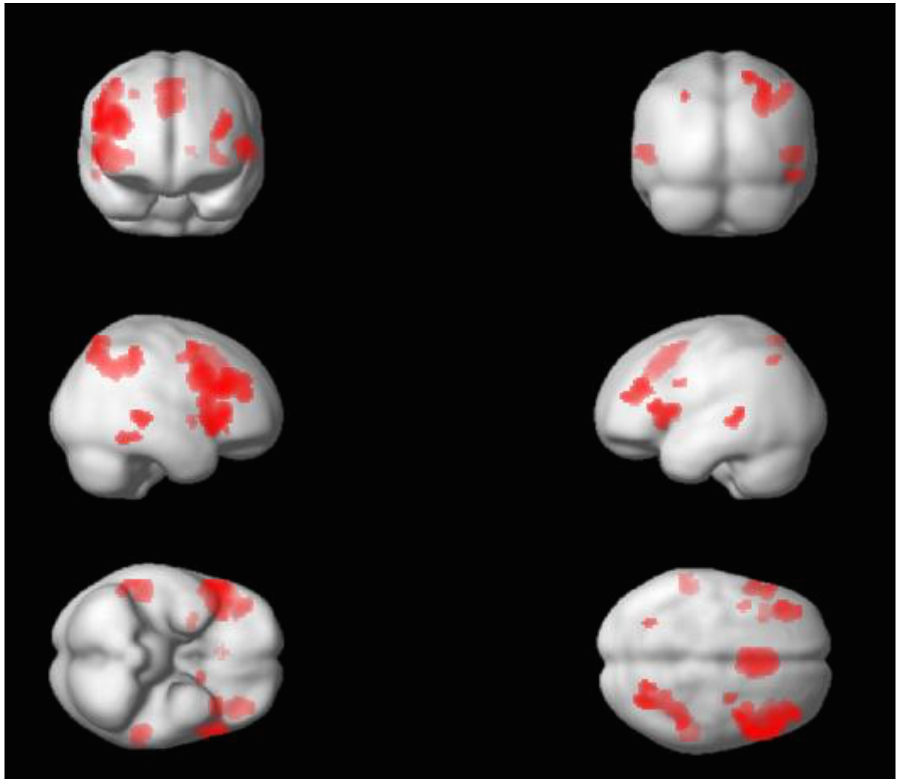


Figure 5.5 – Averaged activation maps from the verbal fluency task for **atypically lateralised adextrals** (*n*=4). These maps were corrected as in figure 5.3. There is a higher concentration of activation in right hemisphere regions. Of course there are fewer participants, but this group appears less bilateral than the typically lateralised adextrals (see figure 5.4).

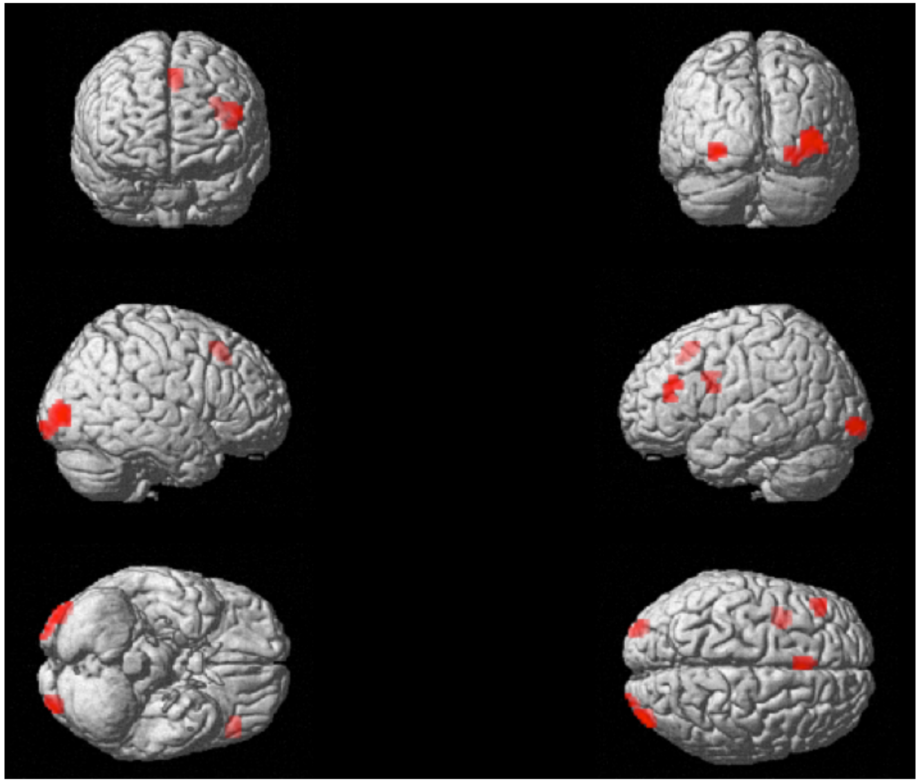


Figure 5.6 – Individual activation maps for participant B0035, a female dextral with an LI of -.036 for fluency. The maps have been thresholded with the same procedures as the average maps. The strongest and largest area of activation here is in the right occipital lobe. For the areas that are most active in the average maps, this participant has more left hemisphere activation, but generally not much activity in these locations.

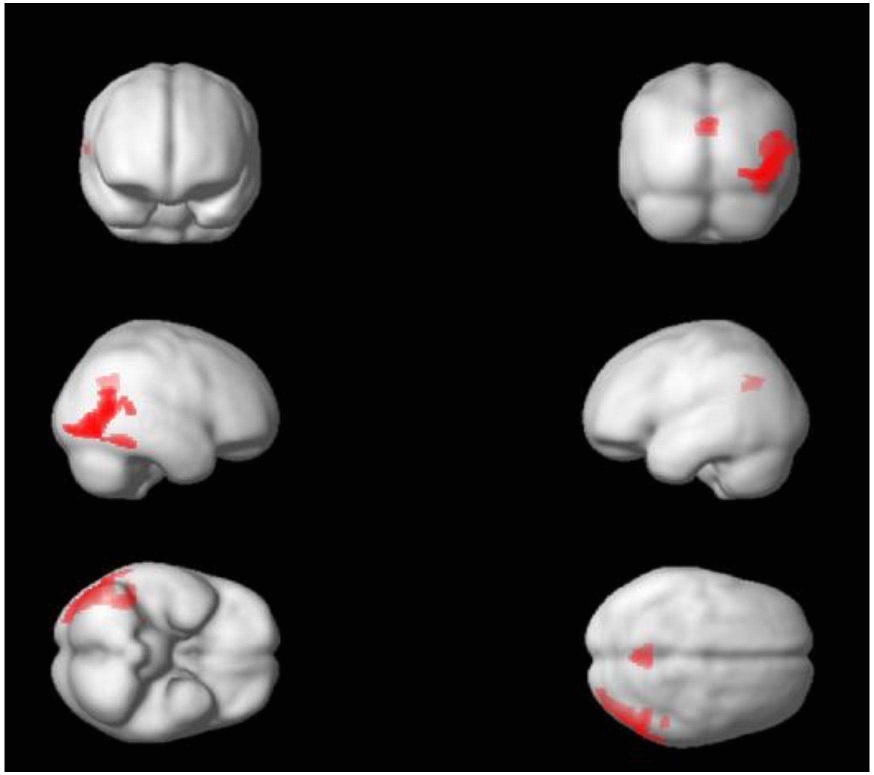


Figure 5.7 – Averaged activation maps from the face localiser for **typically lateralised dextrals** (*n*=16). These maps were corrected as in figure 5.3. There is a higher concentration of activation in right hemisphere regions, and almost no surviving activations in the left hemisphere.

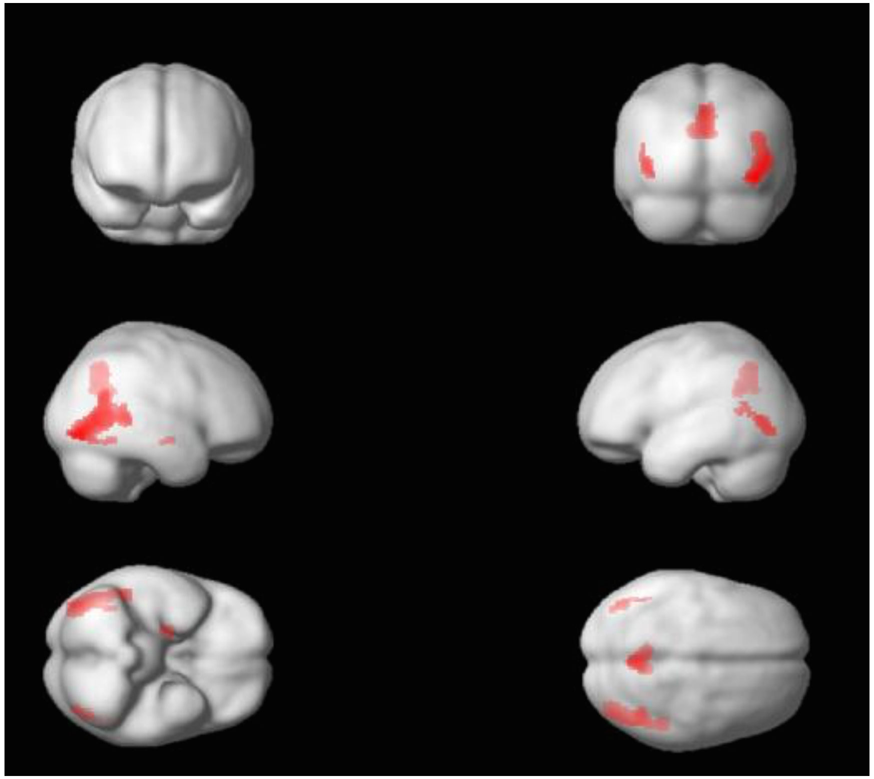


Figure 5.8 – Averaged activation maps from the face localiser for **typically lateralised adextrals** (*n*=21). These maps were corrected as in figure 5.3. There is a higher concentration of activation in right hemisphere regions, but more left hemisphere activations present than in dextral counterparts (fig 5.7).

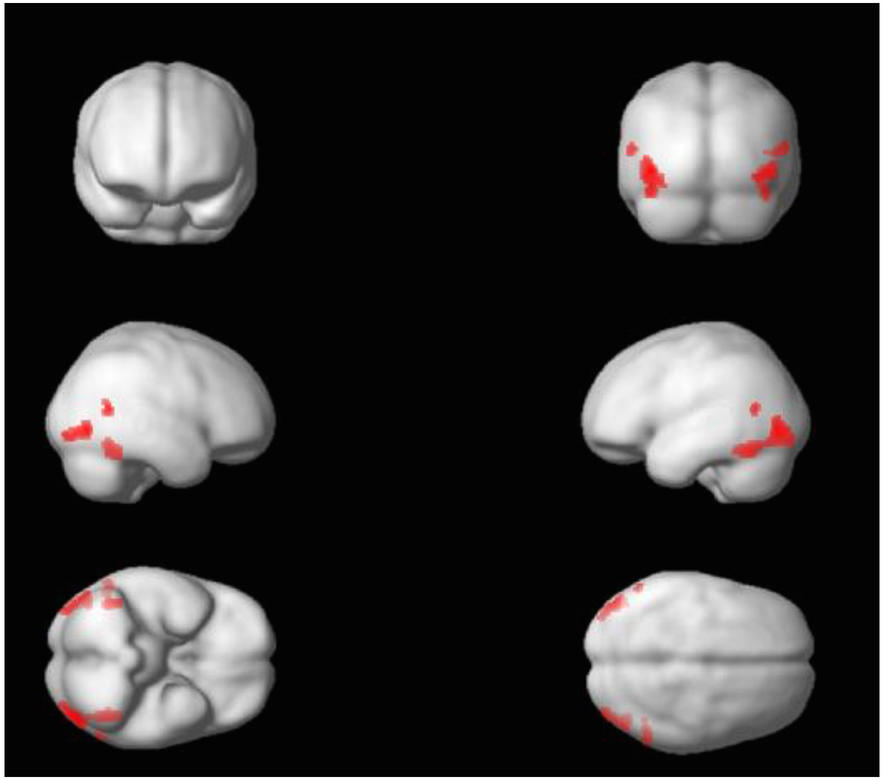


Figure 5.9 – Averaged activation maps from the face localiser for **atypically lateralised dextrals** (*n*=5). These maps were corrected as in figure 5.3. There is a higher concentration of activation in left hemisphere regions, but right hemisphere regions are also relatively active.

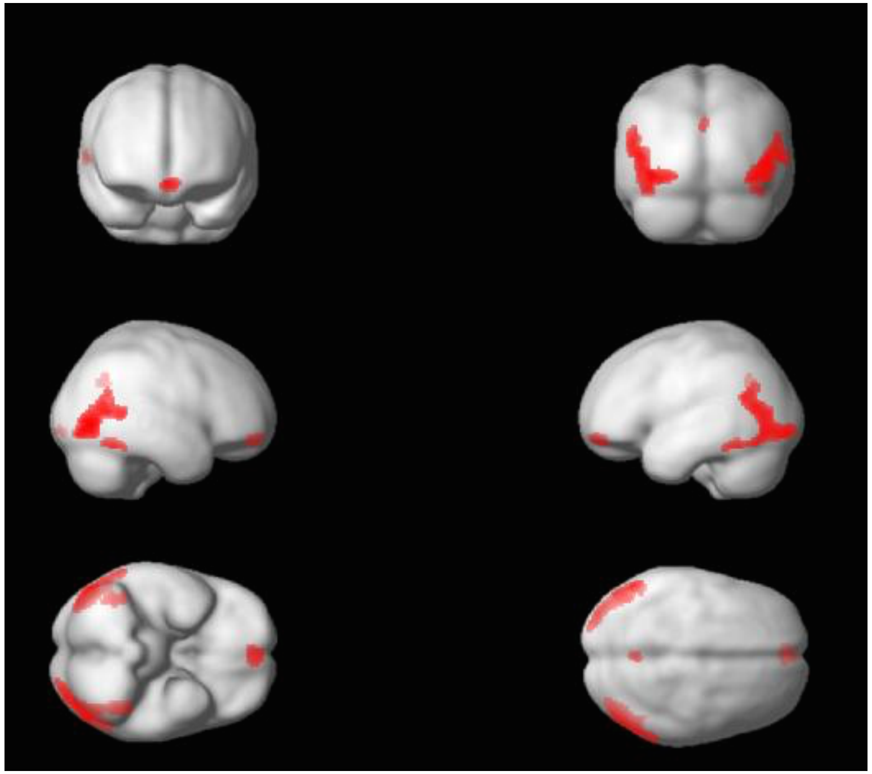


Figure 5.10 – Averaged activation maps from the face localiser for **atypically lateralised adextrals** (*n*=12). These maps were corrected as in figure 5.3. There is a higher concentration of activation in left hemisphere regions, but again, the activity is fairly bilateral.

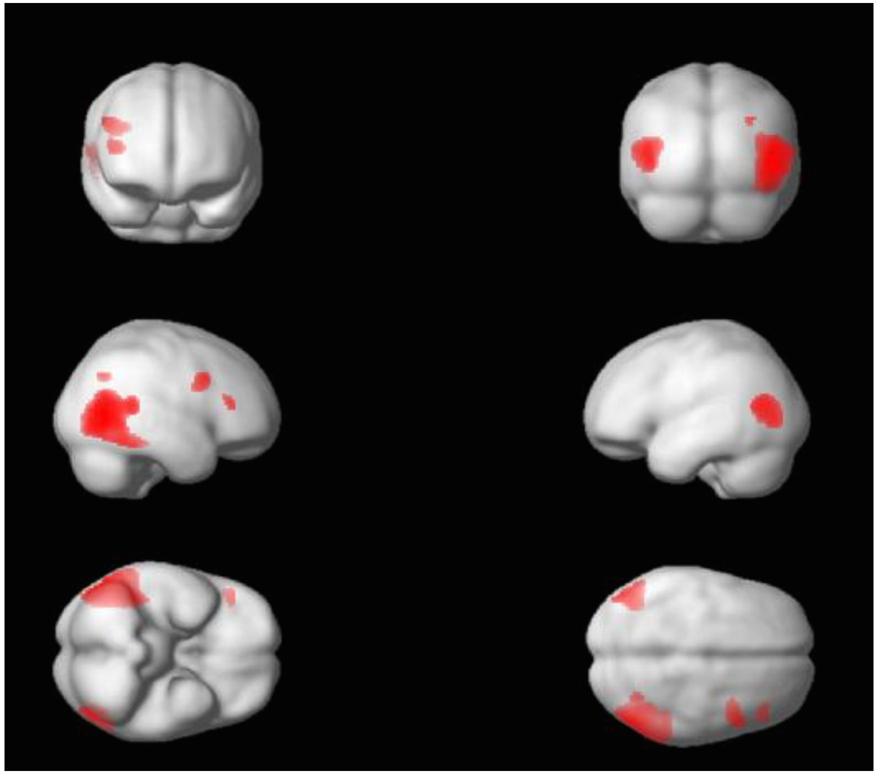


Figure 5.11 – Averaged activation maps from the body localiser for **typically lateralised dextrals** (*n*=20). These maps were corrected as in figure 5.3. Although left hemisphere activations survive the subtraction, there is a higher concentration of activation in right hemisphere regions.

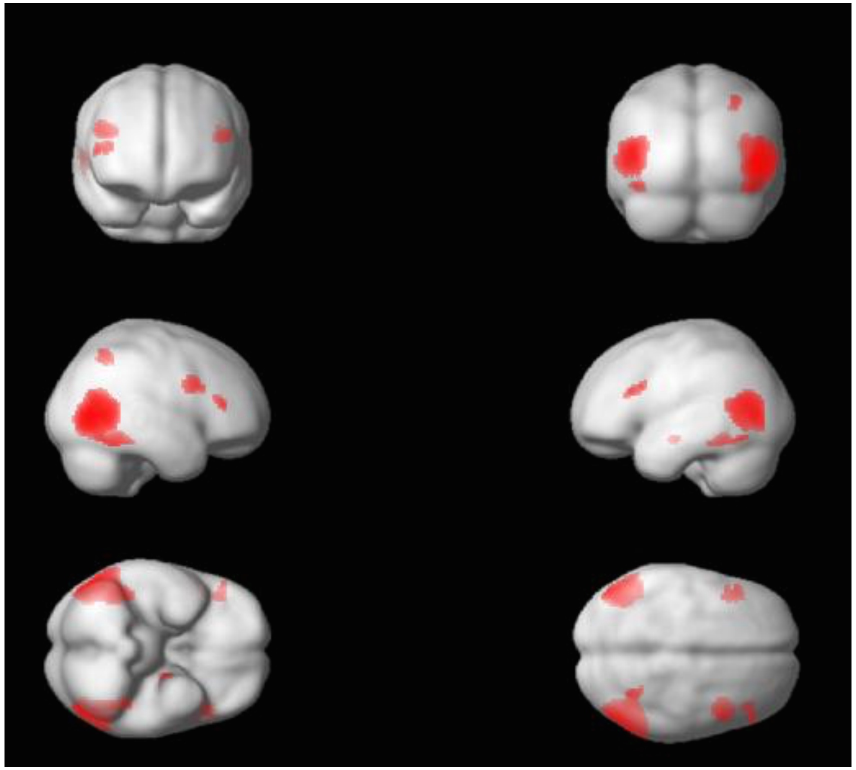


Figure 5.12 – Averaged activation maps from the body localiser for **typically lateralised adextrals** (*n*=23). These maps were corrected as in figure 5.3. There is a higher concentration of activation in right hemisphere regions.

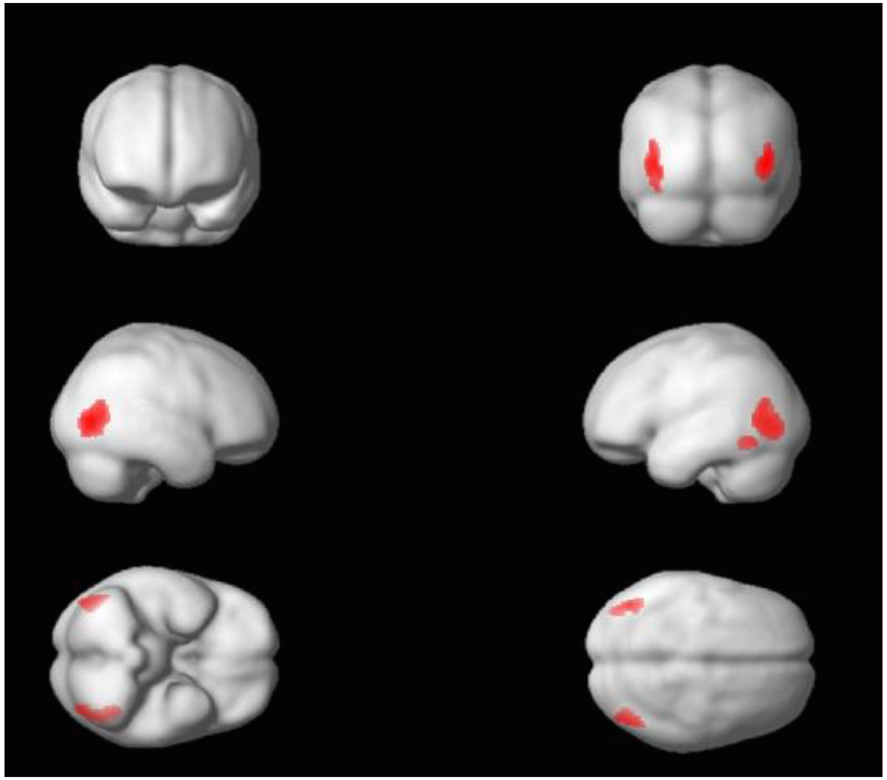


Figure 5.13 – Averaged activation maps from the body localiser for **atypically lateralised adextrals** (*n*=10). These maps were corrected as in figure 5.3. The pattern of activity is quite bilateral, but slightly more left-hemisphere biased.

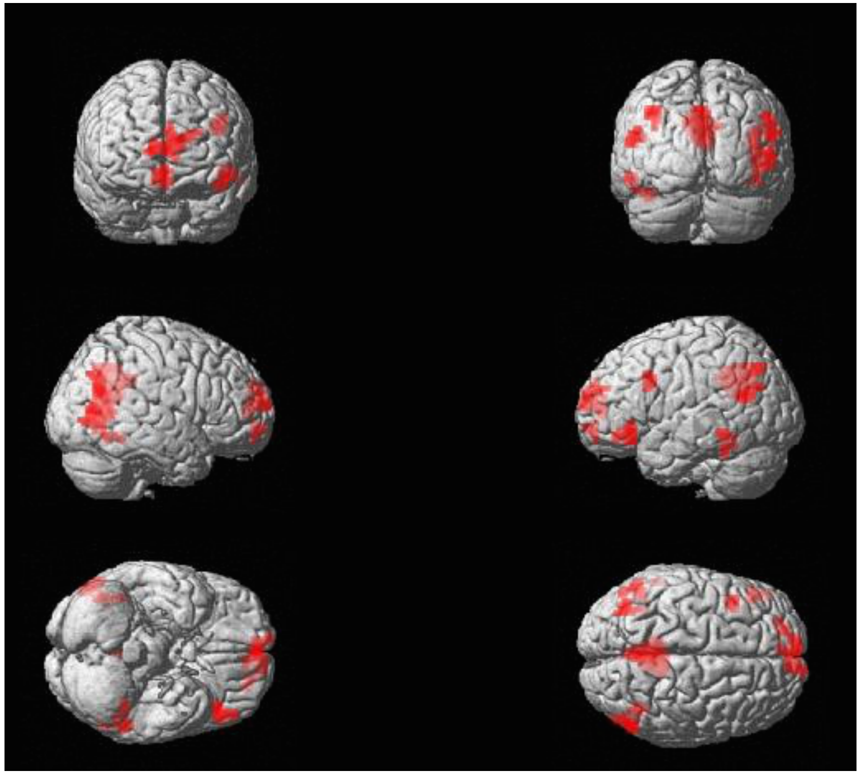


Figure 5.14 – Individual activation maps for participant B0101, a male dextral with an LI of +.037 from the body localiser. These maps were not corrected as in figure 5.3, as only one central region survived thresholding. Therefore for the purposes of this figure activations are thresholded at $p<.001$ uncorrected for FWE. Activity is fairly equally distributed across the hemispheres, with perhaps more right hemisphere activation in body related areas.

5.3.2 Central tendency and proportions

In response to the verbal fluency paradigm, of the 21 dextral participants, all but one had a positive LI for fluency (95%), and the subject with a negative score had an LI of -.034, i.e. there was a 3-4% difference between activation in the hemispheres. As discussed in the introduction, LI boundaries to classify individuals as 'bilateral' are difficult to justify and vary across research groups. Perhaps between +/-0.10 would be a reasonable bilateral category, however we did not decide this a priori. The mean LI in the left hemisphere dominant dextrals was +.65 (SD=.20).

In the adextral participants, four were atypically dominant for fluency, with the remaining 29 (88%) typically lateralised. The mean LI in the typical adextrals was +.56 (SD=.21), whereas the mean LI in the four atypical participants was -.56 (SD=.17) (see figures 5.15 and 5.16 for group mean LIs for each task and percentages of each sample showing the typical response). The mean LI of the typical dextrals was numerically higher than that of the typical adextrals, but this difference was not statistically significant (*t*(47)=1.51, *p*=.07, one-tailed), indicating that typical dextrals are not more lateralised than typical adextrals. To assess whether the atypical group were as lateralised as the typical group the direction of the individual LIs for the atypical language group was inverted, and absolute values were used (i.e. -.63 became .63) and an independent-samples t-test was run comparing the typical scores with the atypical modified scores. The magnitude of lateralisation of the two groups did not significantly differ (*t*(52)=1.36, *p*=.18, two-tailed).

For face processing, as measured by our localiser task, 16/21 (76%) dextrals and 21/33 (64%) adextrals were typically right-hemisphere dominant. The mean LI in the typical participants was -.66 and -.45 for the dextral and adextrals respectively. In those who were atypically lateralised for face processing the mean LI was .25 and .29 for dextrals and adextrals respectively. The difference between mean LI in the typical, right-dominant dextrals and adextrals was statistically significant (*t*(35)=3.32, *p*=.001, one-tailed), indicating that on average the dextrals are more strongly lateralised than the adextrals. Again the magnitude of lateralisation was investigated with an independent-samples t-test. The typical group were more strongly lateralised than the atypical group (*t*(52)=4.34, *p*<.001).

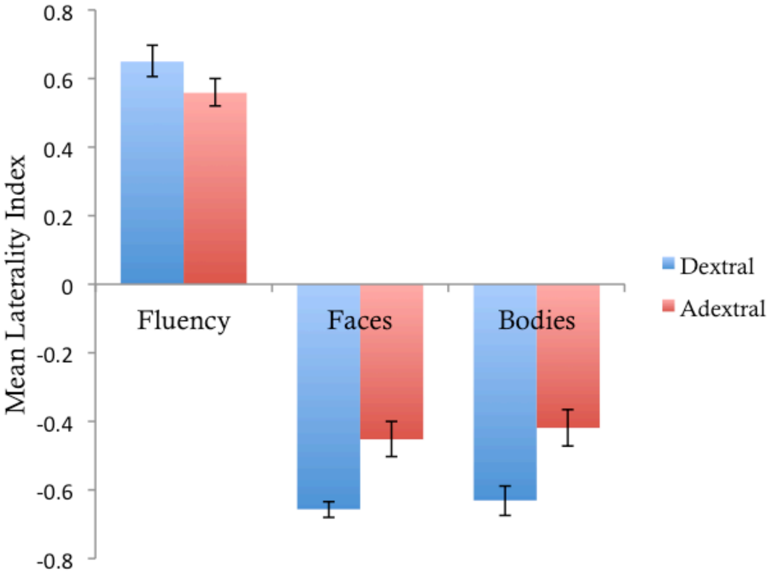


Figure 5.15 – Mean LIs for each handedness group for each fMRI task. A positive score on the *y*-axis indicates more left hemisphere activity, whereas a negative score indicates more right hemisphere involvement. Error bars represent +/-1 standard error of the mean.

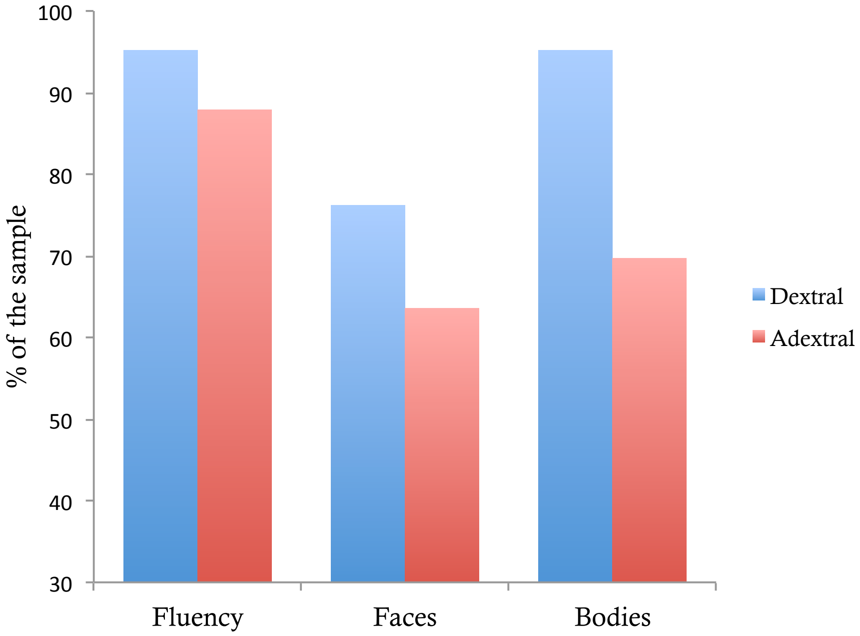


Figure 5.16 – The percentage of each handedness group displaying 'typical' hemispheric dominance on each fMRI task. 'Typical' refers to more left hemisphere dominance on the fluency task and right hemisphere dominance on the face and body localisers.

For body-related activation, 20/21 (95%) dextrals and 23/33 (70%) adextrals were typically right-hemisphere dominant. The mean LI in the typical dextrals and adextrals was -.63, and -.42 respectively. The left hemisphere dominant dextral had an LI of +.037 (as mentioned in the fluency section, scores between +/-.10 should be interpreted carefully – it is also worth noting that this participant is not the same participant who is atypical on fluency; see figure 5.14). The atypical adextrals had a mean LI score of +.23. The difference between mean LI in the typical dextrals and adextrals was statistically significant (*t*(41)=3.02, *p*=.002, one-tailed), indicating that on average the dextrals are more strongly lateralised than the adextrals. Again the magnitude of lateralisation between typical and atypical participants was investigated, finding that the typical group were more strongly lateralised than the atypical group (*t*(52)=3.23, *p*=.002).

As in previous chapters, a *z*-test was used to statistically compare the proportions of dextrals/adextrals showing typical lateralisation for each task (see figure 5.16). The difference in proportion between dextrals and adextrals was not statistically significant for the fluency or face task (*z*=0.87, *p*=.19 and *z*=0.90, *p*=.18 respectively, both one-tailed), however on the body localiser the proportion of the dextral sample that was typically lateralised was significantly higher than that of the adextrals (*z*=2.10, *p*<.02, one-tailed). Of course the sample sizes are small for proportional analyses, particularly in fluency where the data are so skewed towards left hemisphere dominance, but with more participants this would be a useful analysis for determining fMRI factors that really differentiate dextrals and adextrals.

5.3.3 Degree of 'sidedness'

Both eye dominance and preferred kicking foot was recorded from all participants (as in Chapter 2, see page 39 for justification). To investigate what relationship these asymmetries may have to asymmetries on the fMRI tasks participants were split four hand/eye/foot subgroups: right dominant ('RRR'; *n*=13), right handed but left eyed or footed ('R_Mixed'; *n*=7), left handed but right eyed or footed ('L_Mixed'; *n*=19), and finally left dominant ('LLL'; *n*=10). This subgrouping allowed for comparison of the incidence of typical lateralisation for each task across increased right/left sidedness. All four adextrals that were atypical for fluency were left eyed and left footed. Overall typical lateralisation for each measure decreases as left sidedness increases (see figure

5.17). WHQ scores were also recorded for each participant, and this score correlated significantly with each LI measure, see figure 5.18.

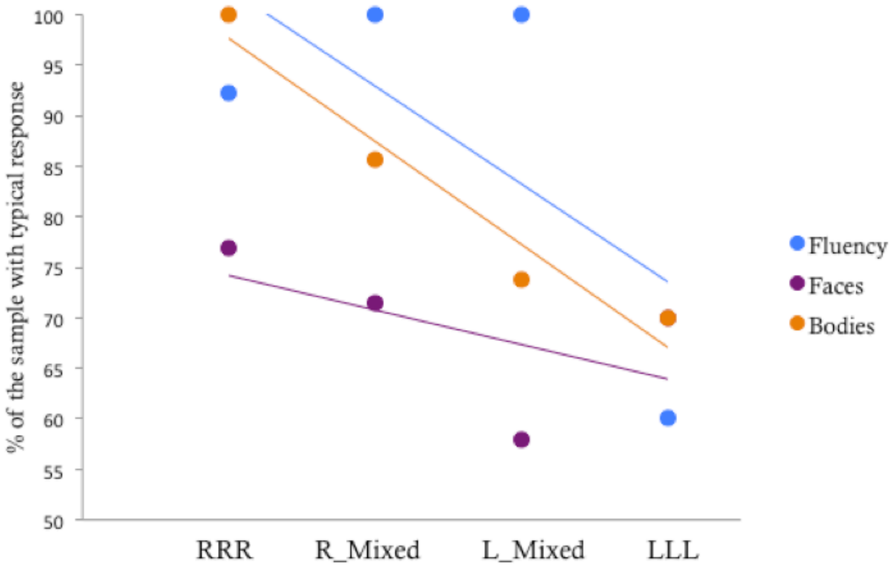


Figure 5.17 – Proportions of each hand/eye/foot group showing typical lateralisation for each fMRI task. RRR indicates the group who are right handed, eyed, and footed. R_Mixed is the group who are right handed, but left eyed, left footed, or both. This convention carries through to the left-handed groups.

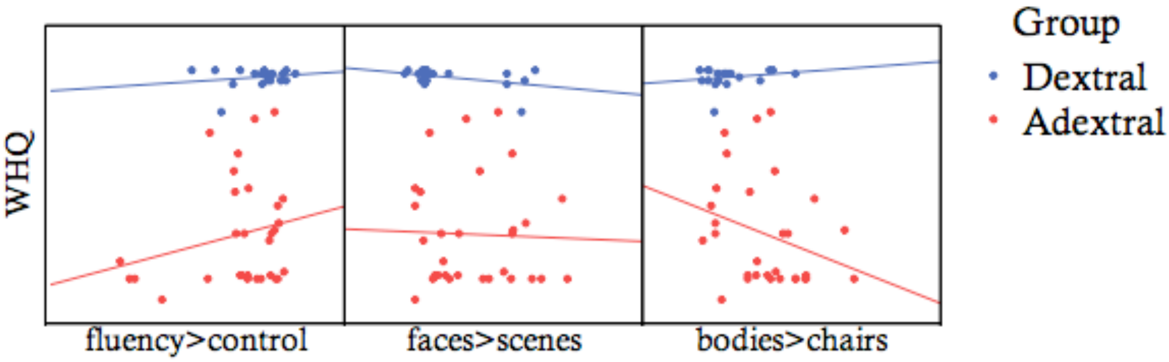


Figure 5.18 – A scatterplot showing WHQ scores (-30 to +30) plotted against LIs (-1.0 to +1.0) for each fMRI task. Scores falling right of centre on the *x*-axis indicate a positive LI (i.e. left brain activations), and scores above centre on the *y*-axis indicate positive WHQ scores (i.e. more right than left hand use). What is immediately apparent is the lack of variability amongst the dextrals as compare with the adextrals. The correlations between WHQ and fluency/face/body LI were all significant: r=.32, p<.02, r=-.28, p<.03, and r=-.52, p<.001 (one-tailed).

5.3.4 Complementary specialisation

It is clear from the proportions reported in section 5.3.1 that perfect complementary hemispheric specialisation between activations in response to the fluency and the face/body task is not present in our sample. We anticipated, however, that perhaps if an individual were strongly lateralised on fluency, for example, s/he would be strongly lateralised in the opposite direction for face or body asymmetry. Our hypotheses, therefore, were a negative correlation between fluency scores and body/face scores, and a positive correlation between the body and face scores. We used bivariate correlation to compare relationships between LIs for all three tasks. When comparing fluency x faces x bodies, the only significant correlation was between faces and bodies (*r* = .49, *p*<.001, one-tailed). Figure 5.19 contains a matrix scatterplot displaying the relationships between LIs on all three tasks, separated by handedness group. What is clear from this figure is that the adextrals are a more heterogeneous group than the dextrals, who are more closely clustered. Subsequently we ran these same correlations separately for the two groups, finding a significant negative correlation between fluency and face

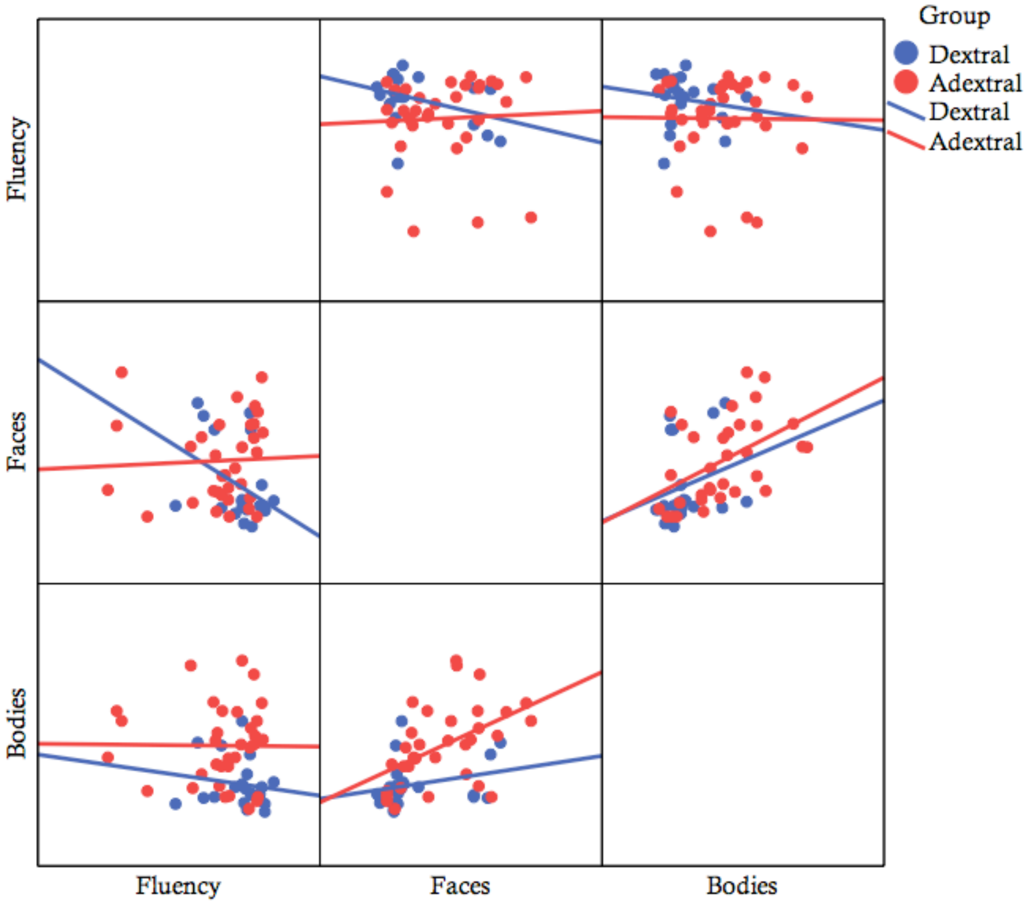


Figure 5.19 – Matrix scatterplot of the LIs for both groups for all tasks. It is clear to see here how much more spread there is amongst the adextral data than that of the dextrals.

scores in the dextrals (*r* = -.39, *p*<.05, one-tailed), and a positive correlation between face and body scores in adextrals (*r* = .49, *p*=.002, one-tailed).

5.3.5 Are fMRI LIs for these tasks a trait or state variable?

To assess the reliability of the LIs found in our sample bivariate correlations were run between LI scores from the first run of a specific task and the LI from the second run, for each of the tasks. All correlations were statistically significant, with fluency having the strongest between-run correlation (*r* = .82, *p*<.001), followed by face asymmetry (*r* = .69, *p*<.001), and finally body asymmetry (*r* = .65, *p*<.001); see figures 5.20-5.22 for scatterplots. As can be seen in figure 5.20, the majority of participants fall in the upper right quadrant, indicating that they had a leftward LI in both runs of the fluency task. Any participants falling in either the top left or bottom right quadrant has reversed the direction of their LI from run 1 to run 2. Using figure 5.20 as an example, only 3/54 participants appear in these quadrants, and interestingly these are all adextrals.

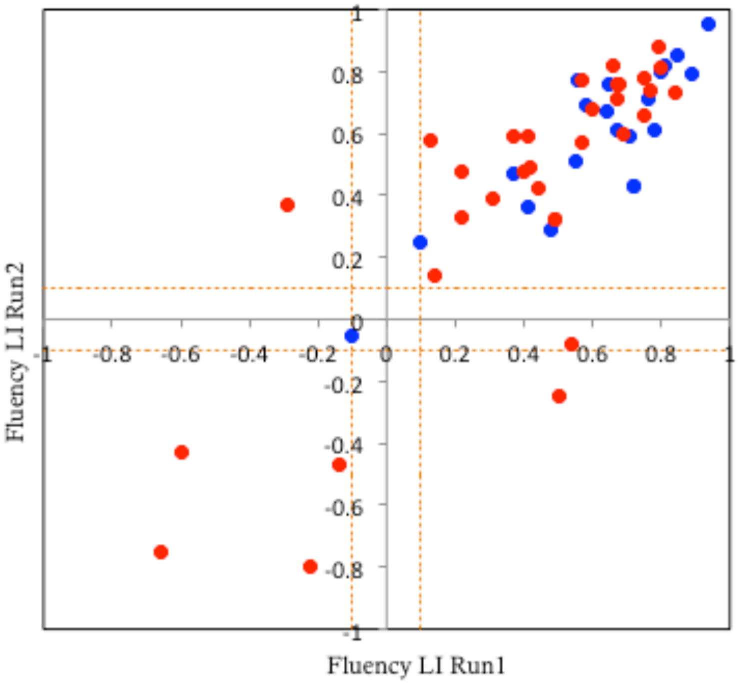


Figure 5.20 – LIs from run 1 of the fluency task, plotted against LIs from run 2. Blue data points are dextral participants and red data points are adextral participants. The dotted lines are positioned at +/-.10 for each run, to indicate an area of potential noise. Participants who fall into the top left or bottom right quadrant are participants with LIs that reversed between runs. This formatting is repeated in figures *5.21* and *5.22*.

In the face task (figure 5.21), nine participants (two dextrals) show opposite laterality across the two runs of the task. The pale orange lines indicate the area between +/-.10, i.e. the boundary between which the difference between activations in the hemispheres is only 10%. Of the ten participants who changed response patterns, six fall within this boundary for run 2, and two fall within this boundary for run 1 (one participant is in both boundaries). Five participants have LIs that reverse direction across runs and are not near zero on either run (i.e. the change in LI is substantial – see bottom right panel of figure 5.21). Of course for individual people we expect some measurement error in fMRI, and this will be discussed later in this chapter. Finally for the body localiser (figure 5.22), twelve participants (three dextrals) reversed lateralisation across the runs. Four of these are extremely close to the zero border, but six fall outside the +/.10 boundary.

Overall these data suggest that LIs across runs are reasonably reliable, particularly for the fluency task where only 6% of participants' LIs changed direction across runs. In the face and body data, several of the participants whose LIs reversed fall close to zero for one of the runs, as opposed to having LIs that reverse both direction and magnitude.

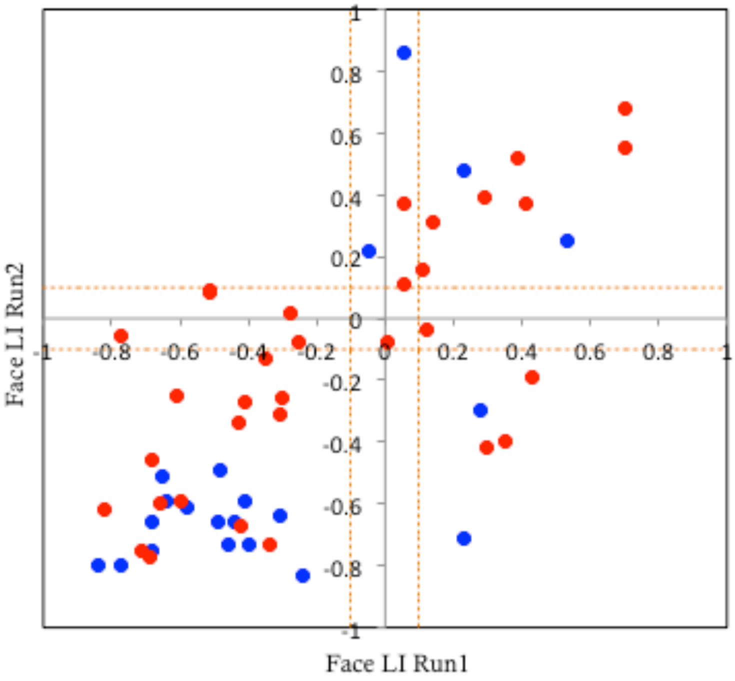


Figure 5.21 – LIs from run 1 of the face task, plotted against the LIs from run 2. Blue data points are dextral participants and red data points are adextral participants. The distribution of LIs present in the face task data is much more spread than that of the verbal fluency LI data in figure 5.20.

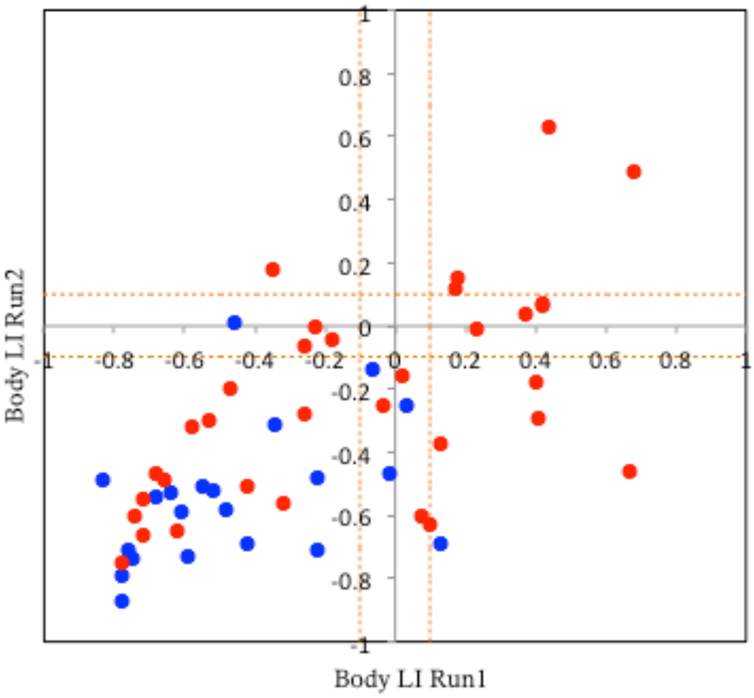


Figure 5.22 – LIs from run 1 of the body task, plotted against LIs from run 2. Blue data points are dextral participants and red data points are adextral participants. Again the distribution of scores here is more spread than that of the verbal fluency LI data in figure 5.20.

6.3.6 A first pass at assessing behavioural predictors

As this is a thesis about factors predicting brain asymmetry, in this chapter we can finally start to analyse the potential predictive value of our behavioural measures. It is obviously crucial to note that our sample size of participants who have undergone our imaging procedures are small (for these statistical purposes at least), so any multivariate analyses are limited. Data on all indirect and fMRI measures are heavily skewed towards responses relating to typical lateralisation, therefore conducting these analyses properly would require large sample sizes with multiple participants with every combination of possible responses/ asymmetries having some cell membership. Ideally the result of this enterprise would be an equation that weighs each predictor appropriately and calculates how likely someone is to be right- or left-brain dominant for a function such as language.

Multiple regression analyses were run to assess the predictive power of our behavioural measures for fluency, face, and body LIs. Three separate regressions were run using LI score from the verbal the fluency, face, and body tasks as the dependent variables in each case, and CV dichotic listening, Efron dichotic listening, the octave illusion, the two measures of the Stroop task, the greyscales task, and the face VHF task scores, as well as the asymmetry of hand differences in RT, peak velocity, duration, and deceleration duration (as difference scores where negative indicated the atypical response) as the independent variables. All participants were included in these analyses, however it is important to note that 45 had data for all predictor variables, however the remaining nine participants had up to three measures missing. In these cases the missing data was replaced with the mean score.

These variables did not statistically significantly predict fluency LI ($F(10,43)=0.99$, $p=.47$), and the analysis gave adjusted R^2 value of -.003. Adjusted R^2 takes into account the number of predictors in a model, and only increases if a measure improves the fit of the model more than chance, and decreases if a measure improves fit less than expected by chance. This data suggests that perhaps we have too few participants for so many predictors. A negative R^2 suggests that the fit of the current model is worse than the fit of the null hypothesis, suggesting the model does not follow the trend of the data (i.e. it fits the data less well than a horizontal line). None of the measures added statistically significantly to the prediction. The correlation table revealed that only Stroop RT variable approached a significant correlation with fluency LI ($r= -.22$, $p=.057$).

In the face LI analysis, the independent variables again could not successfully predict the dependent variable ($F(10,43)=0.58$, $p=.82$, adj. $R^2 =-.09$). None of the independent variables added statistically significantly to the prediction, and no correlations were found between the predictor variables and face LI (the closes relationship being with manual asymmetry in reaction time, $r=.21$, $p=.062$).

When body LI was the dependent variable, the independent variables still did not successfully predict LI ($F(7,46)=1.73$, $p=.10$, adj. $R^2 =.12$), however, this model had a better fit than either the fluency or face models. Only accuracy score on the Stroop task added statistically significantly to the prediction ($t=3.05$, $p=.003$), and was significantly correlated with body LI ($r=-.36$, $p=.004$).

For our purposes, predicting the actual LI for any of these measures is not as relevant as simply predicting the direction of the LI, i.e. the individual's categorical lateralisation for each function. As there are only four atypical participants on our fluency task, unfortunately we are underpowered to carry out analyses such as discriminant function analysis, where variables are assessed on their ability to aid prediction of group membership (i.e. left or right lateralised).

5.4 Discussion

The proportions of left hemisphere/right hemisphere dominance are as one might expect. In the fluency data, 95.2% of the dextrals, and 87.9% of the adextrals are left hemisphere dominant. These proportions are similar to what Rasmussen and Milner (1977) estimate from their Wada test patient series, and to the 90% and 73% that we report in our meta analysis of fMRI, ECT and TDS studies (Carey & Johnstone, 2014). Although the proportion of adextrals who are left hemisphere dominant is slightly higher, a majority of both groups are left hemisphere dominant, and this majority is greater in the dextrals. Our use of a dichotomous classification system could account for this. Whilst we acknowledge that our participants were not a completely random sample (nine participants were preselected for atypical responses on CV dichotic listening or greyscales), no participants were added after statistical analyses of any dependent variables, therefore there is no reason to suspect the proportions of typical/atypical dominance in our samples have been manipulated by preselection.

In the face localiser data, 76.2% of dextrals and 63.6% of adextrals lateralise typically to the right hemisphere. It appears that face processing is less lateralised than fluency, at least when these two localisers provide the asymmetry measures. Finding estimates of how often right or left lateralisation of face functions occurs in dextrals has been difficult, but our proportion of dextrals showing right brain dominance corresponds closely to the 77.4% right brain dominance that Galit Yovel and colleagues (2008) found in their sample of 61 dextrals (Yovel, personal communication 26th January 2015). The incidence of right lateralisation in the adextrals is lower, but still present in a majority as predicted. Typical right-hemisphere lateralisation of body perception related activations was found in 95.2% of dextrals and 69.7% of adextrals. This was arguably the most surprising finding in the proportion data. It was anticipated that body activity to co-lateralise with face processing functions, however, more participants in both groups are right lateralised for bodies than for faces, with the asymmetry following more closely that of fluency. This finding corresponds to the average data reported by Willems, Peelen, and Hagoort (2010) where adextrals were more symmetrical in terms of FFA activation than they were for EBA activation (which was numerically more right lateralised, but this difference did not reach statistical significance – p=.09).

Typically lateralised adextrals had a significantly less asymmetric mean LI than the typically lateralised dextrals for the face and body tasks. For verbal fluency this effect occurred in the predicted direction numerically (with a 9.2% increase in average left lateralisation in dextrals) but did not reach statistical significance (*p*=.07). Given what is known from distributions of scores on handedness questionnaires, for example, most adextrals use their non-dominant hand more than dextrals (see figure 5.18 for WHQ spread in our samples). This difference in hand use suggests that adextrals may be less lateralised, in terms of behaviour, than their dextrals counterparts. Although conclusions that adextrals are less asymmetric than dextrals have been drawn previously, these are usually from group averaged data that may include atypical individuals. To the best of our knowledge this is the first comparison between the magnitude of lateralisation between *typical* dextral and adextrals.

Across participants, the only LIs that significantly correlated with one another were from the face and body tasks, therefore a participant being strongly lateralised on the fluency task does not correspond to them being strongly lateralised in terms of face or body perception activation. Perhaps the verbal fluency task was not really ‘matched’ to the face/body localiser, which in some sense are bound to be correlated in terms of brain activity as they are measured within the same experimental design; identical stimulus presentation times, rest periods, balanced block presentation orders, etc. The verbal fluency task, however, did include an active baseline condition to contrast against, rather than a silent ‘rest’ contrast, making it more similar to the face/body localiser than many other language tasks.

When running correlations between the task LIs within handedness group, fluency and face LIs were negatively correlated in the dextrals, and face and body were positively correlated in the adextrals. The lack of a significant negative correlation between fluency and body LI in the dextrals was not expected considering that 20/21 had typical lateralisation for these tasks. It can be seen from the matrix scatterplot (figure 5.19) that the dextrals are a close cluster, and perhaps a lack of variability within the group prevents a clear correlational relationship.

A strength of our design is that we could provide comparisons between two runs of the same task, a kind of within-session test-retest reliability. These correlations are strong, and strongest between runs of the fluency task. This reliability measure adds to the evidence that the fluency task is successful in producing lateralised activity in individual participants.

Others, such as Cai, Van der Haegen and Brysbaert (2013), only use one run of this task and were able to classify participants as left or right hemisphere dominant. The present data suggests that one run may be sufficient, as LIs are fairly reliable across runs, in terms of direction at least. A potential weakness of this aspect of our design is that the 14 letter items, although being those that begin the most words in English, were presented in a random order across the runs, meaning the runs were not balanced for difficulty. It is possible that more difficult letters require more 'effort' for language regions of the brain while a participant mentally searches, or conversely, difficult letters may result in less activation through less words being mentally articulated. In a future experiment, to examine the real limits of within-scan test-retest reliability, two sets of seven letters balanced for fluency difficulty would be created, and orders would be counterbalanced across participants. If the present participants are included in future studies, an additional run of the fluency paradigm will be carried out to allow for test-retest estimates both within and across testing sessions.

As mentioned in the participant section, nine participants were preselected for looking "atypical" on a behavioural measure (usually CV dichotic listening). Of these individuals, three had reversed lateralisation for fluency. Although the multiple regression analysis suggests that none of our behavioural predictors are in fact predictors of fluency LI, three of the four atypical adextrals, and the atypical dextral, had left earred scores on CV dichotic. A test that is not especially sensitive, and gives 'false positives' is a perfectly acceptable pre-screen measure. However, a test that sometimes 'misses' atypical participants is something we set out to avoid, by employing multiple measures.

The four fluency atypical participants had strongly left-sided WHQ scores (less than -25), were all left eye dominant and left footed. Two of these participants had atypical face and body representation, whilst the remaining two had typical lateralisation of both these functions. This is quite different to the laterality profile of the fluency typical participants, where 70% were right lateralised for face processing and 81% were right lateralised for body perception. Three of the atypical fluency participants also had reversed scores on greyscales and the octave illusion.

If fMRI data were available from more participants, a more data driven-analysis, such as discriminant function analysis could have been used. The advantage of this as opposed to multiple regression is that the dependent measures must be a scale variable, i.e. the laterality index scores. For our purpose of identifying atypical individuals the extent of lateralisation is not of particular importance, we want to predict the direction of it. Discriminant function analysis allows for separation of participants based on one nominal factor (i.e. left or right brain dominance for fluency), and assesses the ability of a combination of predictors to assign individuals to these groups.

This type of sample, including relatively (in the neuroimaging literature at least) substantial numbers of dextrals and adextrals, tested on multiple behavioural and kinematic measures, and three different measures of asymmetry in fMRI data, is the first of its kind in laterality research. Assessing both the behavioural and neuroimaging data at an individual level is a major strength of this project. This dataset is a prime example of how valuable information is lost in the sole reporting of measures of central tendency, a practice that has become so popular in psychological research. These data, if analysed simply comparing mean differences across handedness groups, would have only shown that LIs in adextrals were closer to zero for each task.

Chapter 6 – General discussion

This thesis had one principal aim: to identify potential predictors of hemispheric specialisation for language and face/body processing in individual people. This goal is addressed in each chapter, assessing the relationship between these brain asymmetries and manual asymmetries, lateralised ERPs, and an indirect battery of perceptual tests. An overall theme of this work was that the analytical approach did not restrict itself to the typical inferential statistics that examine measures of central tendency, the default in experimental psychology.

In the manual asymmetries literature, many scientists have argued that right hand advantages in dextrals for measures like duration, peak velocity, and accuracy, are related to left hemispheric mechanisms for speech and limb control (Kimura, 1993). A smaller set of research papers have made similar arguments about the right hemisphere and left hand reaction time advantages in dextrals (Elliott et al., 1993; Barthélémy & Boulinguez, 2001; Barthélémy & Boulinguez, 2002; Carey et al., 2015). One improvement utilised in chapter two was the considerably improved sample size, which allowed for the first ever examination of the proportions of individuals who showed manual asymmetries in the key measures. A second and related improvement was the inclusion of a large, well-matched sample of adextral participants tested in exactly the same way. The data summarised in chapter two do provide evidence for a link between cerebral asymmetries and manual asymmetries in reaching.

Dextrals and adextrals differed on a linear combination of outcome measures (RT, peak velocity, duration, and deceleration duration), and the dependent measure of dominant hand duration contributed the most to this model. In hand (dominant/non dominant) by group ANOVAs, interactions between hand and group were present for all measures. Post hoc *t*-tests revealed that this interaction was always driven by an asymmetry in the dextral group favouring the dominant hand for peak velocity, duration and deceleration duration, and the non-dominant hand for RT. There was no significant difference between the hands of the adextral group for any measure. Additionally, no significant difference between the magnitude of the typical manual asymmetry was found between dextrals and adextrals, however when comparing those with the atypical asymmetry dextrals had significantly lower left hand peak velocity and duration advantages than their adextral counterparts.

The proportions of each group showing these asymmetries were significantly different in the predicted directions for three of the four dependent measures: RT, peak velocity and duration. The participants were regrouped based on hand/eye/foot dominance, and the proportion of the sample showing the ‘typical’ manual asymmetries decreased as left-sidedness increased (these proportions were not inferentially tested).

In spite of these promising results, they are obviously not the strongest evidence that manual asymmetries are a direct consequence of functional cerebral asymmetries. It was anticipated that a majority of adextrals would behave in the same way as the majority of dextrals, however, on each measure of asymmetry the adextral sample was split roughly 50:50 for each hand advantage. In spite of this result, the decrease in prevalence of the ‘typical’ response in each measure as left-sidedness increases, is reasonably encouraging support of the hypothesis that manual asymmetries relate to cerebral asymmetries. Eye and foot preference have no obvious relationship to speed measures of hand movements, and yet they appear to moderate these variables. Therefore it was concluded that measures of manual asymmetry are useful for laterality researchers.

Given the indirect nature of our manual asymmetry evidence, a more direct approach could collect data on manual asymmetries in a larger pool of individuals with *known cerebral asymmetries*. This investigation would provide better estimates of how often the right hand biased manual asymmetries such as duration ‘go with’ cerebral dominance for language. Some fMRI investigations have claimed a typically left hemisphere network activated when dextral participants mentally plan the use of every day tools (Johnson-Frey, Newman-Norlund, & Grafton, 2005; Valyear, Cavina-Pratesi, Stiglick, & Culham, 2007). Research into adextrals has demonstrated a leftward asymmetry, which was not significantly different to that of dextrals, when pantomiming tool use (Vingerhoets et al., 2012). Having manual asymmetries data on participants who have fMRI determined language and praxis localisation would be one logical next step for this research programme. However, using fMRI data to uncover relationships between right hemisphere dominant asymmetries and the left hand RT advantage is more problematic.

Despite the conclusion that the left hand RT advantage is reasonably typical in dextrals (78.4%), there still is not a well-supported hypothesis on what right hemisphere property drives this effect (Carey et al., 2015). It might be that the typically right-lateralised face and body related activity in most dextrals in Chapter 5 is related to this mysterious underlying factor, at least in terms of hemispheric dominance. Although many different paradigms have been used in the magnet related to visuospatial attention, these studies are all reported with averaged data (e.g. Coull & Nobre, 1998; Kim, Gitelman, Nobre, Parrish, LaBar, & Mesulam, 1999; Thiel, Zilles, & Fink, 2004; Shulman et al., 2010), therefore they are difficult to evaluate in terms of whatever is right-hemisphere biased in dextrals relating to left hand RT.

Brysbaert and colleagues (Cai, Van der Haegen & Brysbaert, 2013) used the landmark task as a measure of visuospatial function, reporting that it tends to produce right-lateralised activity in dextrals and left-lateralised activity in adextrals with right-lateralised fluency activation. This result suggests complementary hemispheric specialisation for fluency and the processes underlying the landmark task at least. The landmark task, however, does not push localisation and attentional demands in the same way as, say, visually-guided aiming. It is surprising that there is no behavioural test of visuospatial attention that is lateralised to the LVF that could be used in an fMRI context.

The second project in this thesis investigated potential electrophysiological markers of face and language processing asymmetries. Some research groups already employ N170 lateralisation as a marker of cerebral asymmetry (Dundas, Plaut, & Behrmann, 2014; Dundas, Gabay, Plaut, & Berhmann, 2014; Dundas, Plaut, & Berhmann, 2015), however its validity has not been rigorously tested. Strengths of the research presented in Chapter 3 were the employment of a proportional analysis, the recording of ERPs to face/word stimuli in the same individuals, and the inclusion of some individuals with known cerebral dominance of language and face processing.

The data collected to date suggest that these electrophysiological markers might not be particularly useful for predicting brain asymmetries in individuals. Results from the pilot study were not particularly encouraging, with only 2/6 dextrals having a right-biased N170 to faces, or a left-biased N170 to words (and these were not the same two individuals). It was anticipated that if asymmetry in N170 negativity was related to cerebral organisation, a majority of dextrals should show a right-biased N170 to faces and a left-biased N170 to words.

Improvements were made in the second experiment, including requiring deeper processing of both face and word stimuli. When considering the average waveforms and their amplitude over the two sides of the skull, the commonly-reported finding of a larger N170 over right scalp sites for faces was found, but only in the dextral group (with a significantly *leftward* N170 reported in the adextral group). The proportion of the dextral sample that showed this predicted directional difference was 77.3%, however, the other results in this project were less impressive. Only 50% of the dextral sample had a larger N170 to words over left scalp sites. Whilst the adextral sample was small (*n*=10), seven of these participants had larger N170s to faces over left scalp sites, and seven also had larger N170s to words over left scalp sites (four of these participants overlapped). It must be acknowledged, however, that the adextral sample size is smaller than desirable. The P1 data was also unconvincing. No significant differences were found in the averaged data. A majority (63.6%) of dextrals showed a larger right P1 to faces; however, the same proportion of the sample had a larger right P1 to words.

While a proportion of 77.3% of dextrals showing an asymmetry in the predicted direction would have been branded a success in any other chapter of this thesis, the comparison of ERP data with fMRI measures undermines this piece of evidence. In these 10 individuals, ERP asymmetries were only concordant with fMRI asymmetries in 50% of cases. In addition, the reader might keep in mind that this effect was one of four possible differences all predicted by what is known about cerebral asymmetries for word and face processing.

Considering the small but confident literature of left-biased N170s in response to words, our data are surprising. It could be that this research suffers from the file drawer caveat. If researchers are not interested in asymmetry, scalp amplitude effects unreported, regardless of the direction. Furthermore, if asymmetry is of interest and the data show a reversed pattern, perhaps these results might be received unfavourably by the small number of reviewers in this field, and are less likely to be published.

In the ERP literature, a surprising number of interesting effects that can be modulated by language stimuli occur over central electrode cites (e.g. the N400 and P3; Kutas & Federmeier, 2011). Of course, electrophysiologists mostly acknowledge that identifying underlying sources of ERP waveforms is fraught with difficulty for several reasons including non perfect skull shapes, changes in topography over time, etc (Luck & Kappenman, 2011).

The next chapter summarised test selection and results from a small battery of indirect perceptual tests, all of which have been related to cerebral asymmetries of the left and right cerebral hemispheres, in dextrals at least. Before testing strong one-tailed predictions were made for all the tests selected; specific directional differences in both groups, but of significantly reduced magnitude in the adextrals. By this strict criteria, three of our tests succeed, and are potentially worthy of further investigation.

The CV dichotic, lateralised Stroop task, and the octave illusion have all been related to left-hemispheric processes (Hugdahl & Anderson, 1984; Hugdahl & Franzon, 1985; Deutsch, 1983). In this investigation, significant biases in the predicted direction were present for all three tasks, and these were significantly reduced in the adextral group. Referring back to figure 4.6 (page 87), where prevalence of typical responses is plotted against strength of handedness, the slopes for CV dichotic LI and the lateralised Stroop task accuracy scores are the most convincing. These two measures show the most marked decrease in typical responses as left handedness increases. Having said that, in the Stroop task, the proportion of individuals who had poorer performance in the RVF was much lower than expected if this task really was tapping a left-hemisphere language dominance in 90-95% of dextrals and 70% of adextrals. Obviously none of these tasks was expected to perfectly predict language dominance, achieving as high proportions as suggested by the Wada test and other methods (Carey & Johnstone, 2014). Some undershooting of these ideal proportions was always expected given the likely poor sensitivity of some of these tests. For the lateralised Stroop task, more adextrals were slower/less accurate in the non-hypothesised LVF. The between groups difference is significant, but in this instance it is concluded that this finding is either spurious, unrelated to functional asymmetries, or both.

By the strict criteria outlined above, none of our right hemisphere related tasks successfully differentiated between dextrals and adextrals in the manner predicted. The VHF face task produced a weaker LVF asymmetry in adextrals as predicted, but as with the lateralised Stroop task, the obtained proportions are lower than desirable, assuming face asymmetry largely parallels the asymmetry for speech and language (in fact our imaging data suggests it should in 70% of individuals with left language lateralisation). Some of the limitations of the VHF face task have been discussed in more detail in Chapter 4. The failure of this task to produce robust LVF advantages is one of the outstanding mysteries of this dataset. A fuller analysis of the existing literature might be appropriate, although many of the studies which contrast dextrals and adextrals are actually small *n* chimeric face tasks, largely inspired by the success of Levy, Heller, Banich, and Burton (1983).

One would think that a face task that gives robust LVF advantages would be readily available given the laterality data available from prosopagnosia patients and fMRI research into face perception. Perhaps the inclusion of chimeric faces, allowing for more control over the stimulus than the natural face images used in this thesis would have been more successful.

Despite patient data supporting the working hypothesis that the leftward bias in greyscales results is due to a right-hemispheric attentional asymmetry akin to pseudoneglect (Mattingley et al., 2004), our results do not suggest that this asymmetry is related to brain asymmetry, at least in any way that dextrals and adextrals could be expected to differ in. Relatively robust leftward biases were obtained, but these are present in both handedness groups to the same magnitude, when it was anticipated that a weaker lateralisation (in terms of proportion or group averaged data) would be present in adextrals. Similarly the final right-hemispheric test, Efron dichotic listening, produced relatively robust LEAs, but these did not differentiate handedness groups. For our purposes if a task cannot differentiate between handedness groups it probably is not sensitive enough to differentiate brain asymmetries.

The absence of considerable data on non-verbal asymmetries in either handedness group is unfortunate. It is unknown how often these biases manifest in the right hemisphere of dextrals, let alone adextrals. As a working hypothesis, complementary hemispheric specialisation was assumed, but there is now a wealth of data (the present thesis included) to suggest that causal complementarity is not inevitable. In fact, many of the neuropsychologists who pioneered the use of some of these indirect tests (such as Phil Bryden, 1986) perhaps correctly hypothesised, given the data that they had at that time, that a statistical variant of hemispheric complementarity was the most likely possibility. Although many an inconclusive study has ended with “further research is needed”, in this instance it might be warranted.

This line of research requires studies where large numbers of adextrals are tested with perceptual asymmetry measures, and reliable estimates of the proportions of the sample showing a directional effect, as well as the measures of central tendency can be calculated. A chimeric face task could be included in these studies, although surprisingly, some large-scale investigations of this asymmetry, which interpret it as related to handedness, do not include adextral participants (Bourne, 2008). Although degree of handedness and familial sinistrality were recorded in Bourne (2008), in a dextral sample responses on these measures are highly skewed. A more thorough review of the attention literature (both behavioural and neuroimaging) might uncover potentially useful tasks that would produce robust LVF advantages in dextrals at least. Robust hemispheric differences in emotional processing have been suggested for many years (Jackson, 1878, 1879) and yet neuropsychologists have come to studies of emotion rather late. A large number of neuroimaging studies have also suggested asymmetries using stimuli that vary in emotional prosody for example. In fact, Bryden himself developed one of the earliest emotional asymmetry tests; the emotional words dichotic listening paradigm (Bryden & MacRae, 1989). A small number of similarly motivated experiments followed (e.g. Grimshaw, 1998), but now seem to have largely disappeared from view in the laterality literature.

In spite of the relative failure of our typically right-hemispheric tests, the imaging data to date is quite encouraging in terms of both our left hemispheric task (fluency), and the two right hemispheric asymmetries (face and body perception). Fluency is left lateralised in all but one of dextrals tested to date, and 29/33 adextrals. This strong bias is not just an artefact of our dichotomous split, as most people are strongly lateralised within one hemisphere or the other. In fact, it is lateralised to the same degree in typical and atypical participants. Additionally, correlations between run 1 and run 2 of each test were impressive, particularly for the fluency task.

Although the proportions are not as high as in the fluency data, the majority of dextrals and adextrals have laterality favouring the right hemisphere for faces and bodies. Of course, even with threshold-independent estimates of activation that favour the right hemisphere, better performance in the LVF is not inevitable. Differences between subtraction conditions can obviously affect the amount and location of the resulting activation, and the magnitude of any estimated LI. In fact, in the frontal lobe executive literature in particular, some neuroimagers are content to conclude that ‘less is better’ in terms of activation. In different studies more or less activation can be plausibly linked to superior performance in one group or condition versus another.

A similar criticism could be made about any lateralised language related task and its potential relationship to the LIs calculated for fluency. Hunter and Brysbaert (2008) developed a cued lateralised word reading paradigm which produced a RVF advantage in dextrals and a reduced RVF advantage in adextrals. This task was not used based on the recommendation of the authors of the necessity of using a large number of trials. However, they provided no statistics on the minimum number of trial necessary to provide a stable estimate of a visual field advantage in individual people. This might be an obvious addition to our battery of indirect perceptual tests.

Of course we did have one indirect perceptual measure related to asymmetrical perception of language: CV dichotic listening. This measure is not correlated with the fMRI derived LI for verbal fluency. These two measures may relate to quite distinct processes that differ in their laterality profile. Nevertheless, the ear advantage of the fluency atypicals is distinctly less than the typicals, the vast majority of our participants.

Another cerebral asymmetry, which is arguably the most difficult to connect to an obvious perceptual task, is that of the EBA and related regions. These are largely lateralised to the right hemisphere in the majority of our dextrals and adextrals. It is not obvious what a perceptual task would be that would be related to selective processing of part of the body, that was not heavily ‘verbalisable’, or related to distinct right hemispheric mechanisms that have to do with mental rotation and/or left/right discrimination. There probably are some potentially useful behavioural tasks relating to body parts such as hands (e.g. Parsons, 1987). This type of study, and many more recent ones, may be constrained by their applications to mirror-neuron systems, embodiment and so on, as opposed to body perception per se.

Although noted at a group average level in dextrals before (Downing, Jiang, Shuman, & Kanwisher, 2001), only one study has attempted to quantify the asymmetry of the EBA in adextrals. The same study also to its credit calculated an asymmetry index for a second cerebral asymmetry – faces. However, Willems, Peelen, & Hagoort (2010) only provided group averaged data, which was calculated using traditional threshold-dependent calculations. Although a subgroup of 16 participants is generally laudible in neuroimaging circles, this sample size is more appropriate for dextrals than adextrals, given the latter’s increased heterogeneity in terms of functional organisation.

The right sided activations related to bodies minus chairs is particularly noteworthy for at least two reasons. First, in terms of proportions it appears it is more lateralised than faces. Second, the proportion of each sample showing atypicality for this measure (i.e. more activation in the left hemisphere) produces the largest difference between dextrals and adextrals across the three fMRI measures (see figure 5.16, page

117). These data suggest that there is a relationship between magnitude of the asymmetry in bodies and faces which may be similar in both groups (see far right column in figure 5.19 page 120), however the relationship is statistically significant in adextrals but not in dextrals. This lack of an effect could be due to less variance present in the scores from the dextral sample.

For this line of research to advance, clearly identification of more atypically lateralised individuals is needed. This process will improve our ability to use more sophisticated statistical techniques such as multiple regression or discriminant function analysis to assess the potentially predictive indirect measures of cerebral asymmetry. Perhaps any kind of techniques useful for identifying atypical language dominance in adextrals could also be successful in the proportionally rare atypical *dextrals*. In absolute terms, if the ~5% estimate of speech and language-related atypicality in dextrals is reasonably accurate, then these individuals are more frequent in the general population than atypical adextrals. These individuals are unusual in the same way that *typically* lateralised adextrals are: they have control of their dominant hand in the 'wrong' hemisphere. Groups of these individuals, properly identified, could be important for handedness research. For example, any potential costs of having 'manual praxis' invested in a different hemisphere than 'oral praxis' could be tested for.

In our current neuroimaging dataset, the most valuable indirect measures appear to be strong left-handedness (as measured by a handedness questionnaire), left eye dominance, left kicking foot, and a strong LEA on CV dichotic. Three of our four atypicals have all of these qualities (with the fourth atypical not having a LEA on CV dichotic). No other individuals in our sample have these four characteristics, and only one typical is strongly left handed, left eyed and left footed (and this participant has an REA on CV dichotic). Including more participants in the neuroimaging project, particularly individuals who are left-sided for some or all of these factors, will enable better assessment of predictive power of any of them individually as well as all of them collectively.

Once identification methods of individuals with atypical language lateralisation are better established, a number of studies could be done in the future. Considerable progress has been made in the cognitive neuroscience of language since the 1990s. However, these studies tend to restrict themselves by only focussing on averaged data from dextral subjects. Therefore current hypotheses surrounding properties of language relating to specific anatomical brain regions have been developed using evidence from individuals with typical left hemisphere language lateralisation. Many studies have actively excluded adextrals, the group most likely to contain individuals with atypical language dominance. Any ideas about subregions of the language network and how they interact should in theory be similar in the right hemisphere of a sufficiently large sample of people with atypical language lateralisation. Hicock and Poeppel (2007) proposed a language model where the lateralisation of individual language components to one hemisphere or the other are hypothesised (see figure 6.1). Atypical lateralisation may result in a full reversal of this system, or perhaps some aspects of language remain typically lateralised for these individuals.

Similarly, differences in how different speech functions lateralise in typicals could be literally mirrored in those with atypical dominance. Imaging techniques are now being validated which allow for speech movements to be made in the fMRI scanner,

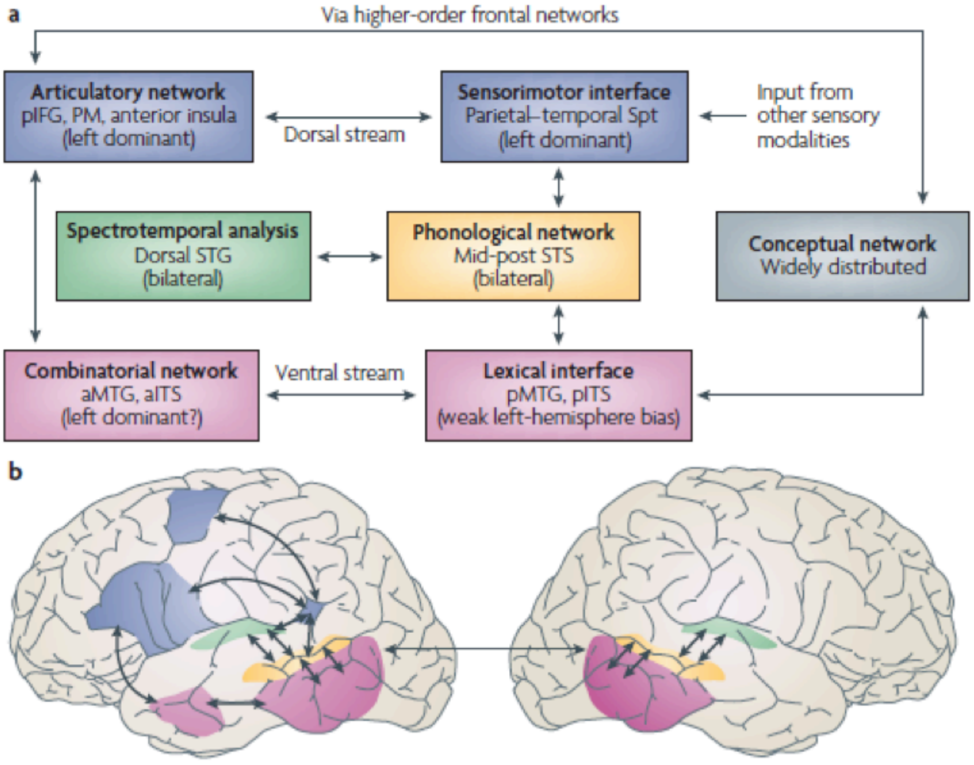


Figure 6.1 – Hickok & Poeppel's (2007) model of the functional anatomy of language. This is one of the few models which hypotheses about components of language which are relatively bilateral versus those which depend more on networks in the left hemisphere. These predictions are all open for exploration in samples of people with atypical cerebral dominance.

despite the problems movements produce in the magnetic field. Some of these use sparse-sampling approaches (Falkenberg, Specht, & Westerhausen, 2011), whereas others attempt to control for movement of the mouth (reviewed in Price, 2012; Simonyan & Fuertinger, 2015). These methods could be used to assess speech asymmetry in atypical individuals. If speech and language regions were *not* reversed in those with atypical dominance, results would suggest that language networks could be organised in at least two distinct patterns. Speech and some aspects of language perception may be relatively more or less lateralised, as suggested in models like that of Hickok and Poeppel (2007), shown in figure 6.1.

This sample is an interesting test case also for examining inter-hemispheric similarities and differences in linguistic and paralinguistic functioning, the latter of which depend more on the right hemisphere in people with typical dominance (Kemmerer, 2015). In some sense, individuals with atypical dominance, if they can be found, are a natural experiment to contrast with any asymmetric properties in 'typical' brains. If at least some of these circuits are relatively innate, then there should be considerable similarities between within hemisphere functions in typically and atypically lateralised individuals.

Reported differences in spatial ability, sex differences, overlap with developmental disorders, eye hand coordination…in fact, just about any kind of study which has historically contrasted handedness groups could be revisited in a new way where meaningful subgroups of adextrals, at least, could be identified, composed, and studied separately. For example, Hugdahl and Franzon (1985) preselected their subgroup of adextrals based on dichotic listening performance, admittedly an indirect measure of cerebral asymmetry for language. The same logic could be applied to imaging data, and has been – see Van der Haegen et al., (2011) and Vingerhoets et al. (2012). In some sense, typical and atypical left handers are the most interesting, if they can be easily identified, and then contrasted on dependent measures of interest.

At the same time that technological advances finally allow us to confront these questions with realistic expectations of some accurate answers, handedness and laterality research has fallen out of favour in neuropsychological research. The results in the preceding empirical chapters suggest that there is considerable potential in using neuroimaging and behaviour to help with understanding the complex relationships between different cerebral asymmetries, and how they interact with handedness. These studies, at least at this stage, may continue to be sample size intensive. However, these studies would not remain large-scale forever, as the data accumulated would allow for more accurate assessment of the ability of various indirect measures to predict cerebral asymmetries.

It is easy, when attempting to explain a body of work of this size, to lose sight of the big picture, and why you opened this line of investigation to begin with. Functions that are essential to the human experience, language, face processing, body perception, and so on, have neural substrates that are asymmetrically represented in the brain. Despite knowledge of this for over 200 years, scientists have failed to explain both how and why this is the case. In addition to this great unknown, humans have been aware of their population level hand-preference since even further back in history, and still again, we are yet to discover both how and why. I hope that after many more adextral subjects, and the subsequent development of reliable predictors of brain asymmetry, this project will reinvigorate the field of laterality research, providing better tools to tackle these questions once again.

References

Abbott, D. F., Waites, A. B., Lillywhite, L. M., & Jackson, G. D. (2010). fMRI assessment of language lateralization: An objective approach. *Neuroimage, 50*(4), 1446-1455.

Aggleton, J. P., Kentridge, R. W., & Neave, N. J. (1993). Evidence for longevity differences between left handed and right handed men: An archival study of cricketers. *Journal of Epidemiology and Community Health, 47*(3), 206-209.

Allison, T., Puce, A., & McCarthy, G. (2000). Social perception from visual cues: Role of the STS region. *Trends in Cognitive Sciences, 4*(7), 267-278.

Annett, M. (1964). A model of the inheritance of handedness and cerebral dominance. *Nature, 204*, 59-60.

Annett, M. (1967). The binomial distribution of right, mixed and left handedness. *The Quarterly Journal of Experimental Psychology, 19*(4), 327-333.

Annett, M. (1978). Genetic and nongenetic influences on handedness. *Behavior Genetics, 8*(3), 227-249.

Annett, M. (1985). *Left, right, hand and brain: The right shift theory.* Hove, East Sussex: Psychology Press.

Annett, M. (2002). *Handedness and brain asymmetry: The right shift theory*. Hove, East Sussex: Psychology Press.

Arning, L., Ocklenburg, S., Schulz, S., Ness, V., Gerding, W. M., Hengstler, J. G., . . . Beste, C. (2013). PCSK6 VNTR polymorphism is associated with degree of handedness but not direction of handedness. *PLoS One, 8*(6), e67251.

Asbjornsen, A. E., & Hugdahl, K. (1995). Attentional effects in dichotic listening. *Brain and Language, 49*(3), 189-201.

Ashton, G. C. (1982). Handedness: An alternative hypothesis. *Behavior Genetics, 12*(2), 125-147.

Badcock, N. A., Nye, A., & Bishop, D. V. (2012). Using functional transcranial doppler ultrasonography to assess language lateralisation: Influence of task and difficulty level. *Laterality: Asymmetries of Body, Brain and Cognition, 17*(6), 694-710.

Badzakova-Trajkov, G., Häberling, I. S., Roberts, R. P., & Corballis, M. C. (2010). Cerebral asymmetries: Complementary and independent processes. *PloS One, 5*(3), e9682.

Bagesteiro, L. B., & Sainburg, R. L. (2002). Handedness: Dominant arm advantages in control of limb dynamics. *Journal of Neurophysiology, 88*(5), 2408-2421.

Barthélémy, S., & Boulinguez, P. (2001). Manual reaction time asymmetries in human subjects: The role of movement planning and attention. *Neuroscience Letters, 315*(1), 41-44.

Barthélémy, S., & Boulinguez, P. (2002). Orienting visuospatial attention generates manual reaction time asymmetries in target detection and pointing. *Behavioural Brain Research, 133*(1), 109-116.

Beaton, A. A. (1997). The relation of planum temporale asymmetry and morphology of the corpus callosum to handedness, gender, and dyslexia: A review of the evidence. *Brain and Language, 60*(2), 255-322.

Behrmann, M., & Plaut, D. C. (2015). A vision of graded hemispheric specialization. *Annals of the New York Academy of Sciences,*

Benke, T., Köylü, B., Visani, P., Karner, E., Brenneis, C., Bartha, L., . . . Bauer, G. (2006). Language lateralization in temporal lobe epilepsy: A comparison between fMRI and the wada test. *Epilepsia, 47*(8), 1308-1319.

Benton, A. L., & Van Allen, M. W. (1968). Impairment in facial recognition in patients with cerebral disease. *Cortex, 4*(4), 344-IN1.

Bentin, S., Allison, T., Puce, A., Perez, E., & McCarthy, G. (1996). Electrophysiological studies of face perception in humans. *Journal of Cognitive Neuroscience, 8*(6), 551-565.

Bentin, S., Mouchetant-Rostaing, Y., Giard, M., Echallier, J., & Pernier, J. (1999). ERP manifestations of processing printed words at different psycholinguistic levels: Time course and scalp distribution. *Cognitive Neuroscience, Journal of, 11*(3), 235-260.

Bentin, S., Taylor, M. J., Rousselet, G. A., Itier, R. J., Caldara, R., Schyns, P. G., . . . Rossion, B. (2007). Controlling interstimulus perceptual variance does not abolish N170 face sensitivity. *Nature Neuroscience, 10*(7), 801-802.

Binder, J. R., Swanson, S. J., Hammeke, T. A., Morris, G. L., Mueller, W. M., Fischer, M., . . . Haughton, V. M. (1996). Determination of language dominance using functional MRI: A comparison with the wada test. *Neurology, 46*(4), 978-984.

Binder, J. R. (1997). Neuroanatomy of language processing studied with functional MRI. *Clinical Neuroscience (New York, N.Y.), 4*(2), 87-94.

Binder, J. R., Swanson, S. J., Hammeke, T. A., & Sabsevitz, D. S. (2008). A comparison of five fMRI protocols for mapping speech comprehension systems. *Epilepsia, 49*(12), 1980-1997.

Binder, J. R., Swanson, S. J., Sabsevitz, D. S., Hammeke, T. A., Raghavan, M., & Mueller, W. M. (2010). A comparison of two fMRI methods for predicting verbal memory decline after left temporal lobectomy: Language lateralization versus hippocampal activation asymmetry. *Epilepsia, 51*(4), 618-626.

Blau, A. (1946). *The master hand: A study of the origin and meaning of left and right sidedness and its relation to personality and language.* (5th ed.). New York, NY: American Orthopsychiatric Association.

Blau, V. C., Maurer, U., Tottenham, N., & McCandliss, B. D. (2007). The face-specific N170 component is modulated by emotional facial expression. *Behavioral and Brain Functions, 3*(7), 1-13.

Blonder, L. X., Bowers, D., & Heilman, K. M. (1991). The role of the right hemisphere in emotional communication. *Brain, 114 (Pt 3)*(Pt 3), 1115-1127.

Blumstein, S., Goodglass, H., & Tartter, V. (1975). The reliability of ear advantage in dichotic listening. *Brain and Language, 2*, 226-236.

Borod, J. C., Cicero, B. A., Obler, L. K., Welkowitz, J., Erhan, H. M., Santschi, C., . . . Whalen, J. R. (1998). Right hemisphere emotional perception: Evidence across multiple channels. *Neuropsychology, 12*(3), 446.

Bötzel, K., Schulze, S., & Stodieck, S. R. (1995). Scalp topography and analysis of intracranial sources of face-evoked potentials. *Experimental Brain Research, 104*(1), 135-143.

Boulinguez, P., Nougier, V., & Velay, J. (2001a). Manual asymmetries in reaching movement control. I: Study of right-handers. *Cortex, 37*(1), 101-122.

Boulinguez, P., Velay, J., & Nougier, V. (2001b). Manual asymmetries in reaching movement control. II: Study of left-handers. *Cortex, 37*(1), 123-138.

Bourne, V. J. (2008). Examining the relationship between degree of handedness and degree of cerebral lateralization for processing facial emotion. *Neuropsychology, 22*(3), 350.

Briggs, G. G., & Nebes, R. D. (1976). The effects of handedness, family history and sex on the performance of a dichotic listening task. *Neuropsychologia, 14*(1), 129-133.

Broadbent, D. E. (1956). Successive responses to simultaneous stimuli. *Quarterly Journal of Experimental Psychology, 8*(4), 145-152.

Broca, P. (1865). Sur le siège de la faculté du langage articulé. *Bulletins De La Société d'Anthropologie De Paris, 6*(1), 377-393.

Bryden, M. (1965). Tachistoscopic recognition, handedness, and cerebral dominance. *Neuropsychologia, 3*(1), 1-8.

Bryden, M. (1967). An evaluation of some models of laterality effects in dichotic listening. *Acta Oto-Laryngologica, 63*(2-3), 595-604.

Bryden, M. P. (1970). Laterality effects in dichotic listening: Relations with handedness and reading ability in children. *Neuropsychologia, 8*(4), 443-450.

Bryden, M. (1986). The nature of complementary specialization. *Two hemispheres—one Brain: Functions of the Corpus Callosum*, 463-469.

Bryden, M., Hecaen, H., & DeAgostini, M. (1983). Patterns of cerebral organization. *Brain and Language, 20*(2), 249-262.

Bryden, M. P. (1988). An overview of the dichotic listening procedure and its relation to cerebral organization. (pp. 1-43). Oxford, England: John Wiley & Sons.

Brysbaert, M. (1994). Lateral preferences and visual field asymmetries: Appearances may have been overstated. *Cortex, 30*(3), 413-429.

Buchanan, T. W., Lutz, K., Mirzazade, S., Specht, K., Shah, N. J., Zilles, K., & Jäncke, L. (2000). Recognition of emotional prosody and verbal components of spoken language: An fMRI study. *Cognitive Brain Research, 9*(3), 227-238.

Bukowski, H., Dricot, L., Hanseeuw, B., & Rossion, B. (2013). Cerebral lateralization of face-sensitive areas in left-handers: Only the FFA does not get it right. *Cortex, 49*(9), 2583-2589.

Burton, M. W., Small, S. L., & Blumstein, S. E. (2000). The role of segmentation in phonological processing: An fMRI investigation. *Journal of Cognitive Neuroscience, 12*(4), 679-690.

Caharel, S., d'Arripe, O., Ramon, M., Jacques, C., & Rossion, B. (2009). Early adaptation to repeated unfamiliar faces across viewpoint changes in the right hemisphere: Evidence from the N170 ERP component. *Neuropsychologia, 47*(3), 639-643.

Cai, Q., Van der Haegen, L., & Brysbaert, M. (2013). Complementary hemispheric specialization for language production and visuospatial attention. *Proceedings of the National Academy of Sciences of the United States of America, 110*(4), E322-30.

Campanella, S., Hanoteau, C., Depy, D., Rossion, B., Bruyer, R., Crommelinck, M., & Guerit, J. M. (2000). Right N170 modulation in a face discrimination task: An account for categorical perception of familiar faces. *Psychophysiology, 37*(6), 796-806.

Carey, D. P. (2001). Vision research: Losing sight of eye dominance. *Current Biology, 11*(20), R828-R830.

Carey, D. P., Hargreaves, E. L., & Goodale, M. A. (1996). Reaching to ipsilateral or contralateral targets: Within-hemisphere visuomotor processing cannot explain hemispatial differences in motor control. *Experimental Brain Research, 112*(3), 496-504.

Carey, D. P., & Johnstone, L. T. (2014). Quantifying cerebral asymmetries for language in dextrals and adextrals with random-effects meta analysis. *Frontiers in Psychology, 5,* 1128.

Carey, D. P., & Liddle, J. (2013). Hemifield or hemispace: What accounts for the ipsilateral advantages in visually guided aiming? *Experimental Brain Research, 230*(3), 323-331.

Carey, D. P., Otto-de Haart, E. G., Buckingham, G., Dijkerman, H. C., Hargreaves, E. L., & Goodale, M. A. (2015). Are there right hemisphere contributions to visually-guided movement? manipulating left hand reaction time advantages in dextrals. *Frontiers in Psychology, 6,* 1203.

Carey, D. P., Smith, D. T., Martin, D., Smith, G., Skriver, J., Rutland, A., & Shepherd, J. W. (2009). The bi-pedal ape: Plasticity and asymmetry in footedness. *Cortex, 45*(5), 650-661.

Carey, D. P., Smith, G., Smith, D. T., Shepherd, J. W., Skriver, J., Ord, L., & Rutland, A. (2001). Footedness in world soccer: An analysis of france'98. *Journal of Sports Sciences, 19*(11), 855-864.

Carmon, A., & Nachshon, I. (1973). Ear asymmetry in perception of emotional non-verbal stimuli. *Acta Psychologica, 37*(6), 351-357.

Carnahan, H. (1998). Manual asymmetries in response to rapid target movement. *Brain and Cognition, 37*(2), 237-253.

Carson, R. G. (1996). Neuromuscular-skeletal constraints upon the dynamics of perception-action coupling. *Experimental Brain Research, 110*(1), 99-110.

Carson, R. G., Chua, R., Elliott, D., & Goodman, D. (1990). The contribution of vision to asymmetries in manual aiming. *Neuropsychologia, 28*(11), 1215-1220.

Carson, R. G., Goodman, D., Chua, R., & Elliott, D. (1993). Asymmetries in the regulation of visually guided aiming. *Journal of Motor Behavior, 25*(1), 21-32.

Carson, R. G., Chua, R., Goodman, D., Byblow, W. D., & Elliott, D. (1995). The preparation of aiming movements. *Brain and Cognition, 28*(2), 133-154.

Cashmore, L., Uomini, N., & Chapelain, A. (2008). The evolution of handedness in humans and great apes: A review and current issues. *Journal of Anthropological Sciences, 86*, 7-35.

Chamberlain, H. D. (1928). The inheritance of left-handedness. *Journal of Heredity, 19*, 557-559.

Chesher, E. (1936). Some observations concerning the relation of handedness to the language mechanism. *Bulletin of the Neurological Institute of New York, 4*, 556-562.

Cole, D. A., Maxwell, S. E., Arvey, R., & Salas, E. (1994). How the power of MANOVA can both increase and decrease as a function of the intercorrelations among the dependent variables. *Psychological Bulletin, 115*(3), 465.

Coltheart, M. (1981). The MRC psycholinguistic database. *The Quarterly Journal of Experimental Psychology, 33*(4), 497-505.

Corballis, M. C. (1991). *The lopsided ape: Evolution of the generative mind.* Oxford University Press.

Coren, S., & Halpern, D. F. (1991). Left-handedness: A marker for decreased survival fitness. *Psychological Bulletin, 109*(1), 90.

Coull, J. T., & Nobre, A. C. (1998). Where and when to pay attention: The neural systems for directing attention to spatial locations and to time intervals as revealed by both PET and fMRI. *The Journal of Neuroscience, 18*(18), 7426-7435.

Cowell, P., & Hugdahl, K. (2000). Individual differences in neurobehavioral measures of laterality and interhemispheric function as measured by dichotic listening. *Developmental Neuropsychology, 18*(1), 95-112.

Critchley, M. (1954). Parietal syndromes in ambidextrous and left-handed subjects. *Zentralblatt Fur Neurochirurgie, 14*(1-2), 4-16.

Curry, F. K. (1967). A comparison of left-handed and right-handed subjects on verbal and non-verbal dichotic listening tasks. *Cortex, 3*(3), 343-352.

Dagenbach, D. (1986). Subject variable effects in correlations between auditory and visual language processing asymmetries. *Brain and Language, 28*(1), 169-177.

Damasio, A. R., Damasio, H., & Van Hoesen, G. W. (1982). Prosopagnosia: Anatomic basis and behavioral mechanisms. *Neurology, 32*(4), 331-341.

David, A. S. (1989). Perceptual asymmetry for happy-sad chimeric faces: Effects of mood. *Neuropsychologia, 27*(10), 1289-1300.

De Renzi, E. (1986). Current issues on prosopagnosia. *Aspects of face processing* (pp. 243-252) Springer.

De Renzi, E., Perani, D., Carlesimo, G. A., Silveri, M., & Fazio, F. (1994). Prosopagnosia can be associated with damage confined to the right hemisphere—an MRI and PET study and a review of the literature. *Neuropsychologia, 32*(8), 893-902.

Deppe, M., Knecht, S., Papke, K., Lohmann, H., Fleischer, H., Heindel, W., . . . Henningsen, H. (2000). Assessment of hemispheric language Lateralization: A comparison between fMRI and fTCD. *Journal of Cerebral Blood Flow & Metabolism, 20*(2), 263-268.

Desmond, J. E., Sum, J. M., Wagner, A. D., Demb, J. B., Shear, P. K., Glover, G. H., … Morrell, M. J. (1995). Functional MRI measurement of language lateralization in wada-tested patients. *Brain, 118*(6), 1411-1419.

Deutsch, D. (1974). An auditory illusion. *Nature, 251*, 307-309.

Deutsch, D. (1980). Music perception. *Musical Quarterly*, 165-179.

Deutsch, D. (1978). Pitch memory: An advantage for the left-handed. *Science (New York, N.Y.), 199*(4328), 559-560.

Deutsch, D. (1983). The octave illusion in relation to handedness and familial handedness background. *Neuropsychologia, 21*(3), 289-293.

Donchin, E., Ritter, W., & McCallum, W. C. (1978). Cognitive psychophysiology: The endogenous components of the ERP. *Event-Related Brain Potentials in Man*, 349-411.

Downing, P. E., Chan, A. W., Peelen, M. V., Dodds, C. M., & Kanwisher, N. (2006). Domain specificity in visual cortex. *Cerebral Cortex, 16*(10), 1453-1461.

Downing, P. E., Jiang, Y., Shuman, M., & Kanwisher, N. (2001). A cortical area selective for visual processing of the human body. *Science (New York, N.Y.), 293*(5539), 2470-2473. doi:10.1126/science.1063414 [doi]

Downing, P. E., Wiggett, A. J., & Peelen, M. V. (2007). Functional magnetic resonance imaging investigation of overlapping lateral occipitotemporal activations using multi-voxel pattern analysis. *The Journal of Neuroscience, 27*(1), 226-233.

Dundas, E. M., Plaut, D. C., & Behrmann, M. (2015). Variable left-hemisphere language and orthographic lateralization reduces right-hemisphere face lateralization. *Journal of Cognitive Neuroscience, 27*(5), 913-925.

Dundas, E., Gabay, Y., Plaut, D., & Behrmann, M. (2014). Altered hemispheric specialization for faces and word in developmental dyslexia. *Journal of Vision, 14*(10), 1438-1438.

Dundas, E. M., Plaut, D. C., & Behrmann, M. (2014). An ERP investigation of the co-development of hemispheric lateralization of face and word recognition. *Neuropsychologia, 61*, 315-323.

Efron, R., Koss, B., & Yund, E. W. (1983). Central auditory processing: IV. ear dominance—Spatial and temporal complexity. *Brain and Language, 19*(2), 264-282.

Efron, R., & Yund, E. W. (1974). Dichotic competition of simultaneous tone bursts of different frequency—I. dissociation of pitch from lateralization and loudness. *Neuropsychologia, 12*(2), 249-256.

Efron, R., & Yund, E. W. (1975). Dichotic competition of simultaneous tone bursts of different frequency—III. the effect of stimulus parameters on suppression and ear dominance functions. *Neuropsychologia, 13*(2), 151-161.

Efron, R., & Yund, E. W. (1976). Ear dominance and intensity independence in the perception of dichotic chords. *The Journal of the Acoustical Society of America, 59*(4), 889-898.

Elias, L. J., Bryden, M. P., & Bulman-Fleming, M. B. (1998). Footedness is a better predictor than is handedness of emotional lateralization. *Neuropsychologia, 36*(1), 37-43.

Eling, P. (1984). Broca on the relation between handedness and cerebral speech dominance. *Brain and Language, 22*(1), 158-159.

Elliott, D., Chua, R., & Pollock, B. J. (1994). The influence of intermittent vision on manual aiming. *Acta Psychologica, 85*(1), 1-13.

Elliott, D., & Roy, E. A. (1996). *Manual asymmetries in motor performance* CRC Press.

Elliott, D., Roy, E. A., Goodman, D., Carson, R. G., Chua, R., & Maraj, B. K. (1993). Asymmetries in the preparation and control of manual aiming movements. *Canadian Journal of Experimental psychology/Revue Canadienne De Psychologie Expérimentale, 47*(3), 570.

Ellis, P., Marshall, E., Windridge, C., Jones, S., & Ellis, S. J. (1998). Left-handedness and premature death. *The Lancet, 351*(9116), 1634.

Falkenberg, L. E., Specht, K., & Westerhausen, R. (2011). Attention and cognitive control networks assessed in a dichotic listening fMRI study. *Brain and Cognition, 76*(2), 276-285.

Fisk, J., & Goodale, M. (1985). The organization of eye and limb movements during unrestricted reaching to targets in contralateral and ipsilateral visual space. *Experimental Brain Research, 60*(1), 159-178.

Flöel, A., Buyx, A., Breitenstein, C., Lohmann, H., & Knecht, S. (2005). Hemispheric lateralization of spatial attention in right-and left-hemispheric language dominance. *Behavioural Brain Research, 158*(2), 269-275.

Foundas, A. L., Corey, D. M., Hurley, M. M., & Heilman, K. M. (2006). Verbal dichotic listening in right and left-handed adults: Laterality effects of directed attention. *Cortex, 42*(1), 79-86.

Foundas, A. L., Leonard, C. M., Gilmore, R., Fennell, E., & Heilman, K. M. (1994). Planum temporale asymmetry and language dominance. *Neuropsychologia, 32*(10), 1225-1231.

Foundas, A. L., Leonard, C. M., & Heilman, K. M. (1995). Morphologic cerebral asymmetries and handedness: The pars triangularis and planum temporale. *Archives of Neurology, 52*(5), 501-508.

Franzon, M., & Hugdahl, K. (1987). Effects of speed vs. accuracy in vocal reaction time to visual half-field presentations of incongruent (stroop) color-words. *Cortex, 23*(4), 615-629.

Galaburda, A. M., Corsiglia, J., Rosen, G. D., & Sherman, G. F. (1987). Planum temporale asymmetry, reappraisal since Geschwind and Levitsky. *Neuropsychologia, 25*(6), 853-868.

Gandour, J., Dzemidzic, M., Wong, D., Lowe, M., Tong, Y., Hsieh, L., . . . Lurito, J. (2003). Temporal integration of speech prosody is shaped by language experience: An fMRI study. *Brain and Language, 84*(3), 318-336.

Geffen, G., Bradshaw, J., & Wallace, G. (1971). Interhemispheric effects on reaction time to verbal and nonverbal visual stimuli. *Journal of Experimental Psychology, 87*(3), 415.

Geschwind, N., & Galaburda, A. M. (1985). Cerebral lateralization: Biological mechanisms, associations, and pathology: I. A hypothesis and a program for research. *Archives of Neurology, 42*(5), 428-459.

Geschwind, N., & Levitsky, W. (1968). Human brain: Left-right asymmetries in temporal speech region. *Science (New York, N.Y.), 161*(3837), 186-187.

Geuze, R. H., Zickert, N., Beking, T., & Groothius, T.*Is performance better when brain functions are typically lateralized?*. Durham, UK: Paper presented at the North Sea Meeting on Brain Asymmetries.

Gilbert, A. N., & Wysocki, C. J. (1992). Hand preference and age in the united states. *Neuropsychologia, 30*(7), 601-608.

Gloning, I., Gloning, K., Haub, G., & Quatember, R. (1969). Comparison of verbal behavior in right-handed and non right-handed patients with anatomically verified lesion of one hemisphere. *Cortex, 5*, 43-52.

Goffaux, V., Gauthier, I., & Rossion, B. (2003). Spatial scale contribution to early visual differences between face and object processing. *Cognitive Brain Research, 16*(3), 416-424.

Goldenberg, G. (2013). Apraxia in left-handers. *Brain : A Journal of Neurology, 136*(Pt 8), 2592-2601.

Goodale, M. A. (1988). Hemispheric differences in motor control. *Behavioural Brain Research, 30*(2), 203-214.

Goodale, M. A. (1990). Brain asymmetries in the control of reaching. *Vision and Action: The Control of Grasping*, 14-32.

Goodglass, H., & Quadfasel, F. A. (1954). Language laterality in left-handed aphasics. *Brain : A Journal of Neurology, 77*(4), 521-548.

Groen, M. A., Whitehouse, A. J., Badcock, N. A., & Bishop, D. V. (2012). Does cerebral lateralization develop? A study using functional transcranial doppler ultrasound assessing lateralization for language production and visuospatial memory. *Brain and Behavior, 2*(3), 256-269.

Haaland, K. Y., & Harrington, D. (1989). The role of the hemispheres in closed loop movements. *Brain and Cognition, 9*(2), 158-180.

Häberling, I. S., Badzakova-Trajkov, G., & Corballis, M. C. (2011). Callosal tracts and patterns of hemispheric dominance: A combined fMRI and DTI study. *Neuroimage, 54*(2), 779-786.

Häberling, I. S., Badzakova-Trajkov, G., & Corballis, M. C. (2013). Asymmetries of the arcuate fasciculus in monozygotic twins: Genetic and nongenetic influences. *PloS One, 8*(1), e52315.

Harrell, H. (1991). Left-handedness and life expectancy. *N Engl J Med, 325*, 1041.

Harris, L. J. (1993). Do left-handers die sooner than right-handers? commentary on coren and halpern's (1991)" left-handedness: A marker for decreased survival fitness.".

Harris, L. J. (1991). Cerebral control for speech in right-handers and left-handers: An analysis of the views of paul broca, his contemporaries, and his successors. *Brain and Language, 40*(1), 1-50.

Hécaen, H., & Piercy, M. (1956). Paroxysmal dysphasia and the problem of cerebral dominance. *Journal of Neurology, Neurosurgery, and Psychiatry, 19*(3), 194-201.

Hécaen, H., & Angelergues, R. (1962). Agnosia for faces (prosopagnosia). *Archives of Neurology, 7*(2), 92-100.

Hellige, J. B. (1990). Hemispheric asymmetry. *Annual Review of Psychology, 41*(1), 55-80.

Hilliard, R. D. (1973). Hemispheric laterality effects on a facial recognition task in normal subjects. *Cortex, 9*(3), 246-258.

Hines, D., & Satz, P. (1974). Cross-modal asymmetries in perception related to asymmetry in cerebral function. *Neuropsychologia, 12*(2), 239-247.

Hiscock, M., & Kinsbourne, M. (1995). Progress in the measurement of laterality and implications for dyslexia research. *Annals of Dyslexia, 45*(1), 247-268.

Hochberg, J. H., & Le May, M. (1974). Arteriographic correlates of handedness. *Neurology, 25*, 218-222.

Hopkins, W. D. (2006). Comparative and familial analysis of handedness in great apes. *Psychological Bulletin, 132*(4), 538.

Hopkins, W. D. (2007). *The evolution of hemispheric specialization in primates* Elsevier.

Hopkins, W. D., & Cantalupo, C. (2004). Handedness in chimpanzees (pan troglodytes) is associated with asymmetries of the primary motor cortex but not with homologous language areas. *Behavioral Neuroscience, 118*(6), 1176.

Hopkins, W. D., Russell, J. L., & Cantalupo, C. (2007). Neuroanatomical correlates of handedness for tool use in chimpanzees (pan troglodytes): Implication for theories on the evolution of language. *Psychological Science, 18*(11), 971-977.

Horton, J. C., & Hoyt, W. F. (1991). The representation of the visual field in human striate cortex: A revision of the classic holmes map. *Archives of Ophthalmology, 109*(6), 816-824.

Hugdahl, K., & Anderson, L. (1984). A dichotic listening study of differences in cerebral organization in dextral and sinistral subjects. *Cortex, 20*(1), 135-141.

Hugdahl, K., & Franzon, M. (1985). Visual half-field presentations of incongruent color-words reveal mirror-reversal of language lateralization in dextral and sinistral subjects. *Cortex, 21*(3), 359-374.

Hugdahl, K., & Andersson, L. (1986). The “forced-attention paradigm” in dichotic listening to CV-syllables: A comparison between adults and children. *Cortex, 22*(3), 417-432.

Hugdahl, K. E. (1988). *Handbook of dichotic listening: Theory, methods and research.* John Wiley & Sons.

Hugdahl, K., Satz, P., Mitrushina, M., & Miller, E. N. (1993). Left-handedness and old age: Do left-handers die earlier? *Neuropsychologia, 31*(4), 325-333.

Hugdahl, K. (1995). Dichotic listening: Probing temporal lobe functional integrity. In R. J. Davidson, & K. Hugdahl (Eds.), *Brain asymmetry* (1st ed., pp. 123-156). Cambridge, Massachusetts: The MIT Press.

Hugdahl, K., & Hammar, Å. (1997). Test-retest reliability for the consonant-vowel syllables dichotic listening paradigm. *Journal of Clinical and Experimental Neuropsychology, 19*(5), 667-675.

Hugdahl, K., Bodner, T., Weiss, E., & Benke, T. (2003). Dichotic listening performance and frontal lobe function. *Cognitive Brain Research, 16*(1), 58-65.

Hugdahl, K. (2003). Dichotic listening: An experimental tool in clinical neuropsychology. *Experimental methods in neuropsychology,* (pp. 29-46) Springer.

Hugdahl, K., & Westerhausen, R. (2010). *The two halves of the brain: Information processing in the cerebral hemispheres*. Cambridge, Massachusetts: MIT Press.

Hugdahl, K., Westerhausen, R., Alho, K., Medvedev, S., Laine, M., & Hämälaäinen, H. (2009). Attention and cognitive control: Unfolding the dichotic listening story. *Scandinavian Journal of Psychology, 50*(1), 11-22.

Humphreys, G. W., & Riddoch, M. J. (1987). *To see but not to see: A case study of visual agnosia* Psychology Press.

Hunter, Z. R., & Brysbaert, M. (2008). Visual half-field experiments are a good measure of cerebral language dominance if used properly: Evidence from fMRI. *Neuropsychologia, 46*(1), 316-325.

Hyde, K. L., Peretz, I., & Zatorre, R. J. (2008). Evidence for the role of the right auditory cortex in fine pitch resolution. *Neuropsychologia, 46*(2), 632-639.

Itier, R. J., & Taylor, M. J. (2004). Source analysis of the N170 to faces and objects. *Neuroreport, 15*(8), 1261-1265.

Jäger, A. O., & Althoff, K. (1994). *Der WILDE-intelligenz-test:(WIT); ein strukturdiagnostikum* Hogrefe, Verlag für Psychologie.

Janecek, J. K., Swanson, S. J., Sabsevitz, D. S., Hammeke, T. A., Raghavan, M., E Rozman, M., & Binder, J. R. (2013). Language lateralization by fMRI and wada testing in 229 patients with epilepsy: Rates and predictors of discordance. *Epilepsia, 54*(2), 314-322.

Johnson-Frey, S. H., Newman-Norlund, R., & Grafton, S. T. (2005). A distributed left hemisphere network active during planning of everyday tool use skills. *Cerebral Cortex (New York, N.Y.: 1991), 15*(6), 681-695.

Johnsrude, I. S., Penhune, V. B., & Zatorre, R. J. (2000). Functional specificity in the right human auditory cortex for perceiving pitch direction. *Brain : A Journal of Neurology, 123*(1), 155-163.

Jordan, H. E. (1914). Hereditary left-handedness with a note on twinning. *Journal of Genetics, 4*, 67-81.

Joseph, R. (1988). The right cerebral hemisphere: Emotion, music, visual-spatial skills, body-image, dreams, and awareness. *Journal of Clinical Psychology, 44*(5), 630-673.

Joyce, C., & Rossion, B. (2005). The face-sensitive N170 and VPP components manifest the same brain processes: The effect of reference electrode site. *Clinical Neurophysiology, 116*(11), 2613-2631.

Kanwisher, N., McDermott, J., & Chun, M. M. (1997). The fusiform face area: A module in human extrastriate cortex specialized for face perception. *The Journal of Neuroscience, 17*(11), 4302-4311.

Karuza, E. A., Newport, E. L., Aslin, R. N., Starling, S. J., Tivarus, M. E., & Bavelier, D. (2013). The neural correlates of statistical learning in a word segmentation task: An fMRI study. *Brain and Language, 127*(1), 46-54.

Kemmerer, D. (2015). Prosody. *Cognitive neuroscience of language* (pp. 189-213). New York, NY: Psychology Press.

Kim, Y., Gitelman, D. R., Nobre, A. C., Parrish, T. B., LaBar, K. S., & Mesulam, M. (1999). The large-scale neural network for spatial attention displays multifunctional overlap but differential asymmetry. *Neuroimage, 9*(3), 269-277.

Kim, H. (1994). Distributions of hemispheric asymmetry in left-handers and right-handers: Data from perceptal asymmetry studies. *Neuropsychology, 8*(2), 148-159. doi:10.1037/0894-4105.8.2.148

Kimura, D. (1961). Cerebral dominance and the perception of verbal stimuli. *Canadian Journal of Psychology/Revue Canadienne De Psychologie, 15*(3), 166.

Kimura, D. (1967). Functional asymmetry of the brain in dichotic listening. *Cortex, 3*(2), 163-178.

Kimura, D. (1973). Manual activity during speaking – I. Right-handers. *Neuropsychologia, 11*(1), 45-50.

Kimura, D., & Archibald, Y. (1974). Motor functions of the left hemisphere. *Brain : A Journal of Neurology, 97*(2), 337-350.

Kimura, D. (1993). *Neuromotor mechanisms in human communication*. New York: Oxford University Press.

King, F. L., & Kimura, D. (1972). Left-ear superiority in dichotic perception of vocal nonverbal sounds. *Canadian Journal of Psychology/Revue Canadienne De Psychologie, 26*(2), 111.

Klein, D., Moscovitch, M., & Vigna, C. (1976). Attentional mechanisms and perceptual asymmetries in tachistoscopic recognition of words and faces. *Neuropsychologia, 14*(1), 55-66.

Knecht, S., Jansen, A., Frank, A., Van Randenborgh, J., Sommer, J., Kanowski, M., & Heinze, H. (2003). How atypical is atypical language dominance? *Neuroimage, 18*(4), 917-927.

Knecht, S., Deppe, M., Ebner, A., Henningsen, H., Huber, T., Jokeit, H., & Ringelstein, E. B. (1998). Noninvasive determination of language lateralization by functional transcranial doppler sonography: A comparison with the wada test. *Stroke; a Journal of Cerebral Circulation, 29*(1), 82-86.

Knecht, S., Drager, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., . . . Henningsen, H. (2000). Handedness and hemispheric language dominance in healthy humans. *Brain : A Journal of Neurology, 123 Pt 12*, 2512-2518.

Knecht, S., Drager, B., Floel, A., Lohmann, H., Breitenstein, C., Deppe, M., . . . Ringelstein, E. B. (2001). Behavioural relevance of atypical language lateralization in healthy subjects. *Brain : A Journal of Neurology, 124*(Pt 8), 1657-1665.

Kompus, K., Specht, K., Ersland, L., Juvodden, H. T., van Wageningen, H., Hugdahl, K., & Westerhausen, R. (2012). A forced-attention dichotic listening fMRI study on 113 subjects. *Brain and Language, 121*(3), 240-247.

Kosslyn, S. M. (1987). Seeing and imagining in the cerebral hemispheres: A computational approach. *Psychological Review, 94*(2), 148.

Kutas, M., & Federmeier, K. D. (2011). Thirty years and counting: Finding meaning in the N400 component of the event-related brain potential (ERP). *Annual Review of Psychology, 62*, 621-647. doi:10.1146/annurev.psych.093008.131123 [doi]

Le May, M., & Kido, D. K. (1978). Asymmetries of the cerebral hemispheres on computed tomograms. *Journal of Computer Assisted Tomography, 2*(4), 471-476.

Leehey, S. C., & Cahn, A. (1979). Lateral asymmetries in the recognition of words, familiar faces and unfamiliar faces. *Neuropsychologia, 17*(6), 619-628.

Levy, J., & Nagylaki, T. (1972). A model for the genetics of handedness. *Genetics, 72*(1), 117-128.

Levy, J., Trevarthen, C., & Sperry, R. W. (1972). Reception of bilateral chimeric figures following hemispheric deconnexion. *Brain : A Journal of Neurology, 95*(1), 61-78.

Levy, J. (1976). A review of evidence for a genetic component in the determination of handedness. *Behavior Genetics, 6*(4), 429-453.

Levy, J., & Reid, M. (1978). Variations in cerebral organization as a function of handedness, hand posture in writing, and sex. *Journal of Experimental Psychology: General, 107*(2), 119.

Levy, J., & Trevarthen, C. (1981). Color-matching, color-naming and color-memory in split-brain patients. *Neuropsychologia, 19*(4), 523-541.

Levy, J., Heller, W., Banich, M. T., & Burton, L. A. (1983). Asymmetry of perception in free viewing of chimeric faces. *Brain and Cognition, 2*(4), 404-419.

Lin, S., Chen, H., Zhao, J., Li, S., He, S., & Weng, X. (2011). Left-lateralized N170 response to unpronounceable pseudo but not false chinese characters—the key role of orthography. *Neuroscience, 190*, 200-206.

Linkenkaer-Hansen, K., Palva, J. M., Sams, M., Hietanen, J. K., Aronen, H. J., & Ilmoniemi, R. J. (1998). Face-selective processing in human extrastriate cortex around 120 ms after stimulus onset revealed by magneto- and electroencephalography. *Neuroscience Letters,253*(3), 147-150.

Lonsdorf, E. V., & Hopkins, W. D. (2005). Wild chimpanzees show population-level handedness for tool use. *Proceedings of the National Academy of Sciences of the United States of America, 102*(35), 12634-12638.

Luck, S. J., & Kappenman, E. S. (2011). *The oxford handbook of event-related potential components* Oxford university press.

Luh, K. E., Rueckert, L. M., & Levy, J. (1991). Perceptual asymmetries for free viewing of several types of chimeric stimuli. *Brain and Cognition, 16*(1), 83-103.

Lundqvist, D., Flykt, A., & Öhman, A. (1998). The karolinska directed emotional faces (KDEF). *CD ROM from Department of Clinical Neuroscience, Psychology Section, Karolinska Institutet,* , 91-630.

Main, J. C., & Carey, D. P. (2014). One hand or the other? effector selection biases in right and left handers. *Neuropsychologia, 64*, 300-309.

Maly, J., Turnheim, M., Heiss, W. -., & Gloning, K. (1977). Brain perfusion and neuropsychological test scores: A correlation study in aphasics. *Brain and Language, 4*(1), 78-94.

Marcel, T., & Rajan, P. (1975). Lateral specialization for recognition of words and faces in good and poor readers. *Neuropsychologia, 13*(4), 489-497.

Marchant, L., & McGrew, W. (1991). Laterality of function in apes: A meta-analysis of methods. *Journal of Human Evolution, 21*(6), 425-438.

Marchant, L. F., & McGrew, W. C. (2013). Handedness is more than laterality: Lessons from chimpanzees. *Annals of the New York Academy of Sciences, 1288*(1), 1-8.

Mattingley, J. B., Bradshaw, J. L., Nettleton, N. C., & Bradshaw, J. A. (1994). Can task specific perceptual bias be distinguished from unilateral neglect? *Neuropsychologia, 32*(7), 805-817.

Mattingley, J. B., Berberovic, N., Corben, L., Slavin, M. J., Nicholls, M. E., & Bradshaw, J. L. (2004). The greyscales task: A perceptual measure of attentional bias following unilateral hemispheric damage. *Neuropsychologia, 42*(3), 387-394.

Mattson, A. J., Levin, H. S., & Grafman, J. (2000). A case of prosopagnosia following moderate closed head injury with left hemisphere focal lesion. *Cortex, 36*(1), 125-137.

Maurer, U., Brandeis, D., & McCandliss, B. D. (2005). Fast, visual specialization for reading in english revealed by the topography of the N170 ERP response. *Behavioral and Brain Functions, 1*(1), 13.

Maurer, U., Rossion, B., & McCandliss, B. D. (2008). Category specificity in early perception: Face and word N170 responses differ in both lateralization and habituation properties. *Frontiers in Human Neuroscience, 2*, 18. doi:10.3389/neuro.09.018.2008

Maurer, U., Zevin, J. D., & McCandliss, B. D. (2008). Left-lateralized N170 effects of visual expertise in reading: Evidence from japanese syllabic and logographic scripts. *Journal of Cognitive Neuroscience, 20*(10), 1878-1891.

Mazzoni, D., & Dannenberg, R. B. (2002). A fast data structure for disk-based audio editing. *Computer Music Journal, 26*(2), 62-76.

McGettigan, C., Eisner, F., Agnew, Z. K., Manly, T., Wisbey, D., & Scott, S. K. (2013). T'ain't what you say, it's the way that you say it—left insula and inferior frontal cortex work in interaction with superior temporal regions to control the performance of vocal impersonations. *Journal of Cognitive Neuroscience, 25*(11), 1875-1886.

McManus, I. (1983). The interpretation of laterality. *Cortex, 19*(2), 187-214.

McManus, I. (1991). The inheritance of left-handedness. *Biological Asymmetry and Handedness, 162*, 251-281.

McManus, I. (1999). Eye-dominance, writing hand, and throwing hand. *Laterality: Asymmetries of Body, Brain and Cognition, 4*(2), 173-192.

McManus, C. (2004). *Right hand, left hand: The origins of asymmetry in brains, bodies, atoms and cultures.* Harvard University Press.

McManus, I., & Bryden, M. (1992). The genetics of handedness, cerebral dominance, and lateralization. In I. Rapin, & S. J. Segalowitz (Eds.), *Handbook of neuropsychology* (pp. 115-144). Amsterdam: Elsevier Science.

McManus, I., & Bryden, M. (1993). The neurobiology of handedness, language, and cerebral dominance: A model for the molecular genetics of behavior.

Meadows, J. C. (1974). The anatomical basis of prosopagnosia. *Journal of Neurology, Neurosurgery, and Psychiatry, 37*(5), 489-501.

Meguerditchian, A., & Vauclair, J. (2006). Baboons communicate with their right hand. *Behavioural Brain Research, 171*(1), 170-174.

Mercure, E., Cohen Kadosh, K., & Johnson, M. (2011). The N170 shows differential repetition effects for faces, objects, and orthographic stimuli. *Frontiers in Human Neuroscience, 5*, 6.

Mercure, E., Dick, F., Halit, H., Kaufman, J., & Johnson, M. H. (2008). Differential lateralization for words and faces: Category or psychophysics? *Journal of Cognitive Neuroscience, 20*(11), 2070-2087.

Moscovitch, M., & Smith, L. C. (1979). Differences in neural organization between individuals with inverted and noninverted handwriting postures. *Science (New York, N.Y.), 205*(4407), 710-713.

Ng, V. W., Eslinger, P. J., Williams, S. C., Brammer, M. J., Bullmore, E. T., Andrew, C. M., . . . Benton, A. L. (2000). Hemispheric preference in visuospatial processing: A complementary approach with fMRI and lesion studies. *Human Brain Mapping, 10*(2), 80-86.

Nguyen, V. T., & Cunnington, R. (2014). The superior temporal sulcus and the N170 during face processing: Single trial analysis of concurrent EEG–fMRI. *Neuroimage, 86*, 492-502.

Ocklenburg, S., Arning, L., Hahn, C., Gerding, W. M., Epplen, J. T., Güntürkün, O., & Beste, C. (2011). Variation in the NMDA receptor 2B subunit gene GRIN2B is associated with differential language lateralization. *Behavioural Brain Research, 225*(1), 284-289.

Parsons, L. M. (1987). Imagined spatial transformations of one's hands and feet. *Cognitive Psychology, 19*(2), 178-241.

Perelle, I. B., & Ehrman, L. (1994). An international study of human handedness: The data. *Behavior Genetics, 24*(3), 217-227.

Persson, P., & Allebeck, P. (1994). Do left-handers have increased mortality?. *Epidemiology, 5*(3), 337-340.

Peters, M., Reimers, S., & Manning, J. T. (2006). Hand preference for writing and associations with selected demographic and behavioral variables in 255,100 subjects: The BBC internet study. *Brain and Cognition, 62*(2), 177-189.

Plaut, D. C., & Behrmann, M. (2011). Complementary neural representations for faces and words: A computational exploration. *Cognitive Neuropsychology, 28*(3-4), 251-275.

Poizner, H. (1990). Language and motor disorders in deaf signers. *Advances in Psychology, 70*, 303-326.

Porac, C., & Coren, S. (1981). *Lateral preferences and human behaviour.* Springer Science & Business Media.

Powell, J. L., Kemp, G. J., & García-Finaña, M. (2012). Association between language and spatial laterality and cognitive ability: An fMRI study. *Neuroimage, 59*(2), 1818-1829.

Price, C., Wise, R., Ramsay, S., Friston, K., Howard, D., Patterson, K., & Frackowiak, R. (1992). Regional response differences within the human auditory cortex when listening to words. *Neuroscience Letters, 146*(2), 179-182.

Price, C. J. (2000). The anatomy of language: Contributions from functional neuroimaging. *Journal of Anatomy, 197*(03), 335-359.

Price, C. J. (2010). The anatomy of language: A review of 100 fMRI studies published in 2009. *Annals of the New York Academy of Sciences, 1191*(1), 62-88.

Price, C. J. (2012). A review and synthesis of the first 20years of PET and fMRI studies of heard speech, spoken language and reading. *Neuroimage, 62*(2), 816-847.

Ramaley, F. (1913). Inheritance of left-handedness. *American Naturalist*, 730-738.

Rasmussen, T., & Milner, B. (1977). The role of early left-brain injury in determining lateralization of cerebral speech functions. *Annals of the New York Academy of Sciences, 299*(1), 355-369.

Riecker, A., Ackermann, H., Wildgruber, D., Dogil, G., & Grodd, W. (2000). Opposite hemispheric lateralization effects during speaking and singing at motor cortex, insula and cerebellum. *Neuroreport, 11*(9), 1997-2000.

Riecker, A., Wildgruber, D., Dogil, G., Grodd, W., & Ackermann, H. (2002). Hemispheric lateralization effects of rhythm implementation during syllable repetitions: An fMRI study. *Neuroimage, 16*(1), 169-176.

Rife, D. C. (1940). Handedness, with special reference to twins. *Genetics, 25*(2), 178-186.

Rossion, B., Delvenne, J. -., Debatisse, D., Goffaux, V., Bruyer, R., Crommelinck, M., & Guérit, J. -. (1999). Spatio-temporal localization of the face inversion effect: An event-related potentials study. *Biological Psychology, 50*(3), 173-189.

Rossion, B., Gauthier, I., Tarr, M. J., Despland, P., Bruyer, R., Linotte, S., & Crommelinck, M. (2000). The N170 occipito-temporal component is delayed and enhanced to inverted faces but not to inverted objects: An electrophysiological account of face-specific processes in the human brain. *Neuroreport, 11*(1), 69-74.

Rossion, B., Joyce, C. A., Cottrell, G. W., & Tarr, M. J. (2003). Early lateralization and orientation tuning for face, word, and object processing in the visual cortex. *Neuroimage, 20*(3), 1609-1624.

Rossion, B., & Jacques, C. (2008). Does physical interstimulus variance account for early electrophysiological face sensitive responses in the human brain? ten lessons on the N170. *Neuroimage, 39*(4), 1959-1979.

Rossion, B., Hanseeuw, B., & Dricot, L. (2012). Defining face perception areas in the human brain: A large-scale factorial fMRI face localizer analysis. *Brain and Cognition, 79*(2), 138-157.

Rugg, M. D., & Coles, M. G. (1995). *Electrophysiology of mind: Event-related brain potentials and cognition.* Oxford University Press.

Rushworth, M. F., Ellison, A., & Walsh, V. (2001). Complementary localization and lateralization of orienting and motor attention. *Nature Neuroscience, 4*(6), 656-661.

Rushworth, M. F., Krams, M., & Passingham, R. E. (2001). The attentional role of the left parietal cortex: The distinct lateralization and localization of motor attention in the human brain. *Journal of Cognitive Neuroscience, 13*(5), 698-710.

Rutten, G., Ramsey, N., Van Rijen, P., Alpherts, W., & Van Veelen, C. (2002). FMRI-determined language lateralization in patients with unilateral or mixed language dominance according to the wada test. *Neuroimage, 17*(1), 447-460.

Sabsevitz, D. S., Swanson, S. J., Hammeke, T. A., Spanaki, M. V., Possing, E. T., Morris, G. L.,3rd, . . . Binder, J. R. (2003). Use of preoperative functional neuroimaging to predict language deficits from epilepsy surgery. *Neurology, 60*(11), 1788-1792.

Salive, M. E., Guralnik, J. M., & Glynn, R. J. (1993). Left-handedness and mortality. *American Journal of Public Health, 83*(2), 265-267.

Sato, S., Demura, S., Sugano, N., Mikami, H., & Ohuchi, T. (2008). Characteristics of handedness in japanese adults: Influence of left-handed relatives and forced conversion. *International Journal of Sport and Health Science, 6*, 113-119.

Scott, S. K., & Johnsrude, I. S. (2003). The neuroanatomical and functional organization of speech perception. *Trends in Neurosciences, 26*(2), 100-107.

Sequeira, S. D. S., Woerner, W., Walter, C., Kreuder, F., Lueken, U., Westerhausen, R., ... Wittling, W. (2006). Handedness, dichotic-listening ear advantage, and gender effects on planum temporale asymmetry—a volumetric investigation using structural magnetic resonance imaging. *Neuropsychologia, 44*(4), 622-636.

Shulman, G. L., Pope, D. L., Astafiev, S. V., McAvoy, M. P., Snyder, A. Z., & Corbetta, M. (2010). Right hemisphere dominance during spatial selective attention and target detection occurs outside the dorsal frontoparietal network. *The Journal of Neuroscience : The Official Journal of the Society for Neuroscience, 30*(10), 3640-3651.

Simon, G., Petit, L., Bernard, C., & Rebaï, M. (2007). N170 ERPs could represent a logographic processing strategy in visual word recognition. *Behavioral and Brain Functions, 3*(21), 1-11.

Simonyan, K., & Fuertinger, S. (2015). Speech networks at rest and in action: Interactions between functional brain networks controlling speech production. *Journal of Neurophysiology, 113*(7), 2967-2978.

Smith, L. C., & Moscovitch, M. (1979). Writing posture, hemispheric control of movement and cerebral dominance in individuals with inverted and noninverted hand postures during writing. *Neuropsychologia, 17*(6), 637-644.

Sommer, I.E.C. (2010) Sex differences in handedness, brain asymmetry, and language lateralization. In Hugdahl, K., & Westerhausen, R. (Eds.), *The Two Halves of the Brain: Information Processing in the Cerebral Hemispheres* (pp. 287-312). Cambridge, Massachusetts: The MIT Press.

Sparks, R., & Geschwind, N. (1968). Dichotic listening in man after section of neocortical commissures. *Cortex, 4*(1), 3-16.

Steenhuis, R. E., & Bryden, M. (1989). Different dimensions of hand preference that relate to skilled and unskilled activities. *Cortex, 25*(2), 289-304.

Steenhuis, R. E., Østbye, T., & Walton, R. (2001). An examination of the hypothesis that left-handers die earlier: The canadian study of health and aging. *Laterality: Asymmetries of Body, Brain and Cognition, 6*(1), 69-75.

Steinmetz, H., & Galaburda, A. M. (1991). Planum temporale asymmetry: In-vivo morphometry affords a new perspective for neuro-behavioral research. *Reading disabilities* (pp. 143-155) Springer.

Steinmetz, H., & Seitz, R. J. (1991). Functional anatomy of language processing: Neuroimaging and the problem of individual variability. *Neuropsychologia, 29*(12), 1149-1161.

Steinmetz, H., Volkmann, J., Jäncke, L., & Freund, H. (1991). Anatomical left-right asymmetry of language-related temporal cortex is different in left-and right-handers. *Annals of Neurology, 29*(3), 315-319.

Strauss, E., & Wada, J. (1983). Lateral preferences and cerebral speech dominance. *Cortex, 19*(2), 165-177.

Subirana, A. (1969). Handedness and cerebral dominance. In P. Vinken, & G. Bruyn (Eds.), *Handbook of clinical neurology* (pp. 248-272). Amsterdam.

Szaflarski, J. P., Binder, J. R., Possing, E. T., McKiernan, K. A., Ward, B. D., & Hammeke, T. A. (2002). Language lateralization in left-handed and ambidextrous people: FMRI data. *Neurology, 59*(2), 238-244.

Tabachnick, B. G., & Fidell, L. S. (2001). *Using multivariate statistics* (4th ed.). Boston, MA: Allyn and Bacon.

Taylor, J. C., Wiggett, A. J., & Downing, P. E. (2007). Functional MRI analysis of body and body part representations in the extrastriate and fusiform body areas. *Journal of Neurophysiology, 98*(3), 1626-1633.

Taylor, J. C., Wiggett, A. J., & Downing, P. E. (2010). fMRI-adaptation studies of viewpoint tuning in the extrastriate and fusiform body areas. *Journal of Neurophysiology, 103*(3), 1467-1477.

Thiel, C. M., Zilles, K., & Fink, G. R. (2004). Cerebral correlates of alerting, orienting and reorienting of visuospatial attention: An event-related fMRI study. *Neuroimage, 21*(1), 318-328.

Thierry, G., Martin, C. D., Downing, P., & Pegna, A. J. (2007a). Controlling for interstimulus perceptual variance abolishes N170 face selectivity. *Nature Neuroscience, 10*(4), 505-511.

Thierry, G., Martin, C. D., Downing, P. E., & Pegna, A. J. (2007b). Is the N170 sensitive to the human face or to several intertwined perceptual and conceptual factors? *Nature Neuroscience, 10*(7), 802-803. doi:10.1038/nn0707-802

Toga, A. W., & Thompson, P. M. (2003). Mapping brain asymmetry. *Nature Reviews Neuroscience, 4*(1), 37-48.

Valyear, K. F., Cavina-Pratesi, C., Stiglick, A. J., & Culham, J. C. (2007). Does tool-related fMRI activity within the intraparietal sulcus reflect the plan to grasp? *Neuroimage, 36*, T94-T108.

Van der Haegen, L., Cai, Q., Seurinck, R., & Brysbaert, M. (2011). Further fMRI validation of the visual half field technique as an indicator of language laterality: A large-group analysis. *Neuropsychologia, 49*(10), 2879-2888.

Vingerhoets, G., Acke, F., Alderweireldt, A., Nys, J., Vandemaele, P., & Achten, E. (2012). Cerebral lateralization of praxis in right-and left-handedness: Same pattern, different strength. *Human Brain Mapping, 33*(4), 763-777.

Wada, J. (1949). A new method for the determination of the side of cerebral speech dominance: A preliminary report on the intracarotid injection of sodium amytal in man. *Igaku Seibutsugaku, 14*, 221-222.

Wada, J. A., Clarke, R., & Hamm, A. (1975). Cerebral hemispheric asymmetry in humans - cortical speech zones in 100 adult and 100 infant brains. *Archives of Neurology, 32*(4), 239-246.

Wada, Y., & Yamamoto, T. (2001). Selective impairment of facial recognition due to a haematoma restricted to the right fusiform and lateral occipital region. *Journal of Neurology, Neurosurgery, and Psychiatry, 71*(2), 254-257.

Warren, J. M. (1980). Handedness and laterality in humans and other animals. *Physiological Psychology, 8*(3), 351-359.

Watson, J. B., & Watson, R. R. (1921). Studies in infant psychology. *The Scientific Monthly*, 493-515.

Whitehouse, A. J., & Bishop, D. V. (2009). Hemispheric division of function is the result of independent probabilistic biases. *Neuropsychologia, 47*(8), 1938-1943.

Willems, R. M., Peelen, M. V., & Hagoort, P. (2010). Cerebral lateralization of face-selective and body-selective visual areas depends on handedness. *Cerebral Cortex (New York, N.Y.: 1991), 20*(7), 1719-1725. doi:10.1093/cercor/bhp234 [doi]

Woodhead, Z. V., Wise, R. J., Sereno, M., & Leech, R. (2011). Dissociation of sensitivity to spatial frequency in word and face preferential areas of the fusiform gyrus. *Cerebral Cortex (New York, N.Y.: 1991), 21*(10), 2307-2312.

Yovel, G., Tambini, A., & Brandman, T. (2008). The asymmetry of the fusiform face area is a stable individual characteristic that underlies the left-visual-field superiority for faces. *Neuropsychologia, 46*(13), 3061-3068.

Zangwill, O. L. (1960). *Cerebral dominance and its relation to psychological function.* Oxford, England: Oliver & Boyd.

Zatorre, R. J. (1989). Perceptual asymmetry on the dichotic fused words test and cerebral speech lateralization determined by the carotid sodium amytal test. *Neuropsychologia, 27*(10), 1207-1219.