Title of PhD Thesis: Mirror-touch synaesthesia: The role of shared representations in social cognition

Michael Joseph Banissy

Institute of Cognitive Neuroscience

University College London

PhD in Cognitive Neuroscience

I, Michael Joseph Banissy, confirm that the work presented in this thesis is my own. Where information has been derived from other sources, I confirm that this has been indicated in the thesis.

TABLE OF CONTENTS

LIST OF FIGURES AND TABLES

ABSTRACT

Synaesthesia is a condition in which one property of a stimulus results in conscious experiences of an additional attribute. In mirror-touch synaesthesia, the synaesthete experiences a tactile sensation on their own body simply when observing touch to another person. This thesis investigates the prevalence, neurocognitive mechanisms, and consequences of mirror-touch synaesthesia. Firstly, the prevalence and neurocognitive mechanisms of synaesthesia were assessed. This revealed that mirror-touch synaesthesia has a prevalence rate of 1.6%, a finding which places mirror-touch synaesthesia as one of the most common variants of synaesthesia. It also indicated a number of characteristics of the condition, which led to the generation of a neurocognitive model of mirror-touch synaesthesia. An investigation into the perceptual consequences of synaesthesia revealed that the presence of synaesthesia is linked with heightened sensory perception - mirror-touch synaesthetes showed heightened tactile perception and grapheme-colour synaesthetes showed heightened colour perception. Given that mirror-touch synaesthesia has been shown to be linked to heightened sensorimotor simulation mechanisms, the impact of facilitated sensorimotor activity on social cognition was then examined. This revealed that mirror-touch synaesthetes show heightened emotional sensitivity compared with control participants. To compliment this, two transcranial magnetic stimulation (TMS) studies were then conducted to assess the impact of suppressing sensorimotor activity on the expression recognition abilities of healthy adults. Consistent with the findings of superior emotion sensitivity in mirror-touch synaesthesia (where there is facilitated sensorimotor activity), suppressing sensorimotor resources resulted in impaired expression recognition across modalities. The findings of the thesis are discussed in relation to neurocognitive models of synaesthesia and of social cognition.

PUBLICATIONS ARISING FROM THESIS

Research Articles:

Banissy, M. J., and Ward, J. (2007). Mirror-touch synaesthesia is linked with empathy. *Nature Neuroscience, 10,* 815-816.

Banissy, M. J., Walsh, V., and Ward, J (2009). Enhanced sensory perception in synaesthesia. *Experimental Brain Research, 196,* 565-571.

Banissy, M. J., Cohen Kadosh, R., Maus, G. W., Walsh, V., & Ward, J. (2009). Prevalence, characteristics, and a neurocognitive model of mirror-touch synaesthesia. *Experimental Brain Research, 198,* 261-272.

Banissy, M. J., Sauter, D. A., Ward, J, Warren, J. E., Walsh, V., and Scott, S. (Submitted). Suppressing sensorimotor activity modulates the discrimination of auditory emotions but not speaker identity. *Journal of Neuroscience*.

Banissy, M. J., Garrido, L., Kusnir, F., Duchaine, B., Walsh, V, and Ward, J. (Submitted). Superior facial expression but not idenitity recognition in mirror-touch synaesthesia. *Journal of Neuroscience*.

Invited Book Chapters and Reviews:

Banissy, M. J., and Ward, J. (2008). On being moved: From mirror neurons to empathy. *Child and Adolescent Mental Health, 13,* 50-51.

Ward, J., Banissy, M. J., and Jonas, C. (2008). Haptic perception in synaesthesia. In *Human Haptic Perception: Basics and Applications*, Edited by M.Grunwald. Birkhäuser, Basel.

ACKNOWLEDGEMENTS

Firstly, I would like Vincent Walsh for his unparalleled support and guidance. I would also like to thank Jamie Ward for providing me with the opportunity to complete this research, for his support, and for his advice. The two of them have shaped my intellectual development and I will be forever grateful.

I am also thankful to a large number of my friends and colleagues at University College London and the University of Sussex for their support. Of note, Roi Cohen Kadosh, Brad Duchaine, Lúcia Garrido, Amir Javadi, Clare Jonas, Ryota Kanai, Neil Muggleton, David Pitcher, Sophie Scott, and Lilli Tcheang. There are also a number of friends and family who have provided me with encouragement and support over the years; Lucy Annett, Edith Cole, Margaret Cole, Stanley Cole, Steven Cole, Claire Doyle, Martin Family, Stephen Ford, Davina Reynolds, and Mark Taylor.

My sincerest thanks and love goes to Sian Fitzpatrick. Her encouragement, support and faith in me have been incredible. I am thankful to you for so many reasons and more grateful than I could ever say.

Finally, deepest thanks go to my parents, for their unconditional support and love throughout the years. To my sister Jasmine and to my brother Jamie – you are both an inspiration and I only wish I had the words to explain how much. Thank you for everything. This is for you all, with love always.

CHAPTER 1: INTRODUCTION

This chapter provides a summary of the motivation to investigate mirror-touch synaesthesia. It proposes that synaesthesia relies upon similar mechanisms of multisensory interactions that are present in non-synaesthetic individuals and can be used to inform normal models of cognitive processing. The condition of synaesthesia is introduced and the prevalence and characteristics of the condition are discussed. An overview of current psychological and neurobiological studies is provided which reveals insights into the neurocognitive mechanisms of synaesthesia and demonstrates how the condition makes use of neural pathways involved in normal sensory perception. Recent research demonstrates that developmental mirror-touch synaesthesia appears to rely upon activation of the same somatosensory representations within the human mirror-touch system that are activated when non-synaesthetic individuals observe another person being touched The aims of this thesis are described. These include i) investigations into the neurocognitive mechanisms of mirror-touch synaesthesia and ii) investigations into the role of sensorimotor simulation processes in emotion processing and empathy.

1.1 Origins of synaesthesia

Derived from the Greek roots *syn* (meaning together) and *aisthesis* (meaning sensation), synaesthesia is a condition in which one property of a stimulus (the inducer) gives rise to a conscious experience of a different attribute (the concurrent; Grossenbacher and Lovelance, 2001). For example, in tone-colour synaesthesia, sounds may elicit the experience of colour (Ward, Huckstep, and Tsakanikos, 2006); in grapheme-colour synaesthesia, the visual presentation of achromatic letters or numbers results in subjective experiences of colour (Simner et al., 2006); and in lexical-gustatory synaesthesia, words trigger synaesthetic experiences of taste (Ward, Simner and Auyeung, 2005).

Accounts of the condition can be traced to the 19th century (c.f. Jewanski, Day, and Ward, 2009). For example, Sachs (1812) describes synaesthesia involving colours for music and simple sequences. Later, Galton (1880) described cases of individuals in whom numbers were consciously visualized in space (spatial number forms) and of synaesthesia involving colour. While early accounts of the condition aroused some interest, failure to develop an objective approach to confirm the phenomenon resulted in a decline in research. It was not until the advent of the development of new behavioural and neurophysiological measures which could be used to corroborate self reports that the topic of synaesthesia returned as a topic of legitimate scientific investigation (Baron-Cohen et al., 1987; Cytowic and Wood, 1982; Marks, 1975; see Ramachandran and Hubbbard, 2001; Rich and Mattingely, 2002; Sagiv, 2004 for reviews).

Since this time, research into the topic of synaesthesia has grown rapidly with a focus moving beyond exploring the reality of the condition to consider how synaesthesia can be used to inform models of typical cognition in domains such as numerical cognition (Cohen Kadosh and Henik, 2007), language (Simner, 2007), multisensory processing (Sagiv and Ward, 2006), imagery (Barnett and Newell, 2008; Spiller and Jansari, 2008), and attention (Treisman, 2004). In this introductory chapter, I will review this literature by describing studies on the prevalence, authenticity and aetiology of synaesthesia. The focus of this thesis is to investigate a newly documented type of synaesthesia, mirror-touch synaesthesia (in which individuals' experience tactile sensations on their own body simply when observing touch to others) and to use this condition to examine more general neurocognitive processes in social cognition. In this chapter, I will introduce research investigating synaesthesia involving touch and consider the evidence that mirror-touch synaesthesia relies upon similar mechanisms to multisensory interactions which are shown in non-synaesthetic individuals. Finally, I will discuss how synaesthesia may be used to inform typical models of cognition and discuss the role of sensorimotor simulation in social cognition.

1.2 Prevalence and characteristics of synaesthesia

Synaesthesia is typically considered as having three defining features; 1) experiences are conscious perceptual or percept-like experiences; 2) experiences are induced by an attribute not typically associated with the conscious experience; 3) these experiences occur automatically (Ward and Mattingley, 2007). Further, the synaesthetic percept tends to co-exist with the percept of the inducing stimulus rather than over-riding it – for example in lexical-gustatory synaesthesia written or heard words are recognised but also result in a simultaneous subjective sensation of taste in the mouth and tongue area (Ward and Simner, 2003). Note that throughout the thesis the terminology of referring to different types of synaesthesia in terms of inducer-concurrent pairs separated with a hyphen is used. As such, touch-colour synaesthesia refers to tactile inducers eliciting a concurrent experience of colour, and vision-touch synaesthesia refers to a visual inducer eliciting a tactile experience.

Cases of synaesthesia can be either developmental or acquired, with developmental cases thought to be dependent upon genetic and environmental factors and acquired cases reflecting synaesthesia following specific environmental influences (e.g. following brain injury or drug ingestion). Developmental forms of synaesthesia have been shown to run in families and previous research suggested that the condition may be more common in women than men, which may reflect an X-linked dominant mode of inheritance (Baron-Cohen, Burt, Smith-Laittan, Harrison, and Bolton, 1996). More recent research indicates that synaesthesia may be equally common within males and females and that previous methodologies may have led to an over inflated male-female ratio (Ward and Simner, 2005; but see Barnett et al., 2008). Similarly, reports of twins discordant for synaesthesia (Smilek, Mofatt, Pasternak, White, Dixon, and Merilke, 2002), as well as evidence that synaesthesia can skip generations (Hubbard and Ramachandran, 2003), and that the proportion of sons or daughters born to synaesthete mothers does not significantly differ (Barnett et al., 2008; Ward and Simner, 2005), suggest that an X-linked dominant mode of inheritance may be an over simplified account of the genetic mechanisms which underlie developmental forms of the condition (Asher et al., 2009).

Current estimates on the prevalence of developmental synaesthesia indicate that the condition has a prevalence rate of at least 4% and a female to male ratio of 1:1 (Simner et al., 2006; Ward and Simner, 2005). Although, depending on whether one includes cases of ordinal linguistic personification (in which individuals attribute genders or personalities to letters or numbers; Simner and Holenstein, 2007) or spatial number forms (Sagiv, Simner, Collins, Butterworth, and Ward, 2006), the prevalence rate of 4% is likely to be much higher (Simner et al., 2006).

A trend of all studies of the prevalence of synaesthesia is to report a higher proportion of synaesthetes who experience colour evoked by letters or other linguistic stimuli (e.g. grapheme-colour / day-colour synaesthesia; Baron-Cohen, Burt, Smith-Laittan, Harrison, and Bolton, 1996; Rich, Bradshaw, and Mattingley, 2005; Simner et al., 2006). It is perhaps not surprising that this variant of synaesthesia has been the topic of much research amongst synaesthesia researchers. Research into this variant of the condition has highlighted a number of interesting individual differences between synaesthetes. For example, distinctions have been made between projector and associator synaesthetes; which distinguishes between synaesthetes whose locus of experienced colour is projected to a specific spatial location (projector synaesthetes) and synaesthetes whose concurrent is perceived internally or in the ‘minds eye’ (associator synaesthetes) (Dixon, Smilek, and Merilke, 2004; see also Ward, Li, Salih, and Sagiv, 2007). Similarly, Ramachandran and Hubbard (2001) have categorised synaesthetes based upon the level of induction of the synaesthesia, distinguishing between higher synaesthetes, in whom conceptual properties of a grapheme trigger colours (e.g. a number name or dice pattern for a particular number), and lower synaesthetes in whom the physical properties of the grapheme (e.g. shape / form) trigger synaesthetic experience. Distinctions such as these may also be valid for other variants of synaesthesia (see below).

1.3 Authenticity and perceptual nature of synaesthesia

1.3.1 Authenticity of synaesthesia

Typically, the authenticity of synaesthesia has been confirmed behaviourally using tests of consistency of synaesthetic associations over time. Synaesthetes tend to show greater consistency in inducer-concurrent pairings (synaesthetes are typically around 90% consistent) compared with non-synaesthetic subjects asked to freely associate or use a particular strategy (i.e. memory or imagery), even when tested over longer time periods (Baron-Cohen, Harrison, Goldstein and Wyke, 1993). This pattern has been shown to be the case in a number of variants of synaesthesia, including grapheme-colour (Baron-Cohen et al., 1996), emotion-colour (Ward, 2004) and lexical-gustatory synaesthesia (Ward and Simner, 2003).

A further paradigm used to confirm the automaticity of the synaesthetic experience has been the modified ‘synaesthetic stroop’ task in which synaesthetic inducers are paired with either a congruent or incongruent concurrent. For example, if a grapheme-colour synaesthete perceives the letter A as red, then this grapheme would be presented in a colour which is either congruent with synaesthetic experience (e.g. A) or a colour which is incongruent with synaesthetic experience (e.g. A). The subject is asked to ignore the synaesthetic colour and name the true colour of the grapheme. Grapheme-colour synaesthetes tend to be faster in the congruent relative to incongruent condition (Mills, Boteler, and Oliver, 1999), while non-synaesthetes do not show this pattern. As with tests of consistency, this pattern of performance has been found for different subtypes of synaesthesia, including not only grapheme-colour synaesthesia, but also music-colour (Ward et al., 2006), music-taste (Beeli, Esslen, and Jäncke, 2005), and mirror-touch (Banissy and Ward, 2007; summarised later in Figure 1.5) variants.

Notably, individuals who have over-learned colour associations may also behave similar to synaesthetes on the synaesthetic stroop task. For example, Elias and colleagues report a single case study in which a non-synaesthetic individual with reliable digit-colour associations, as a result of years of training using coloured numerical codes in cross-stitching, performed comparably to synaesthetic subjects on tests of consistency and stroop interference (synaesthetes differed from the control on functional magnetic resonance imaging [fMRI] measures of synaesthesia in colour selective regions but not on behavioural measures; Elias, Saucier, Hardie, and Sart, 2003). This is consistent with the findings of MacLeod and Dunbar (1988) who trained non-synaesthetic subjects to associate black and white geometric shapes with colour names over thousands of trials. When participants were later presented with a stroop task, involving the geometric shapes presented in a congruent or incongruent colour, the typical stroop interference pattern was observed (MacLeod and Dunbar, 1988). In neither study were subjects experiencing synaesthetic colour interactions, implying that associative (rather than perceptual) components may be able to account for some of the patterns of performance shown by colour synaesthetes on synaesthetic stroop and consistency measures. However, more recent findings suggest that, in colour synaesthetes, the synaesthetic stroop effect may be a consequence of both perceptual and associative components (Nikolić, Lichti and Singer, 2007). Using principles of colour-opponency (Hering, 1868/1964), Nikolic and colleagues varied incongruent stimuli within the synaesthetic stroop by using colour-opponent (i.e. red changed to green) or non-opponent colours (i.e. red changed to blue). If synaesthetic stroop relies upon perceptual processes as well as associative components then one would expect the colour-opponent condition to produce the most interference – this pattern was observed (Nikolić et al., 2007).

1.3.2 Psychophysical studies

In addition to measures of stroop and consistency, other psychophysical measures have been used to investigate how closely synaesthetic perception resembles veridical sensory perception. Again, much of this work has focussed on the perceptual reality of synaesthetic colours in grapheme-colour synaesthesia. These findings indicate that synaesthetic and real colours interact under conditions of binocular rivalry (Kim, Blake, and Palmeri, 2006); that synaesthetic colours can induce orientation contingent colour adapting after-effects such as a synaesthetic 'McCollough Effect' (Blake, Palmeri, Marois, and Kim, 2004; but see Hong and Blake, 2008); that synaesthetic and real colours can combine to produce apparent motion (Kim et al., 2006); and that, in projector synaesthetes, synaesthetic experience can be modulated by background contrast, implying that synaesthesia relies upon early contrast-dependent visual mechanisms (Hubbard, Manohar, and Ramachandran, 2006; Witthoft and Winawer, 2006).

1.3.3 Neuroimaging studies

Aside from behavioural and psychophysical tests, functional brain imaging methods have been used to distinguish between synaesthetic and non-synaesthetic subjects. These have included positron emission tomography (PET) studies of word/grapheme-colour synaesthesia triggered by speech (Paulesu et al., 1995); fMRI studies of grapheme-colour (Aleman, Rutten, Sitskoorn, Dautzenberg, and Ramsey, 2001; Hubbard, Arman, Ramachandran, and Boynton, 2005; Weiss, Zilles, and Fink, 2005; Sperling, Prvulovic, Linden, Singer, and Stirn, 2006; Rich et al., 2006), mirror-touch (Blakemore, Bristow, Bird, Frith, and Ward, 2005), word-colour (Aleman et al., 2001; Nunn et al., 2002; Gray, Parslow, Brammer, Chopping, Vythelingum, and ffytche, 2006), digit-colour (Elias et al., 2003), people-colour (Weiss, Shah, Toni, Zilles, and Fink, 2001), time-colour (Steven, Hansen, and Blakemore, 2006), time-space (Steven et al., 2006), sound-vision (Stewart, Mulvenna, Griffiths, and Ward, in prep), and bidirectional synaesthesia (Cohen Kadosh, Cohen Kadosh, and Henik, 2007). In addition, there have been two diffusion tensor imaging studies (DTI) of grapheme-colour synaesthesia (Rouw and Scholte, 2007; Jäncke, Beeli, Eulig, and Hänggi, 2009).

While there is some inconsistency between studies, the majority point to synaesthetic experience being correlated with activations in brain regions involved in normal perceptual experience. For example, studies investigating synaesthesia involving colour tend to report activation of colour area V4 / V8 for synaesthesia inducing stimuli (e.g. Hubbard et al., 2005; Nunn et al., 2002; Sperling et al., 2006), although not always (i.e. Paulesu et al., 1995; Weiss et al., 2005; Figure 1.1). The reasons behind this inconsistency remain unclear, although they may be related to differences in task demands, statistical power, or qualitative differences between synaesthetic subjects (Hubbard et al., 2005). Moreover, by correlating performance on different synaesthetic psychophysical paradigms with fMRI activations, Hubbard and colleagues (2005) show that synaesthetes who show larger effects on psychophysical tasks show greater activations in colour selective regions of the visual cortex (V4).

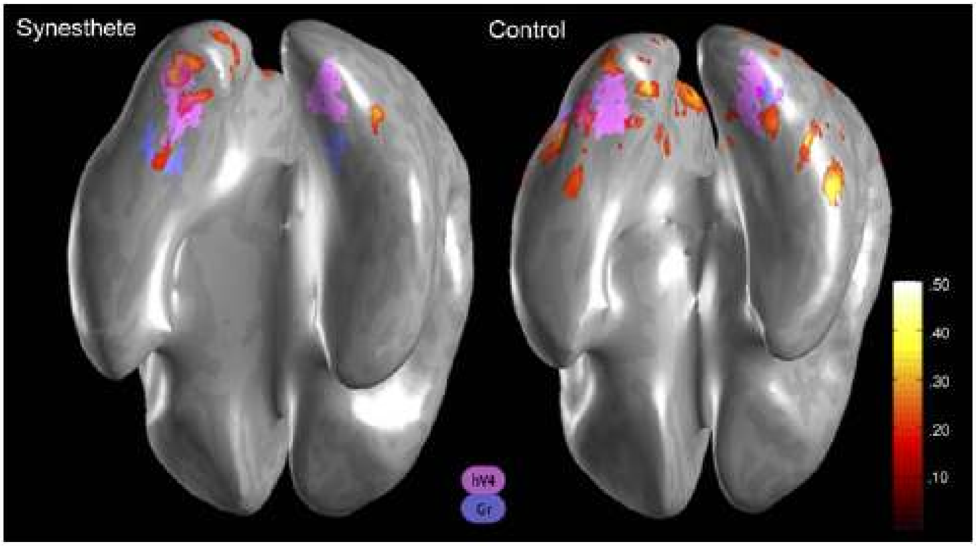


Figure 1.1 fMRI data from a control and grapheme-colour synaesthetic subject when presented with synaesthesia inducing graphemes. Colour area V4 (as per Wade, Brewer, Rieger, and Wandell, 2002) is shown in purple and the grapheme area (Gr) in blue. The synaesthete shows activation in both V4 and Gr, while the control only shows activation in Gr. Taken from Hubbard and Ramachandran (2005).

Recent research making use of DTI techniques is also consistent with the notion that inter-individual differences within the synaesthetic population may contribute to different patterns of brain activation. DTI is a neuroimaging technique which measures the diffusion of water molecules in the living human brain to enable analysis of the degree of structural connectivity between brain regions (Basser, 1995). Using this method, Rouw and Scholte (2007) report that grapheme-colour synaesthesia is linked with increased structural connectivity (as compared with non-synaesthetes) in the left superior parietal cortex, right inferior temporal cortex (adjacent to the fusiform gyrus) and in a bilateral cluster located beneath the central sulcus. Of these four clusters, greater connectivity in the right inferior temporal cortex was found to be strongest in ‘projector’ synaesthetes who saw their colours in the outside world (compared to 'associator' synaesthetes who saw their colours in their mind's eye).

In addition to shared activations in brain regions involved in normal and synaesthetic perceptual experience (e.g. V4 / V8 in colour), a number of common brain activations have been reported across different variants of the condition. Two brain regions of note are the insula and the intraparietal sulcus (IPS). IPS and insula activations have been reported in studies of both visual and auditory grapheme-colour synaesthesia (insula activations - Nunn et al., 2002; Paulesu et al., 1995; IPS activations - Paulesu et al., 1995; Weiss et al., 2005); synaesthesia involving spatial number forms (Tang, Ward, and Butterworth, 2008); and studies of sound-vision synaesthesia (Stewart et al., in prep). Insula activations have also been found in mirror-touch synaesthesia (Blakemore et al., 2005). Both regions have been implicated in multi-sensory processing and integration (Bushara, Grafman, and Hallett, 2001; Hadjikhani and Roland, 1998; Olson, Gatenby, and Gore, 2002), indicating that they may play a role in integrating synaesthesia inducing materials with experience.

1.3.4 Transcranial magnetic stimulation (TMS) studies

TMS is a non-invasive technique that uses induced current to depolarize the cell membrane in the cortex leading to a temporary modulation of neural activity in the stimulated cortex (Walsh and Rushworth, 1999). This method enables examination of the necessity of stimulated brain structures for given cognitive functions. To date, two TMS studies have been conducted to investigate the necessity of parietal cortex activations in grapheme-colour synaesthesia (Esterman, Verstynen, Ivry, and Robertson, 2006; Muggleton, Tsakanikos, Walsh, and Ward, 2007). Esterman et al. investigated the magnitude of synaesthetic interference on a synaesthetic stroop task in two ‘projector’ synaesthetes following TMS to a parieto-occipital region in the right hemisphere, to the corresponding region in the left hemisphere, and to area V1. They found that the magnitude of synaesthetic interference was reduced following TMS to the right parieto-occipital area, but not for the other two brain regions (Esterman et al., 2006). Extending upon this, Muggleton et al. contrasted the effects of TMS over four parietal brain regions (right parieto-occipital, left parieto-occipital, right parietal and left parietal regions) in five grapheme-colour synaesthetes (comprised of one ‘projector’ and four ‘associators’). Consistent with the findings of Esterman et al., these authors also report that the automaticity of synaesthetic experience (as measured using a synaesthetic stroop task) was disrupted following stimulation of the right parieto-occipital area only (Muggleton et al., 2007; Figure 1.2). Therefore both studies suggest that the right parieto-occipital cortex is necessary for the experience of synaesthesia. In non-synaesthetes this brain region has been shown to participate in visual feature binding (Freidman-Hill, Robertson, and Treisman, 1995; Donner, Kettermann, Diesch, Ostendorf, Villringer, and Brandt, 2002) and one explanation for the selective TMS disruption observed is that the right parieto-occipital area may act in the spatial binding of graphemes with synaesthetic colour (Esterman et al., 2006; Muggleton et al., 2007). If so, this suggests that, in grapheme-colour synaesthesia, synaesthetic experience acts upon the same cortical pathways that exist in the non-synaesthetic brain (Cohen Kadosh and Walsh, 2008; Cohen Kadosh, Henik, Catena, Walsh, and Fuentes, 2009). However, even if synaesthetes use common mechanisms of cross-modal binding, it remains unclear whether synaesthetic binding follows the same time-course of processing as veridical cross-modal binding or how the parietal lobe interacts with processing in other cortical areas (i.e. sensory-selective cortical regions) to elicit synaesthetic experience.

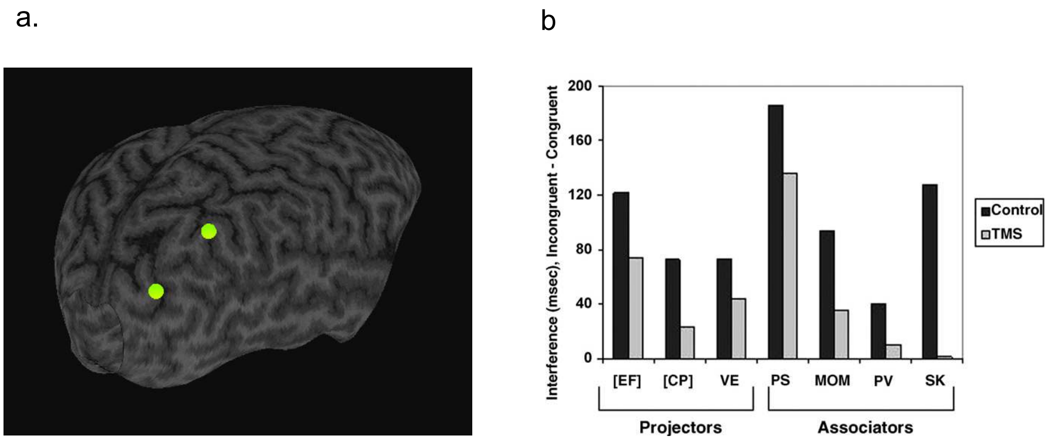


Figure 1.2 Summary of Muggleton et al. (2007). (a) The location of stimulated right parietal-occipital region (RPO; x = 22, y = -71, z = 27) and right parietal region. (b) Interference between real and synaesthetic colours on synaesthetic stroop task. Performance for individual synaesthetes, divided between projectors and associators, following TMS targeted at the RPO region compared to control condition. Synaesthetes EP and CP were reported by Esterman et al. (2006) and are shown for comparison. Adapted from Muggleton et al. (2007) with permission.

1.3.5 Electrophysiological studies

As with TMS studies, to date there have been few studies utilizing electrophysiological techniques to investigate the time course neural activity in synaesthetic experience. Schiltz and colleagues (1999) investigated the electrophysiological correlates of grapheme-colour synaesthesia (n = 17) and reported an increased positivity at frontal and central scalp sites of synaesthetes (relative to controls) occurring around 150 msec after stimulus onset which was sustained until 600 msec. A more recent study by Beeli and colleagues, conducted with grapheme-colour synaesthetes who only experience colours from spoken letters and words (n = 16), revealed differences (reduced amplitude and / or increased latencies) in the auditory N1, P2, and N2 deflections (Beeli, Esslen, and Jäncke, 2008). Source localization implicated intracerebral sources of these components to lay in inferior temporal and orbitofrontal brain regions (although few electrode sites were available). These authors interpret their finding as evidence for increased cortical wiring in synaesthetes (c.f. Ramachandran and Hubbard, 2001; Bargary and Mitchell, 2008), but may also be consistent with accounts of synaesthesia which posit differences in local mechanisms of cortical inhibition (Cohen Kadosh and Walsh, 2008).

In addition to this, two single case studies and one group study have investigated auditory-visual synaesthesia. In a single case study of acquired auditory-visual synaesthesia, Rao and colleagues report that synaesthesia inducing sounds resulted in a modulation of the auditory evoked N1 deflection (Rao, Nobre, Alexanader and Cowey, 2007). Rizzo and Eslinger (1989) investigated the electrophysiological correlates of a single case of developmental auditory-visual synaesthesia, but restricted analysis to three electrode sites (O1/2, or Oz). No abnormal potentials were found at these three sites, but this does not rule out the possibility that abnormal potentials may occur at alternative electrode sites. A more recent group study of tone-colour synaesthesia (n = 10; Goller, Otten, and Ward, 2009) revealed early onset (around 100msec after stimulus onset) differences in deflections of the auditory evoked potential (auditory N1, N2, and P2). No posterior difference was observed, implying that synaesthetic experience may be generated locally (potentially through mechanisms of local differences in cortical inhibition; c.f. Cohen Kadosh and Walsh, 2008).

1.3.6 Neurocognitive models of synaesthesia

While much research has determined the authenticity of synaesthesia, the neurocognitive mechanisms which underpin synaesthesia are a subject of uncertainty. A current area of dispute in the synaesthesia literature is whether synaesthetic experience is due to additional structural connectivity (i.e. structural differences), malfunctions in cortical inhibition (i.e. functional but not structural differences) or a combination of both (Bargary and Mitchell, 2008; Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001; Hubbard and Ramachandran, 2005; Rouw and Scholte, 2007; Smilek, Dixon, Cudahy, and Merikle, 2001).

Supporting evidence for structural connectivity accounts is provided by a DTI study which reports greater white matter coherence in grapheme-colour synaesthetes compared to non-synaesthetic control subjects - grapheme-colour synaesthetes show increased structural connectivity in inferior-temporal, parietal and frontal brain regions when compared to non-synaesthetes (Rouw and Scholte, 2007). Some authors have interpreted these findings to be consistent with accounts of synaesthesia which argue in favour of aberrant connectivity between adjacent cortical regions (Ramachandran and Hubbard, 2001; Hubbard, 2007). For example, given that the brain regions involved in the visual recognition of graphemes (i.e. the putative visual word form area; Cohen and Dehaene, 2004) lie adjacent to brain areas involved in colour perception (i.e. human V4 - Wade et al., 2002), it has been suggested that grapheme-colour synaesthesia may arise from direct cross-activation between these regions as a result of either increased connectivity between adjacent brain regions or reduced inhibition between adjacent regions. This local cross-activation account has also been extended to explain sequence-space synaesthesia (i.e. number forms), in terms of cross-activation between adjacent parietal regions (Ramachandran and Hubbard, 2001), and may also be important for other variants of synaesthesia (e.g. lexical-gustatory synaesthesia; Ward, Simner and Auyeung 2005). However, it is of note that the generality of enhanced structural connectivity in grapheme-colour synaesthesia is debatable (e.g. see Jäncke et al., 2009) and the extent to which these differences extend to other variants of synaesthesia (e.g. mirror-touch synaesthesia) or play a causal role in generating synaesthetic experience remains unknown.

In contrast to aberrant cortical connectivity accounts, other authors have argued in favour of feedback accounts of synaesthesia which explain the condition in terms of malfunctions in cortical inhibition, either within (Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008) or between brain regions (e.g. from a multisensory cortical nexus; Grossenbacher and Lovelace, 2001). According to this view, synaesthesia is mediated by the same cortical pathways that exist in the non-synaesthetes' brain (i.e. aberrant connectivity is not necessary to induce synaesthesia), but unmasking of these pathways due to alterations in cortical inhibition results in synaesthetic experience (Grossenbacher and Lovelace, 2001; Cohen Kadosh and Walsh, 2006; Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008; Cohen Kadosh, Henik, Catena, Walsh, and Fuetnes, 2009). Evidence that TMS disruption of the parietal lobe impairs synaesthetic stroop performance (Esterman et al., 2006; Muggleton et al., 2007); that synaesthetic-like experiences can be induced following hallucinogenic drugs (i.e. in the absence of altered cortical connectivity; Aghajanian and Marek, 1999); and that colour synaesthesia can be induced in non-synaesthetes (individuals without aberrant connectivity) using post-hypnotic suggestion (Cohen Kadosh et al., 2009) are consistent with this.

1.4 Synaesthesia involving touch

Synaesthesia involving touch has been less well documented than other variants of synaesthesia. Despite this, there are some reports of both developmental and acquired synaesthesia involving either a tactile inducer or concurrent. These cases are discussed below.

1.4.1 Synaesthesia involving tactile inducers

To date much research on synaesthesia involving tactile inducers has centred on cases of touch-vision synaesthesia in which touch results in visualised photisms. For example, Armel and Ramachandran (2001) report a case of acquired touch-vision synaesthesia shown by a patient who suffered blindness due to retinitis pigmentosa. One year after becoming completely blind the patient began to experience synaesthetic visual photisms from haptic stimuli. Such sensations were projected onto the spatial location of the body part touched irrespective of the location of the body part in space (e.g. a touch to the right hand in left space would elicit photisms in left space). Detailed investigations indicated that the intensity of tactile stimulation required to induce synaesthesia was lower when body parts were presented in front of the patient relative to behind the head (i.e. moving the hands from in front of the head to behind the head), suggesting that despite the patient being blind a preference was shown for when the inducer was "in view". This may be indicative of a body-based spatial reference that incorporates information about gaze and head orientation. Such findings are consistent with evidence from non-synaesthetes on normal multi-sensory interactions between touch and vision indicating that the spatial reference frame which processes current hand position is modulated by gaze direction (Armel and Ramachandran, 2001).

In addition to this, cases of blind synaesthetes for whom Braille reading elicits a visual concurrent have been reported (Wheeler and Cutsforth, 1921; Steven and Blakemore, 2004). In the latter case, synaesthete JF, who suffered from retinitis pigmentosa leading to blindness, consistently experienced coloured visual photisms both when reading Braille and when thinking about Braille characters (Steven and Blakemore, 2004). Similar geometrical arrangements of Braille dots evoked similar colours, but photisms were not elicited when touching other textures or objects. Notably, it has been reported that J.F experienced visual synaesthesia from childhood (i.e. since before losing his sight; Steven, Hansen, and Blakemore, 2006) so it may be the case that his synaesthesia reflects a different manifestation of grapheme-colour synaesthesia in which graphemes are processed haptically rather than visually (Ward, Banissy, and Jonas, 2008).

There have been relatively few documented cases of developmental touch-vision synaesthesia. While Day (2005) reports that 4% of synaesthetes report ‘coloured-touch’ these figures are based on self reported cases only (a failure to objectively confirm these self reports with tests of genuiness may mean that this 4% claim includes false positive cases; c.f. Simner et al., 2006) and no information is given regarding the nature of these cases (i.e. developmental or acquired cases). Recently, two cases of developmental touch-vision synaesthesia in which touch triggers visual sensations of colour (TV and EB) have been investigated more systematically (Ward et al., 2008). Each case indicated important distinctions between the spatial representations which underpin synaesthetic experience. Moreover, for synaesthete TV coloured photisms were projected onto the spatial location of the body part touched, whereas for EB photisms were perceived in her mind’s eye. This distinction appears similar to the projector / associator distinction in grapheme-colour synaesthesia outlined above (Dixon et al., 2004).

It is of note that while synaesthetes TV and EB appeared consistent on a test of consistency for their synaesthesia, involving 40 different tactile stimuli across two testing sessions; they were not shown to be significantly more consistent than control subjects. This is likely to be related to elevated levels of control consistency (c.f. Kusnir, MSc Thesis, University of London, 2008) indicating that the touch-vision synaesthesia reported by TV and EB may rely upon similar multi-sensory principles which underpin non-synaesthetic touch-vision interactions (Ward et al., 2008). Moreover, cross-modal correspondences between roughness and luminance (rougher textures associated to darker colours) and pressure and luminance (higher pressure associated with darker colours) were found for both synaesthetes and control subjects. Consistent with this, previous reports of touch-vision synaesthesia have indicated a relationship between pressure and luminance, in which the synaesthete experienced dark coloured photisms to hard objects (i.e. higher pressure) and lightly coloured photisms to soft objects (i.e. lower pressure) (Smith, 1905). Thus, it may be the case that developmental touch-vision synaesthesia relies upon similar mechanisms of cross modal transfer as observed in non-synaesthetic multi-sensory interactions between touch and vision. This would be consistent with findings indicating that other variants of synaesthesia appear to act upon the 'normal' architecture for cross-modal interactions (e.g. Ward, Huckstep, and Tsakanikos, 2006; Blakemore et al., 2005; Sagiv and Ward, 2006).

1.4.2 Synaesthesia involving a tactile concurrent

As with cases of synaesthesia in which touch acts to induce synaesthetic experience, cases of synaesthesia involving a tactile concurrent are less well documented than other more common variants of synaesthesia. Despite this, there are reports of acquired auditory-tactile synaesthesia in which sounds elicit tactile sensations (Ro et al., 2007) and of both acquired and developmental mirror-touch synaesthesia in which observed touch results in tactile experiences on the observer's own body (Halligan, Hunt, Marshall, and Wade, 1996; Bradshaw and Mattingley, 2001; Blakemore et al. 2005; Banissy and Ward, 2007). There is also evidence that the presence of synaesthesia for colour is linked to a greater incidence mitempfindung (the referral of a tactile sensation away from the stimulation site; Burrack, Knoch, and Brugger, 2006).

Synaesthetic interactions involving hearing and touch have rarely been documented, however recently Ro et al. (2007) report a single case of acquired auditory-tactile synaesthesia in a female patient following a discrete neurological lesion to the right ventrolateral thalamus. The synaesthesia was first reported 18 months post lesion when the patient began to feel tactile sensations in response to sounds. The synaesthetic somatosensations were typically experienced on the patient's left upper part of the body and a test of consistency (across three testing sessions separated by 35 and 15 days) indicated that they were generally consistent over time. Magnetic resonance imaging (MRI) and diffusion tensor imaging (DTI) conducted at approximately 3 years post lesion indicated disorganised fibre bundles in the right ventrolateral thalamus (lesion site) - at 3 years post onset DTI tracking from the unaffected left hemisphere showed direct projections to motor / premotor cortices, whereas fibre bundles in the lesioned hemisphere were disorganised and smaller compared to the unaffected hemisphere. DTI conducted at 1.3 years post onset (i.e. before synaesthetic experiences were reported) indicated no white matter differences between the right and left ventrolateral thalamus. The authors suggest that this disorganisation in cortico-callosal pathways may account for synaesthetic experiences (Ro et al., 2007; see Chapter 9).

In addition to cases of acquired auditory-tactile synaesthesia there are a number of accounts of acquired synaesthesia involving vision-touch interactions. For example, patient D.N., suffered paralysis and loss of sensation in the left side of his body following stroke. This resulted in D.N. being unable to feel any tactile stimulation presented to the left side when the touch was hidden from view, however if tactile stimulation was made visible then D.N. was able to feel touch to the left side. Similarly, when observing previous videos of his arm being touched and informed that this reflected live video feedback D.N. reported being able to feel his arm being touched despite the fact that the experimenter was not actually touching him. In this sense, observed bodily touch attributed to the patient lead to tactile sensations, indicating that in some conditions vision alone can be sufficient to elicit tactile stimulation (Halligan et al., 1996). Such findings appear consistent with research in the non-synaesthetic population which indicates that observing one's own body can lead to enhancements in one's own tactile sensitivity (Taylor-Clarke, Kennett, and Haggard, 2004) and with evidence provided by Rorden and colleagues (1999) of a patient whose tactile detection increased when observing a flash of light to a rubber hand seen in the same orientation and directly above the patient's concealed hand (i.e. when the rubber hand was attributed to the participant's own body). Taken collectively these findings highlight the important role of vision, and more so of observing one's own body, on haptic perception.

In addition to cases of acquired vision-touch synaesthesia involving one's own body there is also one case report involving an interaction between observed and actual pain ("mirror pain"). This anecdotal report, given to clinicians posthumously by the patient's wife, describes a man who experienced observed pain to others as actual pain to himself (Bradshaw and Mattingley, 2001). Here the inducer is observed touch to another's body rather than to one's own body as described above. The patient was known to have suffered widespread cancer, but as this case was reported post-mortem no information about the neural circuitry involved was available. More recently however, evidence for the interpersonal sharing of observed pain has been provided (Singer, Seymour, O'Doherty, Kaube, Dolan, and Frith, 2004; Morrison, Lloyd, di Pellegrino, and Roberts, 2004; Avenanti, Beuti, Galati, and Aglitoi, 2005). For example, Avenanti and colleagues (2005) report that observing pain to another person results in significant reductions in motor evoked potentials (MEPs). The modulation of MEP amplitude correlated with subjective ratings of the sensory aspects of pain attributed by the observer to the actor and was somatotopically organised such that the reduced amplitude was specific to the muscles observed in a painful event. These authors suggest that the findings provide evidence for a mirror-pain resonance system in which observed pain is matched to the observer's own sensorimotor representation of pain. Such interpretation builds upon the findings of mirror neurons within the monkey premotor cortex and inferior parietal lobule, which respond both when a monkey performs an action and when the monkey watches another person perform a similar action (Gallese, Fadiga, Fogassi, and Rizzolatti, 1996; Rizzolatti and Craighero, 2004) and evidence for similar mirror systems in the human brain for not only action (Buccino et al., 2001), but also touch (Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004; Blakemore et al., 2005; Ebisch, Perucci, Ferretti, Del Gratta, Luca Romani, and Gallese, 2008), pain (Singer et al., 2004; Aventani et al., 2005), disgust (Wicker, Keysers¸ Plailly, Royet, Gallese, and Rizzolatti, 2003) and other emotions (Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003).

Similar to the case of acquired "mirror pain" described above; developmental cases of vision-touch or "mirror-touch" synaesthesia have also been documented (Blakemore et al., 2005; Banissy and Ward, 2007). First reported in a single case fMRI study (Blakemore et al., 2005), mirror-touch synaesthesia refers to cases of synaesthesia in which observing touch to another person leads to tactile sensations on the equivalent part of the synaesthete's own body. In the original study by Blakemore and colleagues (2005) the case of synaesthete C was described. C reports experiencing touch on her own body when observing another person being touched, but not when observing inanimate objects being touched. These experiences have been described as being automatic, in so far as they occur whenever she observes another person being touched, and to have occurred throughout her lifetime. Her experiences mirror observed touch to another person, such that observing touch to another person's left facial cheek leads to a sensation of touch on her own right facial cheek (i.e. as if looking at a mirror reflection of herself). Using fMRI Blakemore and colleagues investigated the neural systems underlying C's synaesthetic experience by contrasting brain activity when watching videos of humans relative to objects being touched (the latter did not elicit synaesthesia) in the synaesthete and in 12 non-synaesthetic control subjects. In controls a network of brain regions were activated during the observation of touch to a human relative to an object, including primary and secondary somatosensory cortex, premotor regions and the superior temporal sulcus. Similar brain regions were also activated during actual touch, indicating that observing touch to another person activates a similar neural circuit as actual tactile experience – a "mirror touch" system. A comparison between synaesthete C and non-synaesthetic subjects indicated that the synaesthete showed hyper activity within a number of regions within this network (including primary somatosensory cortex) and additional activity in the anterior insula (Figure 1.3). Thus suggesting that mirror-touch synaesthesia is a consequence of increased neural activity in the same mirror-touch network that is evoked in non-synaesthetic controls when observing touch to another person (Blakemore et al., 2005).

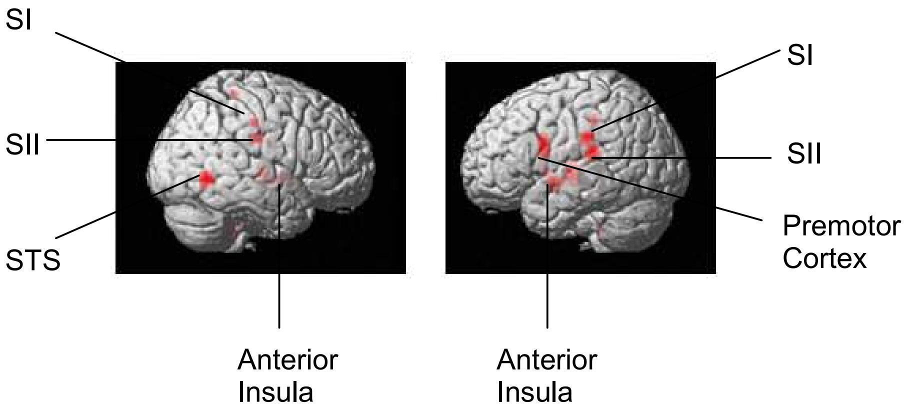


Figure 1.3 Activations resulting from the interaction between mirror-touch synaesthete ‘C’ and non-synaesthetic control participants. The subtraction shown indicates the brain regions more active in synaesthete ‘C’ compared to non-synaesthete controls when observing touch to a human relative to an object. The primary (SI) and secondary somatosensory cortex (SII), bilateral anterior insular and the left premotor cortex were significantly more active in C than in the control group (Blakemore et al., 2005).

More recently, Banissy and Ward (2007) report a behavioural study of ten developmental mirror-touch synaesthetes, including C. Notably, while all synaesthetes report similar experiences (i.e. tactile sensations when observing touch to another person) some important individual differences were found between them. It appears that mirror-touch synaesthetes can be divided into two subgroups based upon the spatial mapping between observed and felt (synaesthetic) touch (Figure 1.4). Some synaesthetes report that an observed touch to the left cheek is felt on their right cheek (as if the other person is a mirror reflection of oneself – hereafter referred to as the ‘specular’ subtype) whereas others report synaesthetic touch on their left cheek when observing touch to another person’s left cheek (as if self and other share the same anatomical body space – hereafter referred to as the ‘anatomical’ subtype). The automaticity of these experiences was confirmed by the development of a visuo-tactile synaesthetic stroop experiment. In the task synaesthetes and matched non-synaesthetic controls were asked to detect a site touched on their own body (either facial cheeks or hands) while observing touch to another person's cheek/hands or to a corresponding object. Participants were asked to report the site of actual touch (left, right, or no touch) and to ignore observed touch. For synaesthetes, but not controls, observed touch to humans elicited a tactile sensation whose location was either in the same position as actual touch (congruent condition – as determined by synaesthetic self reports) or in a different spatial location (incongruent condition). Synaesthetes, but not control participants, were faster at detecting the location of actual touch during the congruent condition relative to the incongruent condition (Figure 1.5b). Further, synaesthetes produced a higher percentage of errors consistent with their synaesthesia (hereafter referred to as mirror-touch errors; i.e. reporting touch on trials involving no actual touch) compared to other error types and to control participants (Figure 1.5c).

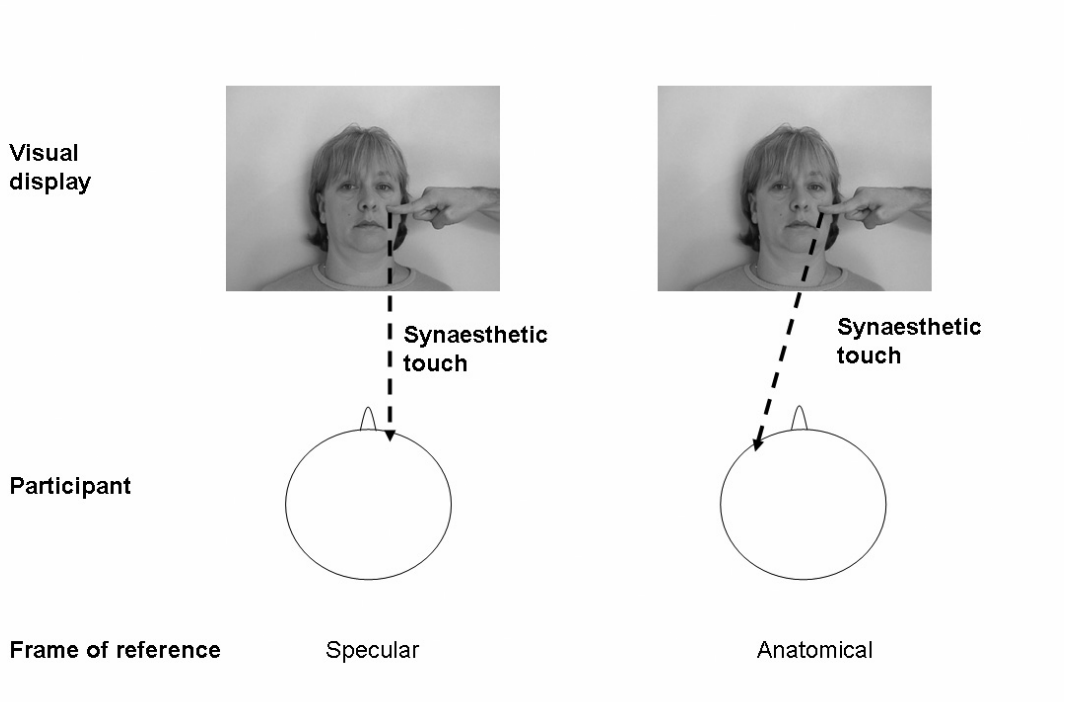


Figure 1.4 Specular and anatomical spatial mappings reported by mirror-touch synaesthetes (c.f. Banissy and Ward, 2007). Under a specular frame of reference, mirror-touch synaesthetes report synaesthetic touch as if looking in a mirror. Under an anatomical frame of reference synaesthetic experience is as if self and other share the same anatomical body space.

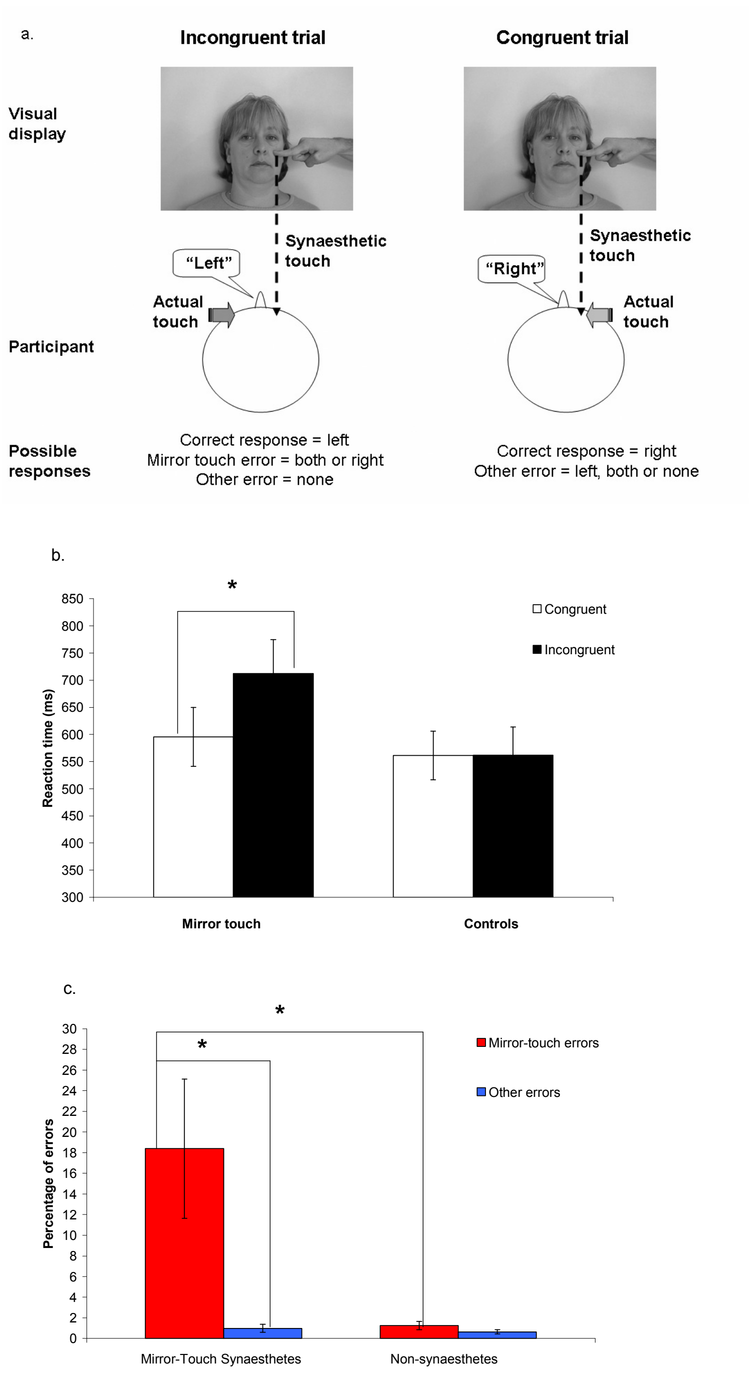


Figure 1.5 Summary of Banissy and Ward (2007). (a) Task Protocol. Participants were required to report the site upon which they were actually touched (i.e. left cheek, right cheek, both cheeks or no touch) while ignoring observed touch (and the synaesthetic touch induced from it). Note that although the example given is for a specular mirror-touch synaesthete, both subtypes were tested and congruency was determined according to each synaesthetes' self-reports. (b) Mirror-touch synaesthetes, but not controls, were significantly faster at detecting the site of real touch in the congruent relative to incongruent condition. (c) Mirror-touch synaesthetes also produced significantly more mirror-touch errors than controls (errors consistent with their synaesthesia), but not other error types. * = $p < .05$.

1.5 Synaesthesia and models of typical cognition

The preceding sections reviewed evidence for the authenticity of synaesthesia. While this is now well established, there is growing interest in using the condition to inform us about non-synaesthetic perceptual and cognitive processing. Following the logic of cognitive neuropsychology, the positive symptoms related to synaesthesia may be able to constrain theories on multisensory interactions and inform about the relationship between multisensory processing and other aspects of cognition (Ward and Mattingley, 2006; Cohen Kadosh and Henik. 2007).

So far, a number of examples have been cited whereby synaesthetic interactions have been shown to rely upon similar neurocognitive mechanisms as those observed in non-synaesthetes and therefore may inform us about general principles of multisensory interactions (e.g. feature binding in grapheme-colour synaesthesia; cross-modal interactions in touch-colour synaesthesia; heightened visual-tactile interactions in mirror-touch synaesthesia). Non-random associations, which are similar to those found in non-synaesthetic subjects, have also been found between pitch and lightness in tone-colour synaesthetes (individuals who experience colour sensations in response to tones) – both synaesthetes and non-synaesthetes show a tendency to associate low pitches with dark colours and high pitches with light colours, although only synaesthetes experience these colours consciously (Ward et al., 2007; also see Parise and Spence, 2009). Evidence of non-random associations in other variants have also been documented, including number and lightness in digit-colour synaesthesia (Cohen Kadosh and Walsh, 2008); word form properties and colour associations in linguistic-colour synaesthesia (Barnett, Feeney, Gormley, and Newell, 2009); and phonology and tastes in lexical-gustatory synaesthesia (Ward and Simner, 2003).

Further, in the case of feature binding in synaesthesia, it has been suggested that an integration of synaesthesia and patient-based research may contribute to our understanding of the binding problem – how two independently processed features are combined to be perceived as a unified experience (Robertson, 2003). In the numerical domain, digit-colour synaesthesia and spatial number-form synaesthesia have been successfully used as models to make inferences about the mental representation of two-digit numbers (Seron, Pesenti, Nöel, Deloche, and Cornet, 1992; Sagiv et al., 2006), the spatial representation of number (Sagiv et al., 2006), and whether numerical representations are compressed or linear (Cohen Kadosh et al., 2007).

One aim of this thesis is to use mirror-touch synaesthesia as a model to make inferences about the role of visual-tactile interactions in cognition and perception. As noted previously, mirror-touch synaesthesia is thought to arise because of hyper-activation of the same cortical network (the mirror-touch system) which is active in non-synaesthetes when observing touch to others (Blakemore et al., 2005). In recent years there has been much interest in the role brain systems with mirror properties (e.g. the mirror-touch system) may play in social cognition (Gallese, Keysers, and Rizzolatti, G, 2004; Gallese, 2006; Keysers and Gazzola, 2006). Moreover, it has been suggested that brain systems with mirror properties (i.e. common brain regions in the experience and observation of a particular sensation) may act as a neurophysiological candidate to facilitate sensorimotor simulation of another's experience and thereby promote an understanding of another's emotions / experience (Gallese, Keysers, and Rizzolatti, G, 2004; Gallese, 2006; Keysers and Gazzola, 2006). Given that mirror-touch synaesthesia has been linked to neural mechanisms common to us all when observing touch to another person (i.e. hyper activity within the tactile mirror system), this variant of synaesthesia highlights one means in which synaesthesia may be used to investigate vision-touch interactions more generally – namely what is the impact of heightened sensorimotor simulation on affective processing. Moreover, mirror-touch synaesthesia is currently one of the only forms of synaesthesia which depends upon interpersonal interaction and therefore offers a unqiue opportunity to assess mechanisms of social perception.

1.6 Aims of thesis

This thesis has two primary aims. The first is to investigate cases of mirror-touch synaesthesia and to document neurocognitive and perceptual profiles associated with the condition. This includes investigations into the prevalence, characteristics, and perceptual processing of mirror-touch synaesthesia. The second is to investigate the function of sensorimotor simulation mechanisms (thought to underpin mirror-touch synaesthesia) in cognition. This aspect of the thesis aims to evaluate the importance of somatosensory resources for social cognition and examine the hypothesis that sensorimotor simulation is critical for understanding the emotions and thoughts of others (Adolphs, 2002; Adolphs, 2003; Gallese, Keysers, and Rizzolatti, G, 2004; Gallese, 2006; Gallese and Goldman, 1998; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007). Studies involving non-synaesthetic individuals and studies using synaesthetic participants to inform us about the role of sensorimotor simulation in affective processing shall be presented.

CHAPTER 2: PREVALENCE AND CHARACHTERISTICS OF MIRROR-TOUCH SYNAESTHESIA

In so-called 'mirror-touch synaesthesia', observing touch to another person induces a subjective tactile sensation on the synaesthete's own body. It has been suggested that this type of synaesthesia depends on increased activity in neural systems activated when observing touch to others. This is the first study on the prevalence of this variant of synaesthesia. The findings indicate that this type of synaesthesia is just as common, if not more common than some of the more frequently studied varieties of synaesthesia such as grapheme-colour synaesthesia. Additionally, behavioural correlates associated with the condition are examined further. In a second experiment, it is shown that synaesthetic experiences are not related to somatotopic cueing - a flash of light on an observed body part does not elicit the behavioural or subjective characteristics of synaesthesia. Finally, a neurocognitive model to account for these characteristics is proposed and the implications of the findings are discussed in relation to general theories of synaesthesia.

2.1 Introduction

As noted in chapter 1, the term synaesthesia is used to describe a condition in which one property of a stimulus (the inducer) results in conscious experiences of an additional attribute (the concurrent). This inducer-concurrent relationship can occur either within or between modalities. For example, in grapheme-colour synaesthesia a visually or auditorily presented grapheme can result in synaesthetic experiences of colour (Ramachandran and Hubbbard, 2001; Cohen Kadosh and Henik, 2007; Rich and Mattingley, 2002), whereas in lexical-gustatory synaesthesia written or heard words trigger a subjective sensation of taste (Ward and Simner, 2003).

Early research on the prevalence of synaesthesia indicated that the condition may have a minimum prevalence rate of 1 in 2000 with a female-to-male ratio of 6:1 (Baron-Cohen, Burt, Smith-Laittan, Harrison, and Bolton, 1996; Rich, Bradshaw, and Mattingley, 2005). These studies assessed the prevalence of the condition based upon the number of respondents to newspaper advertisements who pass an objective measure of synaesthesia (relative to newspaper circulation figures). This method of assessment does not permit inferences about non-responders and may also lead to an over inflated female to male ratio. More recent studies, which overcome these difficulties by screening a large population and supplementing this with the use of objective measures of different variants of synaesthesia, suggest a higher prevalence rate of 4% and a female to male ratio of 1:1 (Simner et al., 2006; Ward and Simner, 2005). These studies indicate that the most common forms of the condition include day-colour synaesthesia (estimated to have a prevalence of 2.8%; Simner et al., 2006) and grapheme-colour synaesthesia (estimated to have a prevalence of 2%; Simner et al., 2006).

Since these studies, a new variant of synaesthesia has been documented in which observing touch to another person induces a tactile sensation on the synaesthete's own body (mirror-touch synaesthesia). A single case fMRI study suggests that this variant of synaesthesia is a consequence of increased neural activity in a network of brain regions which are also activated in non-synaesthetic control subjects when observing touch to another person (Blakemore, Bristow, Bird, Frith, and Ward, 2005). In that study, the authors contrasted brain activity in a single mirror-touch synaesthete with twelve non-synaesthetic control subjects while observing humans relative to objects being touched. This indicated that while similar brain regions were active in the observed touch condition as when participants were touched (a mirror-touch system present in non-synaesthetes), the synaesthete showed increased activity within bilateral primary somatosensory cortex (SI), secondary somatosensory cortex (SII), left premotor cortex and additional activity in the anterior insula relative to non-synaesthetes. In view of this, it was argued that mirror-touch synaesthesia reflects hyper-activation of normal (i.e. non-synaesthetic) visual-tactile interactions in the mirror-touch network (i.e. SI, SII, premotor cortex). Notably, the general role of SI activations in the mirror-touch system in non-synaesthetes remains to be clarified, with some authors reporting SI activity when non-synaesthetes observe touch to another's face (Blakemore et al., 2005) or arm (McCabe, Rolls, Bilderbeck, and McGlone, 2008), others reporting SII, but not SI, activation following observed touch to the legs (Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004), and others reporting SI activity when non-synaesthetes observe intentional but not unintentional touch (Ebisch, Perrucci, Ferretti, Del Gratta, Romani, and Gallese, 2008).

Extending the single case report, a group study of ten mirror-touch synaesthetes showed that individuals with mirror-touch synaesthesia can be divided into two subtypes based upon the spatial mapping between observed and synaesthetically induced touch. Some synaesthetes report a spatial mapping as if looking in a mirror (i.e. observed touch to another person's left cheek induces synaesthetic touch on their right cheek - *specular* subtype), while others report a spatial mapping as if self and other share the same anatomical body space (i.e. experiencing synaesthetic touch on their left cheek when observing touch to another person's left cheek – *anatomical* subtype; (Banissy and Ward, 2007).

Authenticity and characteristics of synaesthesia

When considering the prevalence of mirror-touch synaesthesia it is important to note what constitutes synaesthesia in general and the methods used to confirm the authenticity of the condition. Synaesthesia is typically considered as having three defining features; 1) experiences are conscious perceptual or percept-like experiences; 2) experiences are induced by an attribute not typically associated with that conscious experience; 3) these experiences occur automatically (Ward and Mattingley, 2006). In line with this, mirror-touch synaesthesia requires the conscious experience of a tactile stimulus which occurs automatically following the observation of touch to another person (or possibly an object; see Banissy and Ward, 2007). There are several ways to determine the validity of mirror touch synaesthetes, for example, with regards to automaticity, Banissy and Ward (2007) developed a visuo-tactile congruity experiment to explore this aspect of synaesthesia (for description see Chapter 1; also see Blakemore et al., 2005 methods to assess validity mirror-touch synaesthesia).

Synaesthesia has a number of other important characteristics that also appear to be found in the mirror-touch variety. Synaesthetic experiences tend to be consistent over time (e.g. if 'A' is red at time 1 then it will be at time 2 several weeks or months later; Baron-Cohen, Wyke, and Binnie, 1987). Mirror-touch synaesthetes report their experiences to be enduring and an individual's spatial sub-type (i.e. whether they belong to the specular or anatomical category) is consistent both across time and across different body parts. Further, whilst it was once believed that synaesthetic experiences reflect random but consistent associations this view is no longer widely held. For example, non-random associations have been found between; pitch and lightness (Ward, Huckstep, and Tsakanikos, 2006); number and lightness (Cohen Kadosh, Henik, and Walsh, 2007); grapheme frequencies and colour (Simner et al., 2005); and phonology and tastes (Ward and Simner, 2003). More overt semantic links are also found: it is not uncommon for the word "sausage" to taste of sausage (and similarly for other food names; Ward, Simner and Auyeung 2005) or for the word "red" to be coloured red (and similarly for other colour names; Gray et al., 2002; Rich et al., 2005). The mappings in mirror-touch synaesthesia are non-arbitrary in that somatotopy is generally preserved between the observed and felt touch.

Here two studies investigating the prevalence and the characteristics of mirror-touch synaesthesia are presented. In Experiment 1, the prevalence of mirror-touch synaesthesia is investigated by screening a large population and confirming self reports using a behavioural paradigm designed to test for the authenticity of the condition. Then potential factors which may contribute to the behavioural correlates observed are addressed. Experiment 2 examines the nature of the synaesthetic inducer and considers the role of somatotopic cueing on synaesthetic experience. Finally, the factors which may underpin synaesthetic experience are discussed and a neurocognitive model of mirror-touch synaesthesia is outlined.

2.2 Experiment 1: Prevalence of mirror-touch synaesthesia

This study investigates the prevalence of mirror-touch synaesthesia and compares new cases with previously studied cases of mirror-touch synaesthesia (Banissy and Ward, 2007) to ascertain the main cognitive characteristics of the condition.

Method

All participants (n = 567) were recruited from the University College London and University of Sussex undergraduate communities. Each participant was given a written and verbal description of synaesthesia including examples of what did and did not constitute synaesthesia. Participants were then administered a questionnaire asking about different variants of synaesthesia with one question specifically related to mirror-touch synaesthesia (Appendix 1). Participants were asked to indicate on a five point scale the extent to which they agreed with the question “Do you experience touch sensations on your own body when you see them on another person’s body?” Following initial screening, all participants who gave positive responses to the above question (n = 61; approximately 10.8% of all subjects) were contacted and interviewed about their experiences. This included them being shown a series of online videos showing another person, object, or cartoon face being touched.

Participants were asked to indicate the location (if any) in which they experienced a tactile stimulus and the type of experience. Typical responses of potential mirror-touch synaesthetes (n = 14; approximately 2.5% of all subjects) included reports that observing touch elicits a tingling somatic sensation in the corresponding location on their own body, and that a more intense and qualitatively different sensation is felt for painful stimuli (i.e. videos of a pin pricking a hand rather than observed touch to the hand).

In an attempt to investigate reports of mirror-touch synaesthesia the performance of each potential synaesthete was compared to ten age and gender matched non-synaesthetic control subjects on the paradigm developed by Banissy and Ward (2007). In the task, participants were required to detect a site touched on their own face (left, right, both or none) while observing touch to another person's face or to a corresponding object (a lamp). For synaesthetes, but not for controls, observed touch elicited a synaesthetic sensation in a congruent or incongruent location as actual touch (Figure 2.1). The tactile stimuli were administered via two miniature solenoid tappers attached to the face with a Velcro strap. Each tapper was controlled using a Dual Solenoid Tapper Controller (MSTC3-2, M and E Solve) and the intensity of taps was filtrated to account for individual sensitivity of the participant (as in Banissy and Ward, 2007). The visual stimuli were presented on a 17" CRT monitor with a refresh rate of 100Hz, were sized to fit the screen, and consisted of two presentations of 100 ms each followed by a third stimulus which remained on the screen until the participant responded. The first two stimuli showed the approach of the hand towards the face and the third showed contact with the face. After a 10 ms presentation of the final slide participants received a tap to either their left, right or both cheeks. The location of the felt touch (left, right, both or none) was indicated with a button press and the need for both speed and accuracy was emphasised. Following this, there was a gap of 1500 ms with a fixation cross before the start of the next trial. A train of white noise was presented via headphones for the duration of each trial in order to prevent participants from using auditory cues (i.e. the sound of the taps) to determine the location of actual touch (c.f. Banissy and Ward, 2007 for more details on task methodology) .

A total of 80 congruent trials, 80 incongruent trials and 80 trials involving no actual touch were completed. For each potential synaesthete, congruency was determined according to self reports when observing videos showing another person being touched. Within each condition, 60 trials involved observed touch to either a female or male actor, with the remaining 20 trials involving observed touch to a corresponding object. The order of trials was randomised over 3 blocks of 80 trials (preceded by 5 practice trials). Reaction times and error rates were measured. Based upon previous findings synaesthetes were expected to be faster at identifying a site touched in the congruent compared to incongruent condition and / or to show a higher proportion of mirror-touch errors compared to non-synaesthetic controls. The control data were scored according to the reported sub-type of the corresponding mirror-touch synaesthete (i.e. anatomical versus specular congruency).

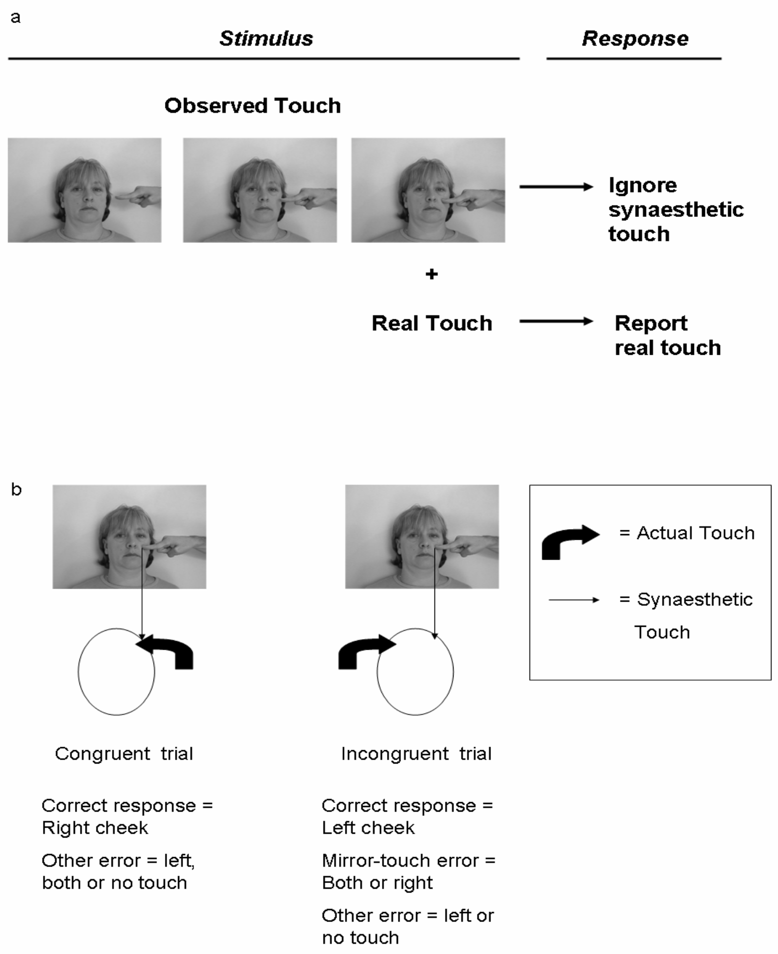


Figure 2.1 (a) Summary of the task used to confirm potential cases of mirror-touch synaesthesia in experiment 1. Participants were asked to detect the site of real touch while observing another person being touched. For mirror-touch synaesthetes observed touch elicited a tactile sensation which could either be in a congruent or incongruent location as the site real touch. (b) Example of congruent and incongruent trials including error types for a specular mirror-touch synaesthete. On a congruent trial, real touch was applied to the same side of the face as synaesthetic experience. On an incongruent trial real touch was applied to the side of the face which was opposite to synaesthetic experience. Participants were asked to report the location of real touch and to ignore synaesthetic touch. 'Mirror-touch' errors could be produced on incongruent trials if the subject was to report real touch to both cheeks (despite real touch being applied to one cheek only) or if the subject was to report synaesthetic rather than real touch. All other error types were classified as 'Other' error types.

Results and Discussion

Behavioural performance of each potential synaesthete was compared to an age and gender matched non-synaesthetic control group using Crawford's modified t-test (Crawford and Garthwaite, 2002). Reaction time performance (filtered prior to analysis, ± 3 s.d. and all errors removed) and the percentage of error types on human and object trials were compared separately (Table 2.1). For reaction time performance, the size of congruency effect (incongruent minus congruent reaction time) was used as an index of synaesthetic experience. For errors, the percentage of mirror-touch errors (errors consistent with synaesthetic experience) and other error types were compared. Subjects who showed either significantly larger reaction time differences or significantly more mirror-touch errors relative to controls were counted as synaesthetes. Using this method nine cases (seven female)[1] of mirror-touch synaesthesia were confirmed on reaction time performance, the percentage of mirror-touch errors produced, or both (Table 2.1). This indicates a prevalence rate of 1.6%. In comparison to previous prevalence estimates of other types of synaesthesia this places mirror-touch synaesthesia as one of the most common forms of synaesthesia along with grapheme-colour synaesthesia (1.4% prevalence) and day-colour synaesthesia (2.8% prevalence; Simner et al., 2006).

Comparison of the prevalence group with previously reported cases

In order to ensure that these cases were consistent with previously reported cases of mirror-touch synaesthesia, these characteristics of synaesthetic experience were considered further by contrasting synaesthetes recruited through the prevalence study (n = 9) with mirror-touch synaesthetes recruited via self referral including some

---

[1] Participants came from courses with a higher female-male ratio and gender information for non-respondants was not available, so no empirical claims about female-male ratio of mirror-touch synaesthetes are made.

previously reported cases (n = 12). Reaction time (Congruency x Group) and the percentage of error types (Error Type x Group) were compared separately using a 2 x 2 ANOVA (Figure 2.2a, 2.2b – for comparison non-synaesthetic control data, n = 20, is also shown, but not included in analysis). One participant from the self referral group was withdrawn from analysis of reaction times due to an insufficient number of correct responses (< 25% correct responses in any one condition).

Analysis of reaction time data revealed a significant main effect of congruency, with subjects performing faster overall on trials which were congruent with their synaesthesia compared to incongruent trials [$F(1, 18) = 13.98$, $p = < .01$]. Analysis of error type data revealed a significant main effect of error type, which was due to a higher proportion of mirror-touch errors being produced relative to other error types [$F(1, 19) = 11.18$, $p = < .01$]. No significant interaction or main effect of group was found for reaction time (*Group:* [$F(1, 18) = .048$, $p = .829$]; *Group x Cong:* [$F(1. 18) = .095$, $p = .761$]) or error type analysis (*Group:* [$F(1, 19) = 2.77$, $p = .113$]; *Group x Cong:* [$F(1. 19) = 2.75$, $p = .114$]). This indicates that the prevalence and self-referred mirror-touch synaesthete group come from the same population with regard to congruency effects. Therefore, both prevalence and self-referred cases are combined to consider additional cognitive characteristics of mirror-touch synaesthesia.

For the majority of cases, the effects of spatial congruity are found for bodies but not objects and this corresponds well with their phenomenological reports. There are, however, a minority of synaesthetes who do report tactile experiences when watching objects being touched (4 out of 21). For some of these synaesthetes, this experience is reported in the finger tip that is touching the objects, but for others synaesthetic touch is mapped onto particular body locations which are thought to spatially correspond to the object being touched (e.g. when looking directly at a monitor the experience maps onto the face, but when standing in front of the monitor the experience maps onto the trunk). In addition, another minority of synaesthetes (6 out of 21, including I., Z. and H.G. in Table 2.1) show an effect of spatial congruity for both bodies and objects despite initially claiming to experience synaesthesia for touched bodies alone. One possibility is that this reflects the fact that object trials are interleaved with the more frequent human trials and this leads to objects being treated more like human bodies than expected. In the normal population, fMRI studies suggest that the tactile mirror system does respond to objects under some circumstances (Ebisch et al., 2008; Keysers et al., 2004).

Of the 21 cases of mirror-touch synaesthesia reported to date, seventeen (nine of which come from the prevalence sample) report a specular frame of reference and four report an anatomical frame of reference. This finding is consistent with studies on imitation behaviour which demonstrate that both adults and children tend to imitate in a specular mode (Schofield, 1976; Franz, Ford, and Werner, 2007). The relative bias in synaesthetes could be due to the fact that one's own head is only ever seen from a mirror-reflected perspective and this regularity may drive the choice of spatial frame. However, it is to be noted that those synaesthetes who adopt a specular frame for the head also do so with the hands (Banissy and Ward, 2007) even though this part of one's own body is not normally viewed from a reflected perspective.

A general characteristic of synaesthesia is that different variants of synaesthesia tend to co-occur (Simner et al., 2006). Some preliminary evidence based upon self reports suggests that this may also be the case with mirror-touch synaesthetes. While, some mirror-touch synaesthetes only report mirror-touch synaesthesia (implying that the overall prevalence of synaesthesia may be higher than the previously assumed 4% estimate), nine of the twenty-one mirror-touch synaesthetes sampled also report genders or personalities for graphemes and/or certain other linguistic stimuli (e.g. 3 is a bossy male; Simner and Holenstein, 2007; Smilek, Malcolmson, Carriere, Eller, Kwan, and Reynolds, 2007). Five of these cases have been confirmed using behavioural tests for this phenomenon (N. Sagiv, personal communication). Additionally, seven report synaesthetic experiences of colour for linguistic stimuli. Notably, this data is preliminary because the sample contains a mixture of randomly (i.e. prevalence group) and non-randomly sampled participants (i.e. self-referred group), and because members of the prevalence group were not systematically tested for other variants of synaesthesia.

Synaesthete	**Human Trials**			**Object Trials**		
	Reaction time	**% Mirror-touch**	**% Other**	**Reaction time**	**% Mirror-touch**	**% Other**
D	431.24^{***}	5.81^{**}	0.58	11.26	0	0
I	38.97	10.29^{***}	3.43^{**}	-51.11	10.34^{***}	5.17^{*}
Z	-34.98	6.86^{**}	0.57	-28.52	6.67^{**}	1.67
E	79.45^{*}	1.14	0	-18.2	0	0
K	84.84^{*}	2.25	4.49^{***}	-20.2	1.67	0
J	53.96	6.62^{***}	0.60	7.77	0	1.75
R	532.13^{***}	6.43^{***}	0.58	54.38	0	0
H.S	214.25^{***}	0.68	0.68	-7.05	0	0
H.G	136.38^{**}	24.02^{***}	0.56	52.67	10.17^{***}	1.69

Table 2.1 Reaction time performance (incongruent condition reaction time minus – congruent condition reaction time) and percentage of mirror-touch and other error types for potential synaesthetes when observing a human or corresponding object being touched. Three synaesthetes showed behavioural correlates of mirror-touch synaesthesia on reaction time only, three on mirror-touch errors only, and three on both reaction times and errors (* $p = < 0.05$; ** $p = < 0.01$; *** $p = < 0.001$ relative to control performance).

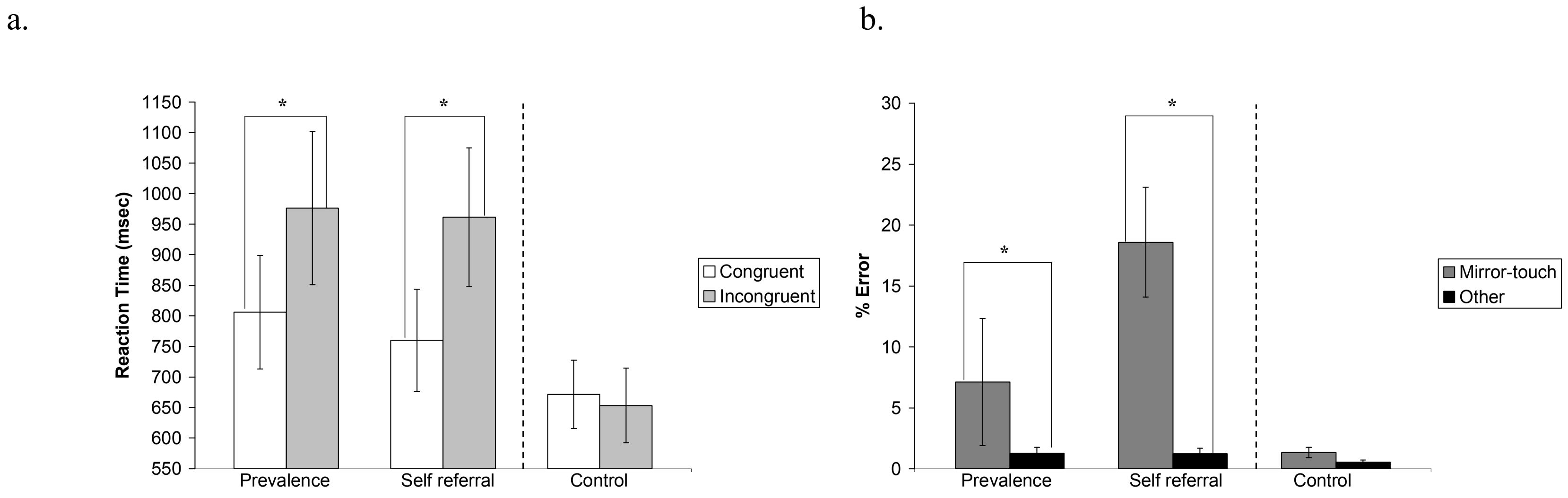


Figure 2.2 Mean reaction time performance (a) and percentage of error types (b) on human trials for mirror-touch synaesthetes recruited within the prevalence study compared to synaesthetes recruited via self-referral (control group performance is shown for comparison). ± s.e.m (* $p =< 0.05$).

2.3 Experiment 2: Behavioural correlates and somatotopic cueing

While the results from experiment 1 establish evidence for the authenticity of mirror-touch synaesthesia and suggest that behavioural correlates are related to ‘observed bodily touch’, it remains unclear if the behavioural data could also be consistent with ‘observed bodily cueing’ – whereby an observed visual event cues a particular location on the body. There is growing evidence from research investigating visual-tactile interactions that non-informative vision associated with one’s own body can influence tactile processing (e.g. Johnson, Burton, and Ro, 2006). In order to establish whether the findings could be related to somatotopic cueing, the performance of mirror-touch synaesthetes and non-synaesthetic subjects was compared on a condition in which a human face is observed but is accompanied by a flash of light on the cheek rather than a touch. As these stimuli did not induce synaesthesia it was expected that the pattern of effects shown by synaesthetes on experiment 1 would be related specifically to ‘observed bodily touch’ and that differences between synaesthetes and non-synaesthete controls would not be found for ‘observed bodily cueing’.

Method

Ten mirror-touch synaesthetes (7 females and 3 male, mean age ± Std. Error = 30.1 ± 11.17 years; 1 anatomical and 9 specular) and ten non-synaesthetic controls matched for age and gender (7 females and 3 males, mean age ± Std. Error = 31 ± 13.23 years) took part. Congruency was determined according to synaesthetes’ self reports when observing touch to another person. Controls were randomly allocated to either a specular or anatomical congruency group to match the synaesthetic group.

The experimental task and procedure was the same as Experiment 1, with the exception of the stimuli presented (Figure 2.3). For the human trials, rather than observing touch to the cheek(s), a flash of light appeared on the observed person's cheek(s). As before, the visual stimuli consisted of 3 frames which were sized to fit the screen. The first stimulus, lasting 100 ms, depicted a male or female face. The second stimulus, also lasting 100 ms, was the same as the first except that a patch of white light appeared on the person's left/right/both cheek(s). The flash was then removed for the third stimulus which remained on the screen until the participant responded. The tactile stimulus was applied 10 ms after the flash, i.e. at the onset of the third stimulus. For the control trials, all pictures of the person were replaced by a blank screen with a 100ms flash of light on the left, right or both sides of space immediately before the tactile event. A total of 306 trials were completed, of which 180 involved human stimuli and 126 involved control stimuli.

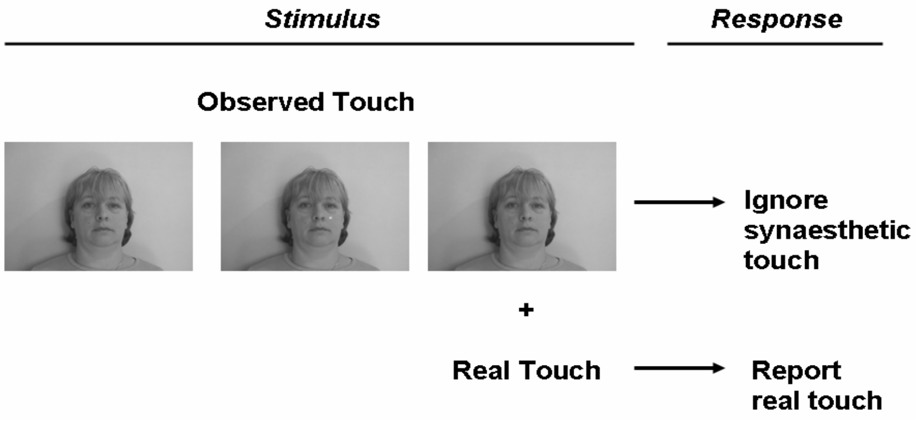


Figure 2.3 Summary of the task used for somatotopic cueing experiment. Participants observed a flash of light on the left/right/or both cheek(s) of another person. Immediately following the light flash, subjects were touched on their own facial cheeks (either left, right or both cheeks). Participants were asked to report the site of real touch.

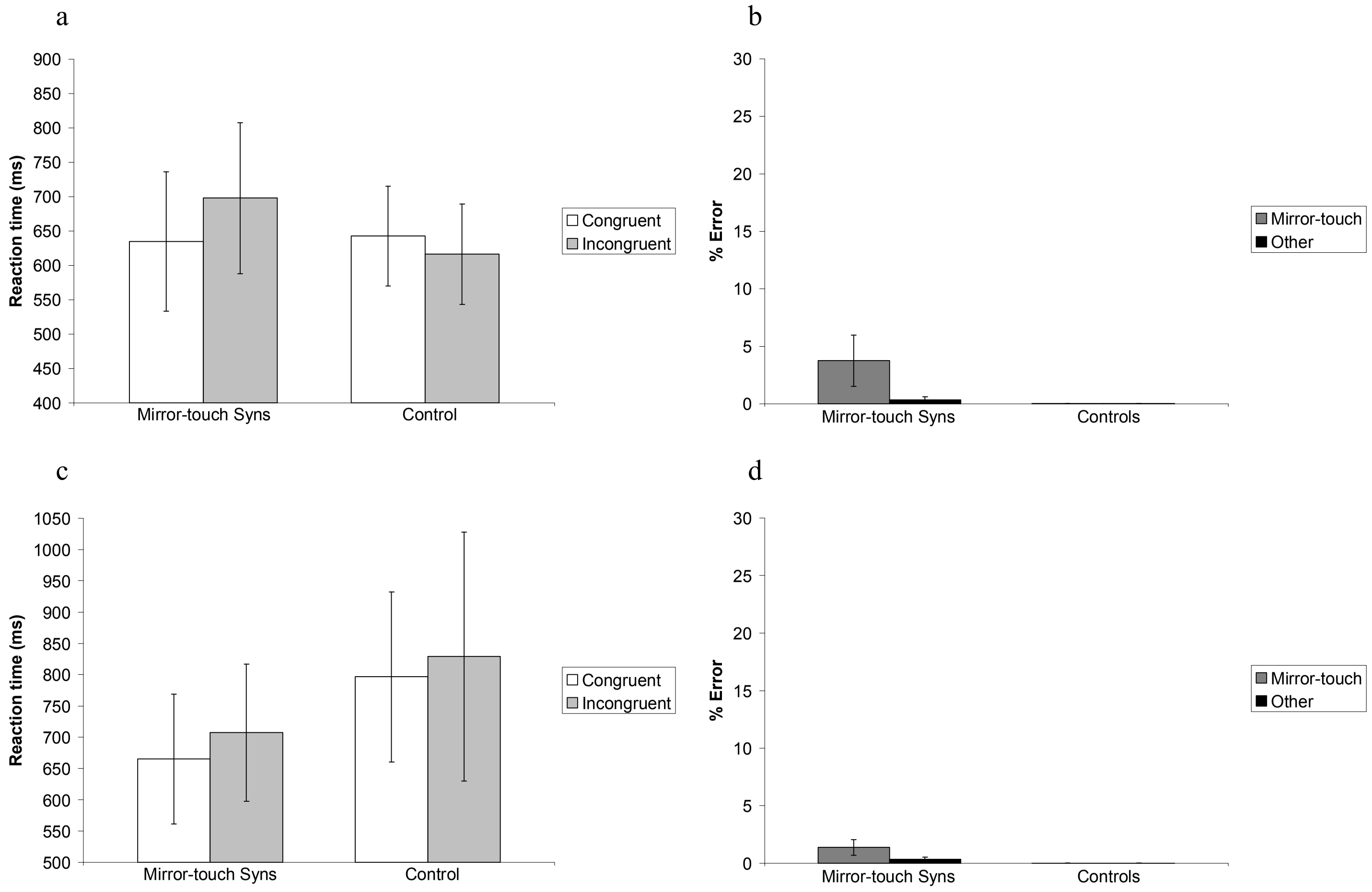


Figure 2.4 Mean reaction time performance and percentage of error types for mirror -touch synaesthetes and non-synaesthetic control subjects observing a light flash on another person's face (a; b) or a light flash only (c; d). ± s.e.m.

Results and Discussion

The results are summarised in Figure 2.4. Reaction times and error rates were measured. Reaction time data were filtered prior to analysis (± 3 s.d. and all errors removed). A 2 (Group) x 2 (Congruency) ANOVA conducted on reaction times revealed no significant main effects or interactions (p = > .05 in all cases; Figure 2.4a). Although the direction of the effect was the same as in Experiment 1 the effect was not significant. Analysis of the percentage of error types made by participants on human trials also revealed no significant main effects or interactions (p = > .05 in all cases; Figure 2.4b). Similarly, no significant differences were observed on control trials (Figure 2.4c, d). These findings are unlikely to be due to the fact that the flash of light is less salient than the hand, because the synaesthetes also failed to show an effect in Experiment 1 when a hand was used on a non-human object.

To further validate that the performance of mirror-touch synaesthetes significantly differed between experiment 1 and 2 a within-group comparison on the size of congruency effect (incongruent minus congruent trial reaction time) shown by synaesthetes across each task was conducted. This revealed that synaesthetes showed a significantly greater effect of congruency on trials involving observed touch to a human face in experiment 1 (mean ± s.e.m = 208.24 ± 52.32 msec) compared to a flash of light shown on a human face in experiment 2 (mean ± s.e.m = 51.49 ± 34.18 msec), [t(9) = 2.98, p = < .02]. Thus the findings from Experiment 1 are related specifically to ‘observed bodily touch’ and cannot be attributed to somatotopic cueing.

2.4 General Discussion

Taken together, these measures detail the prevalence and characteristics of mirror-touch synaesthesia. In relation to prevalence, the findings suggest that:

- mirror-touch synaesthesia is one of the more common forms of synaesthesia
- there are two sub-types (specular and anatomical) depending on the visuo-tactile spatial transformation used
- the specular (mirror-reflected) sub-type is the more common
- the effects are quite specific to observed touch to a human body.

In many respects, mirror-touch synaesthesia shares common ground with other types of synaesthesia; for instance, with regards to phenomenology, automaticity, consistency (of the spatial mapping), reliability over time, and possibly with regards to associated traits (e.g. attributing personalities and genders to graphemes). However, when one turns to consider its neural basis the similarities are less apparent. A current area of debate in the synaesthesia literature is whether synaesthetic experience is due to cross-activation between brain regions or cortical disinhibition (Bargary and Mitchell, 2008; Cohen Kadosh, Henik, Catena, Walsh, and Fuetnes, 2009; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001; Hubbard and Ramachandran, 2005; Rouw and Scholte, 2007). Thus far, accounts of synaesthesia in terms of cross-activation have mainly focussed on grapheme-colour synaesthesia and highlight the role of adjacency between visual grapheme and colour processing areas in the fusiform gyrus (Ramachandran and Hubbard, 2001). It is possible that adjacency is one of several biasing principles that influence which forms of synaesthesia will, and will not, be found. Another biasing principle may be the ‘normal’ architecture for multi-sensory interactions. As noted before, there is now good evidence for a visuo-tactile mirror system in humans (Blakemore et al., 2005; Ebisch et al., 2008; Keysers et al., 2004) and mirror-touch synaesthesia could be construed as hyper-activity within this network (either as a result of cortical disinhibition or cross-activation).

Below I propose a model of this type of synaesthesia.

A Neurocognitive Model of Mirror-Touch Synaesthesia: What, Who, Where.

In this model, mechanisms thought to underpin synaesthetic experience are divided into processes involved in identifying the visual stimulus touched ("what" mechanism – shown in red boxes), discriminating between self and other ("who" mechanism – shown in blue boxes), and locating where on the body and in space observed touch occurs ("where" mechanism – shown in green boxes). Connections between processes common to all subjects are shown in black; connections between processes necessary for an anatomical reference frame in purple; connections between processes contributing to a specular reference frame are shown in orange (Figure 2.5).

Visual Encoding: "What" Mechanisms

With regards to the tactile mirror system, the putative "what" mechanisms are needed to implement several discriminations. Is this a human or object? Is this a face or body? One potential brain region which may be crucial to human body perception in mirror-touch synaesthesia is the extrastriate body area (EBA; Downing, Jiang, Shuman and Kanwisher, 2001). The EBA is a body-selective visual region which responds more to bodies and body parts, than faces, objects and object parts (Downing et al., 2001). This is in contrast to the fusiform body area (FBA; Peelen and Downing, 2005), a further body selective visual region, which appears more important for processing body parts into wholes (Taylor, Wiggett and Downing, 2007).

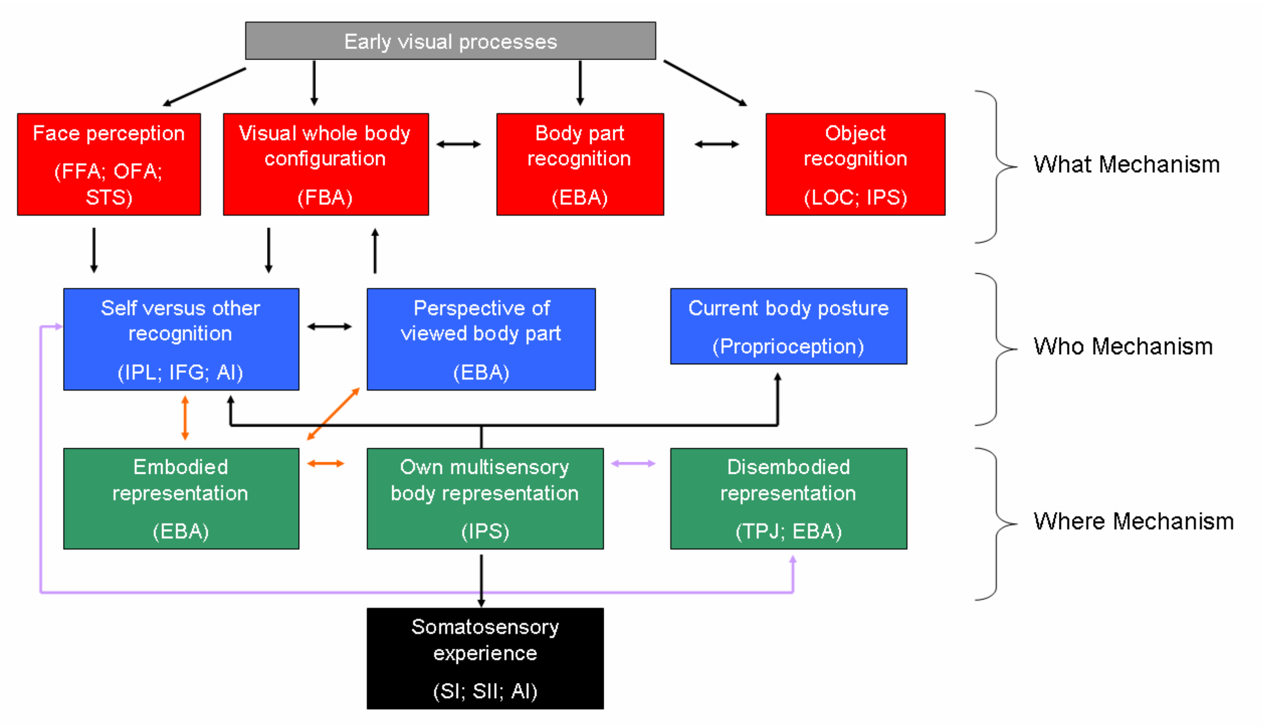


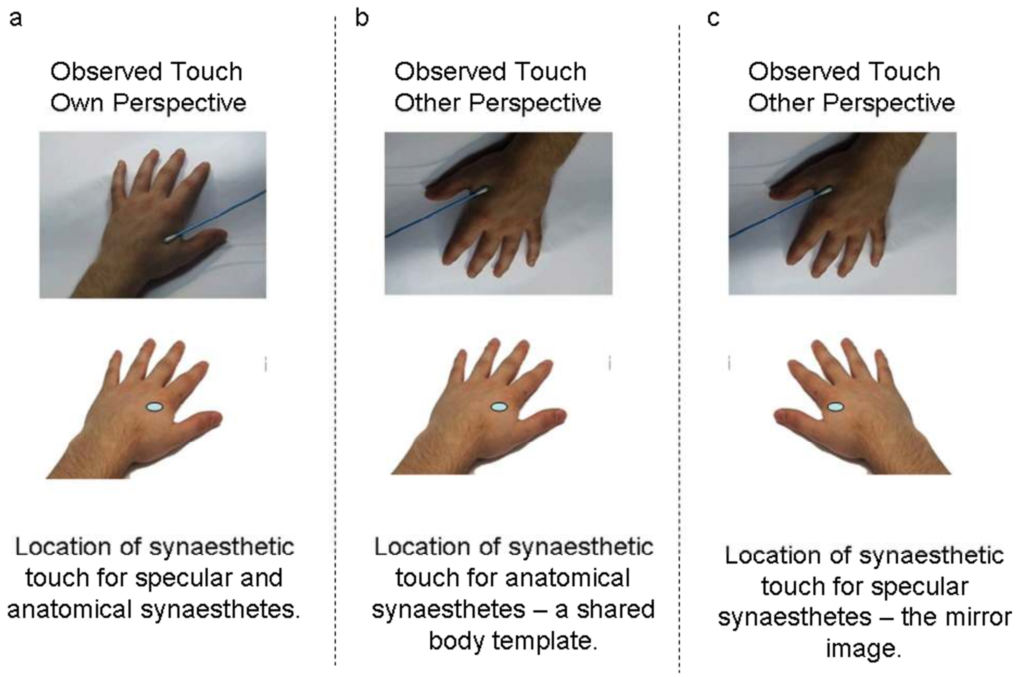
Figure 2.5 The 'What, Who, Where Model of Mirror-Touch Synaesthesia'. 'What' mechanisms are shown in red boxes and are involved in defining the stimulus touched. 'Who' mechanisms implement discriminations between self and other, and are shown in blue boxes. 'Where' mechanisms are shown in green boxes and are involved in locating where on the body and in space observed touch occurs. Processes necessary for all subjects are shown with black arrows, necessary for specular mirror-touch synaesthetes with orange arrows, and for anatomical mirror-touch synaesthetes with purple arrows. Brain regions represented are considered with regard to importance for mirror-touch synaesthesia. AI = Anterior Insula; EBA = Extrastriate Body Area; FBA = Fusiform Body Area; FFA = Fusiform face area; IFG = Inferior Frontal Gyrus; IPL = Inferior Parietal Lobule; IPS = Intraparietal Sulcus; LO = Lateral Occipital Cortex; SI = Primary Somatosensory Cortex; SII = Secondary Somatosensory Cortex; STS = Superior Temporal Sulcus; TPJ = Temporoparietal Junction.

In addition to the EBA, object selective visual regions and their interactions along higher-order visual systems may then be crucial for distinguishing between those synaesthetes for whom observing touch to objects elicit synaesthetic interactions and for those in which no synaesthetic interaction is experienced. In cases where observing touch to objects evokes synaesthesia, the processing of object information via the dorsal stream to areas along the medial bank of the intraparietal sulcus (IPS; Konen and Kaster, 2008) may be particularly important. The IPS forms part of the tactile mirror system (Blakemore et al., 2005) and is known to contain visual-tactile body maps which are important for dynamic multisensory body representations (Bremmer et al., 2001; Duhamel, Colby and Goldberg, 1998; Iriki, Tanaka and Iwamura., 1996; Macaluso and Driver, 2003; also see Colby, 1998; Maravita and Iriki, 2002 for review). Therefore the degree to which observing touch to an object is able to elicit visual-tactile synaesthetic interactions may depend upon the extent to which the object is incorporated into visual-tactile representations of the body, potentially within the IPS.

Visual Encoding: "Who" Mechanisms

The most crucial distinction to be made by the putative "who" mechanism is that between self and other. Is it my body/face that is seen?

One can consider mirror-touch synaesthesia as a breakdown in the mechanisms that normally distinguish self from other. A dedicated module to distinguish between self and other is not proposed; rather, this discrimination will emerge out of other processes involved in linking visual representations with internal representations of bodies. Namely, there may be a tendency to over-incorporate viewed bodies within the observer's current body schema (Coslett, 1998; Gallagher, 1995; Head and Holmes, 1911-1912; Sirigu, Grafman, Bressler, and Sunderland, 1991). This process is likely to depend on a variety of factors: the perspective of the viewed body part; the current posture of the mirror-touch synaesthete; and the similarity (facial or otherwise) between the perceiver and perceived.



Location of synaesthetic touch for specular and anatomical synaesthetes.

Location of synaesthetic touch for anatomical synaesthetes – a shared body template.

Location of synaesthetic touch for specular synaesthetes – the mirror image.

Figure 2.6 The influence of perspective on synaesthetic experience. (a) Observing touch to another person from one's own perspective induces touch on an anatomically corresponding hand for both the anatomical and specular subtypes (i.e. observing touch to another's left hand evokes synaesthesia on the synaesthete's left hand). (b) For anatomical mirror-touch synaesthetes, synaesthetic touch is still evoked on the anatomically corresponding hand when observing touch to another person's hand from another's perspective (i.e. observing touch to another's left hand evokes synaesthesia on the synaesthete's left hand). (c) For specular mirror-touch synaesthetes, this not the case. When observing touch to another person's hand from another's perspective, synaesthesia is evoked on the mirrored right hand (i.e. observing touch to another's left hand evokes synaesthesia on the synaesthete's right hand). See Banissy and Ward (2007). Blue dots correspond to the location of the synaesthetic sensation evoked.

The perspective of the seen body part provides one way of discriminating between self and other. The importance of discriminations between first-person and third-person perspectives (Figure 2.6) also varies between synaesthetic subtypes when observing touch to body parts (excluding the face) and this may require more computations for specular compared to anatomical synaesthetes. For specular synaesthetes, touch to the hands from a first-person perspective induces synaesthetic touch to the anatomically corresponding hand (i.e. right hand to right hand), but from a third-person perspective induces synaesthetic touch to the mirrored hand (i.e. right hand to left hand). In contrast, for anatomical synaesthetes, observed touch from either perspective elicits synaesthetic touch to the anatomically corresponding hand (c.f. Kusnir, MSc Thesis, University of London, 2008). The response of the right EBA is greater for body parts in the third-person than first-person perspective (Saxe, Jamal and Powell, 2006) and this brain region may contribute to this distinction. .

With regards to faces, viewing one's own face activates a different network of brain regions from other faces including famous or personally familiar ones (Uddin, Iacoboni, Lange, and Keenan, 2007). FMRI research has highlighted the role of a right-fronto-parietal network in this process, including the right inferior parietal lobule (IPL) and right inferior frontal gyrus (IFG; Sugiura, Watanabe, Maeda, Matsue, Fukuda, and Kawashima, 2005; Uddin, Kaplan, Molnar-Szakacs, Zaidel, and Iacoboni, 2005). These two regions form part of the classical mirror neuron system in humans (Rizzolatti and Craighero, 2004) and it has been suggested that they may be necessary to not only establish shared representations, but also to implement mechanisms to distinguish between self and other (Uddin, Molnar-Szakacs, Zaidel, and Iacoboni, 2006). It may be the case that this same sensorimotor network is over-active in mirror-touch synaesthetes when viewing faces other than their own, causing the body part to be incorporated into the observer's own body representations. One prediction is that mirror-touch synaesthetes (at least the specular sub-type) will show little behavioural or phenomenological differences on the spatial congruity task used here if the unfamiliar faces were replaced with images of their own faces[2]. However, controls may begin to show similar behavioural performance to the synaesthetes if images of their own face are displayed. In accordance with this, Serino and colleagues (2008) report that, for non-synaesthetes, observing touch to one's own or another's face increases tactile sensitivity on the observers own face (also see Haggard, 2006 for similar evidence of interpersonal enhancements of touch). This visual-tactile enhancement was maximised when observing touch to one's own face rather than another's face, indicating that self-similarity can modulate the extent of visuo-tactile resonance (Serino, Pizzoferrato, and Làdavas, 2008).

Perspective Taking: "Where" Mechanisms

The third class of mechanism that is considered to be relevant involves linking visual representations of body with tactile representations based on proprioception and somatosensation. One distinction that has been made in the literature is between "embodied" and "disembodied" representations of body (Giummarra, Gibson, Georgiou-Karistianis, and Bradshaw, 2007; also see Brugger, 2002 for a discussion of similar spatial aspects of autoscopic phenomena). Evoked potential mapping indicates that the right temporoparietal junction (TPJ) is related to disembodied perspective taking (judging left/right from someone else's perspective), while left EBA activation is linked with embodied perspective taking (judging left/right from own perspective; Arzy, Thut, Mohr, Michel and Blanke, 2006). Moreover, stimulation of the TPJ has been shown to lead to disembodied experiences in neurological patients (Blanke, Landis, Spinelli and Seeck, 2004; Blanke, Ortigue, Landis and Seeck, 2002).

---

[2] The predictions for synaesthetes with the anatomical sub-type are unclear because their usual synaesthetic phenomenology would contradict their own prior experiences of observing their own face in a mirror (e.g. when shaving or putting on make-up).

This distinction is similar to the specular-anatomical division between mirror-touch synaesthetes. For the specular sub-type, the visual representation of the other body is spatially processed as if it is a mirror-image of one's own (embodied) body. For the anatomical sub-type, the spatial mapping is more disembodied in that one's own body is placed in the perspective of the other person (or one's own body and that of the other person are copied into some other shared bodily template). If this is the case, it makes a specific and testable prediction - namely, that the anatomical sub-type will be associated with greater activity in the TPJ than the specular sub-type.

Somatosensory Processes

A final component within the model is the role of somatosensation in mirror-touch synaesthesia. Previous fMRI findings indicate that the condition is linked with increased activations in SI, SII and additional activations in bilateral anterior insula (Blakemore et al., 2005). The specific role of these regions in the experience of synaesthetic touch remains unclear. For example, the anterior insula is connected with both somesthetic cortex and visual association areas (Mesulam and Mufson, 1982; Mufson and Mesulam, 1982) which may make this brain region a potential candidate for accounts of mirror-touch synaesthesia in terms of mechanisms of disinhibition or hyper-connectivity. This brain region also contains tactile receptive fields in the absence of activations of primary somatosensory cortices (Olausson et al., 2002) and is important in processing the affective consequences of touch (Craig, 2002). In this sense, anterior insula activations observed in mirror-touch synaesthesia may reflect processing of tactile and affective consequences of synaesthetic experience; self reports indicate that the synaesthetic tactile sensation varies with the type of touch observed (i.e. pain versus touch) and has differing affective consequences accordingly. Alternatively, the anterior insula is also important in distinguishing between self and other (Fink, Markowitsch, Reinkemeier, Bruckbauer, Kessler, and Heiss, 1996; Kircher et al., 2001; Ruby and Decety, 2001) and this region could be involved in misattributing observed touch to oneself through mechanisms of self-other discrimination (Blakemore et al., 2005). The use of brain imaging to investigate more closely the interactions between activations in the anterior insula and primary somatosensory cortices observed in mirror-touch synaesthesia may shed light on these issues.

Summary

In summary, by investigating the prevalence and characteristics of mirror-touch synaesthesia it has been shown that this variant of the condition may be one of the most common forms of synaesthesia. Furthermore, there are a number of important characteristics which indicate that the condition goes beyond a simple one to one mapping between observed and synaesthetic touch. A neurocognitive model is proposed (Figure 2.5), which distinguishes between subtypes of mirror-touch synaesthesia and suggest potential neural mechanisms to account for how differences in the interpersonal body maps adopted may lead to different cognitive processes related to synaesthetic experience.

CHAPTER 3: SENSORY PROCESSING IN SYNAESTHESIA

The studies presented in chapter 2 explored the prevalence and characteristics of mirror-touch synaesthesia. Here I investigate the perceptual characteristics associated with the presence of mirror-touch synaesthesia. Previous findings imply that synaesthetic experience may have consequences for sensory processing of stimuli that do not themselves trigger synaesthesia. For example, synaesthetes who experience colour show enhanced perceptual processing of colour compared to non-synaesthetes. This study aimed to investigate whether enhanced perceptual processing was a core property of synaesthesia by contrasting tactile and colour sensitivity in synaesthetes who experience either colour, touch, or both touch and colour as evoked sensations. For comparison the performance of non-synaesthetic control subjects was also assessed. There was a relationship between the modality of synaesthetic experience and the modality of sensory enhancement. Synaesthetes who experience colour have enhanced colour sensitivity and synaesthetes who experience touch have enhanced tactile sensitivity. These findings suggest the possibility that a hyper-sensitive concurrent perceptual system is a general property of synaesthesia and are discussed in relation to theories of the condition.

3.1 Introduction

As noted previously, synaesthesia is a developmental condition in which one property of a stimulus results in conscious perceptual or ‘percept like’ experiences of an additional attribute. The authenticity of the condition is now well established (for reviews see Cohen Kadosh and Henik, 2007; Hubbard and Ramachandran, 2005; Rich and Mattingley, 2002) and a number of psychophysical studies indicate that synaesthetic experience resembles veridical sensory perception (but see Hong and Blake, 2008), e.g. in grapheme-colour synaesthetes, synaesthetic and real colours interact in binocular rivalry (Kim, Blake, and Palmeri, 2006); can induce orientation contingent colour adaption after-effects such as a synaesthetic ‘McCollough Effect’ (Blake, Palmeri, Marois, and Kim, 2004); and can combine to produce apparent motion (Kim et al., 2006). Under certain circumstances, synaesthetic experience may also aid veridical sensory perception. Vision-sound synaesthetes (synaesthetes for whom seeing visual motion triggers auditory perception) show an advantage at perceiving visually presented rhythmic patterns compared to non-synaesthetes. Typically, non-synaesthetes are superior at recognising auditory compared to equivalent visual rhythmic patterns, but vision-sound synaesthetes recode the visual information aurally leading to superior visual rhythm perception (Saenz and Koch, 2008).

Recent ERP evidence indicates that the presence of synaesthesia may also exert a wider influence over veridical sensory processing (Barnett et al., 2008; Goller, Otten, and Ward, 2009; Yaro and Ward, 2007). Barnett and colleagues (2008) report that, compared to non-synaesthetes, linguistic-colour synaesthetes show differences in early components of the visual evoked potential (VEP) when presented with simple visual stimuli which do not evoke synaesthesia. VEP differences were observed following the presentation of high spatial frequency Gabor patches which preferentially activate the parvocellular pathways (pathways highly responsive to colour; Kaplan, 1991) of the visual system (Barnett et al., 2008). Goller et al. (2009) report similar early VEP differences between tone-colour synaesthetes and non-synaesthetic controls following the presentation of coloured visual stimuli. These findings indicate electrophysiological differences in two groups of synaesthetes for stimuli which do not themselves trigger synaesthetic experience, implying that synaesthesia may be linked with general differences in veridical sensory perception. Behavioural correlates of this may include enhanced perceptual processing for stimuli related to synaesthetic experience. For example, Yaro and Ward (2007) report that synaesthetes who experience colour show better perceptual discrimination of colour relative to non-synaesthetic control subjects.

Although synaesthetic experiences are nearly always unidirectional in terms of conscious experience (e.g. graphemes or sounds trigger colour but not vice versa) there is good evidence of implicit bidirectionality (Cohen Kadosh and Henik, 2006; Cohen Kadosh, Cohen Kadosh and Henik, 2007). It is possible that previously reported sensory enhancements in colour processing (Yaro and Ward, 2007) are not localised within the colour domain but reflect back-coding, e.g. into the verbal domain. As such it is important to test other varieties of synaesthesia in which this possibility is less likely. For example, 'mirror-touch' synaesthetes experience tactile sensations on their own body when observing touch to another person (Banissy and Ward, 2007; Blakemore, Bristow, Bird, Frith, and Ward, 2005). To address this, the current study investigates tactile and colour perception in three groups of synaesthetes and a group of non-synaesthetic control subjects. The experiment was a 2x2 between subjects design in which I contrasted presence/absence of mirror-touch synaesthesia with presence/absence of synaesthetic colour experiences (including but not limited to grapheme-colour synaesthesia). The group reporting an absence of both types of synaesthesia are termed 'normal' control group. The three synaesthetic groups either have both types (hereafter referred to as dual-synaesthetes), or only one of these types. Based on previous research synaesthetes were expected to show enhanced perceptual sensitivity, but it remains to be shown whether this is specific to the modality (or modalities) that participate in the synaesthesia.

3.2 Methods

Participants

The touch-synaesthete group were comprised of six mirror-touch synaesthetes who do not experience any other forms of synaesthesia (4 female and 2 male; mean age ± s.e.m = 35.5 ± 3.93 years). Eight mirror-touch synaesthetes who also experience some form of colour synaesthesia (i.e. grapheme-colour, digit-colour, tone-colour) formed the dual-synaesthete group (6 female and 2 male; mean age ± s.e.m = 39.14 ±

3.74 years). Eight synaesthetes who experience synaesthetic perceptions of colour only (7 digit-colour synaesthetes and 1 letter-colour synaesthete who also reports digit-colour) were recruited for the colour-synaesthete group (7 female and 1 male; mean age ± s.e.m = 30.83 ± 3.01 years). None of the colour synaesthetes reported that colour elicited synaesthesia (e.g. colour-to-sound). Additionally, 20 non-synaesthetic control subjects were recruited for the experiment (16 female and 4 male; mean age ± s.e.m = 31.4 ± 3.66 years).

Cases of mirror-touch synaesthesia were confirmed on a visual-tactile spatial congruity paradigm designed to provide evidence for the authenticity of the condition (Banissy and Ward, 2007; described in Chapter 1 and 2). All cases of synaesthesia involving colour were confirmed using tests of consistency over time, with subjects demonstrating test-retest consistency of 85% (for letters, numbers, or other verbal stimuli) or a score of ≤ 0.75 on the Eagleman Synaesthesia Test Battery (Eagleman, Kagan, Nelson, Sagaram, and Sarma, 2007).

Materials and Procedure

Subjects completed two tests of sensory perception in a counterbalanced order: The Farnsworth-Munsell Colour Hue Test and the Gratings Orientation Test (Van Boven and Johnsen, 1994).

The Farnsworth-Munsell Colour Hue Test is a test of colour discrimination. The apparatus is a palette of different colour hues with identical luminance and saturation. Each hue is presented as a coloured cap and when arranged correctly the set forms a regular colour series transforming from one hue to another. Four colour series are presented in different trays, each containing 23 or 24 colours showing a distinct colour transformation. The procedure for the task is as follows. For each tray, the coloured caps are removed and arranged on the table in front of the participants.

Two coloured caps remain in the tray, which represent the two end points of the colour sequence (e.g. a purple and pink cap). The participant is given 2 minutes to arrange the remaining caps into an ordered colour series from one hue to another (e.g. purple through violet through pink). The correct order for the hues can be identified by the experimenter from the numeric coding on the underside of each cap. A deviation score is calculated by considering how far each colour cap deviates from the correct location in the sequence. For example, in a correct ordering such as 4–5–6; colour number "5" has a score of 2 because it is 1 unit from 4 and 1 unit from 6. An incorrect ordering such as 2–5–9 would yield a score of 7 for colour "5" because it is 3 units from "2" and 4 units from "9". The error score is the difference between the actual score obtained and the expected score based on flawless ordering. The same procedure was used for each of the four trays and the order of trays was randomized across participants.

In order to investigate tactile discrimination, the Gratings Orientation Test (GOT) was used to measure tactile acuity on the index finger tip. The GOT is a well established method for measuring the spatial resolution of touch. It consists of a series of square wave gratings with varying ridge widths (0.35mm – 3mm; Van Boven and Johnsen, 1994). Each grating is applied to the finger tip in one of two orthogonal orientations (across or along the axis of the finger tip). The task is to report the orientation of the probe. Typically as ridge width decreases, accuracy decreases. The GOT is thought to reflect cortical representations of the finger tip in SI (Van Boven and Johnsen, 1994) and in this vein provides a method for accurate threshold estimates of sensory function.

Six spatial grating probes (0.35mm, 0.5mm, 0.75mm, 1mm, 1.25mm, 1.5mm) were used to investigate each participant's tactile sensory threshold. Using a blocked design (20 trials per block; Van Boven and Johnsen, 1994) each probe was applied manually to the participant's right index finger tip in one of two different orientations (across or along the axis of the finger tip). Manual application was chosen because performance in spatial resolution is generally insensitive to the force of application (Johnsen and Philips, 1981) and the receptive fields of the afferent population involved in grating orientation detection are relatively independent of skin indentation (Vega-Bermudez and Johnsen, 1999). Participants were asked to indicate the orientation of each probe by giving a verbal response (i.e. "across" or "along"). In total participants completed 20 trials per probe (120 trials in total) which were randomised across blocks. For each probe half of the trials were orientated across the finger tip and the remainder were applied along the finger tip. Participants were blindfolded during the task to prevent any visual cues to orientation. Prior to threshold measurement, participants completed two practice blocks, using 2mm and 3mm gratings, in which feedback was given on participants' responses. No feedback was given on trials involved in threshold detection.

3.3 Results

Farnsworth-Munsell Colour Hue Test

The results from the Farnsworth-Munsell Colour Hue Test are shown in figure 3.1. The test is measured according to a total error score (TES) based on the deviation from the expected ordering (it is not a percentage error). Superior performance is reflected by a lower TES.

To investigate if the presence of synaesthesia for colour or touch was linked with superior performance, a 2 (presence/absence of colour synaesthesia) x 2 (presence/absence of touch synaesthesia) ANOVA was conducted. It was predicted that synaesthetes who experience colour would show superior performance on the colour perception task compared to those who do not. This was found to be the case, a significant main effect of Colour Group was found [$F_{(1,38)} = 4.61$, $p = <.05$]. The presence of colour synaesthesia was linked with a lower TES (mean ± s.e.m = 48.22 ± 7.7), and therefore better colour discrimination, than the absence of colour synaesthesia (mean ± s.e.m = 75.54 ± 10.1). This replicates previous reports (Yaro and Ward, 2007). No main effect of touch group or any interaction between groups was found. Therefore, the presence of colour synaesthesia, but not touch synaesthesia, was linked with enhanced colour discrimination.

To further delineate the contribution of different variants of synaesthesia to performance, the performance between each subgroup of subjects (colour-synaesthetes; touch-synaesthetes; dual-synaesthetes; non-synaesthete controls) was compared using a one-way ANOVA (Figure 3.1). The main effect of group approached significance [$F_{(3,38)} = 2.45$, $p = .078$]. In order to examine the basis of this strong trend, and to test the a priori assumption that synaesthetes would show enhanced colour sensitivity relative to control subjects, a series of planned t-tests were carried out (cf. Howell, 2002, pg. 372-373). This revealed that synaesthetes who experience colour (but not touch) as their induced experience showed superior colour discrimination relative to non-synaesthetic control subjects [$t_{(26)} = 2.04$, $p = <.05$]. This was also true of dual-synaesthetes – synaesthetes who experience touch and colour significantly outperformed non-synaesthetic control subjects [$t_{(25.90)} = 2.47$, $p = <.05$]. No significant differences were found between the colour discrimination abilities of synaesthetes who only experience touch-synaesthesia and non-synaesthetic control subjects [$t_{(24)} = .62$, *nsig*]. This indicates that the presence of 'colour' synaesthetic experience (rather than synaesthesia per se) is related to enhancements in the perceptual processing of colour relative to non-synaesthetic control subjects.

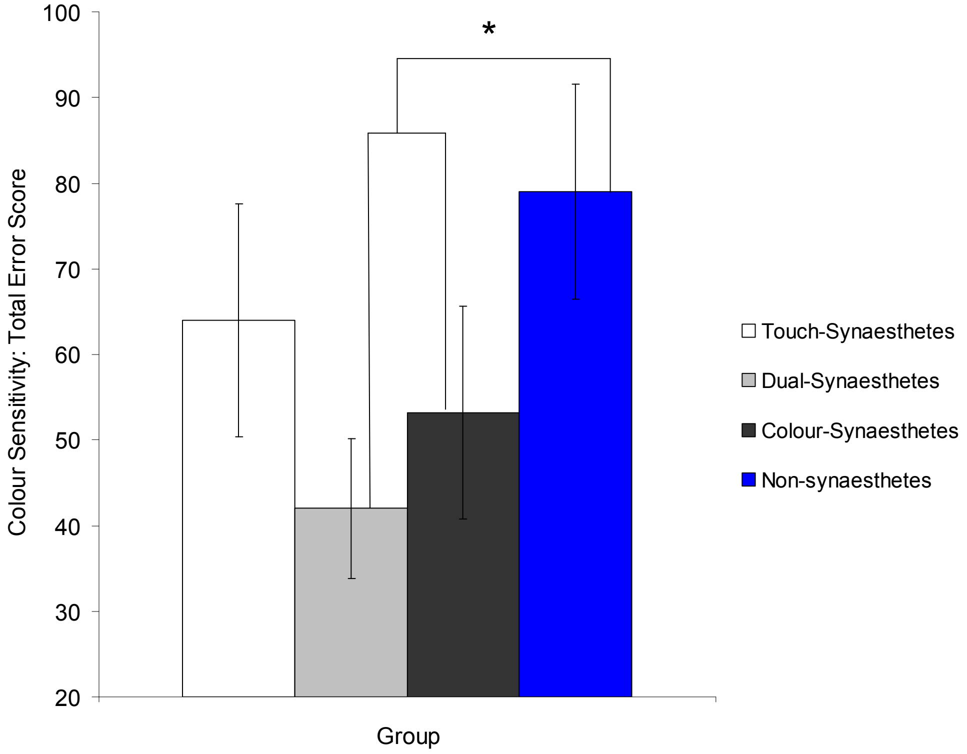


Figure 3.1 Synaesthetes who experience colour outperformed individuals who do not experience synaesthetic colour on a measure of colour perception (a). This pattern of performance was shown by synaesthetes who experience colour only relative to non-synaesthetic controls and by synaesthetes who experience both colour and touch relative to non-synaesthetic controls, but not by synaesthetes who experience touch only relative to controls (b). Error scores are based on the deviation from the expected ordering of hues. Superior colour performance is indicated by a lower error score. * = $p < .05$.

Gratings Orientation Test

Figure 3.2 shows the average tactile discrimination thresholds for all subjects on the gratings orientation test. Enhanced tactile discrimination is reflected in a lower threshold value (in millimetres). Thresholds were calculated using the following formula and provide an estimate of the grating level which would lead to a 75% response level:

$g_{75} = g_{low} + ((0.75 - p_{low})/(p_{high} - p_{low}))\ (g_{high} - g_{low})$

g = grating spacing

p = trials correct / n
n = number of trials
high=the grating spacing on the lowest grating spacing on which the participant responded correctly **better than** 75% of the time.
low=the grating spacing on the highest grating spacing on which the participant responded correctly **less than** 75% of the time.
$\mathbf{g}_{75}$ =the interpolated grating spacing on which the subject would have scored 75% had it been present.

A 2 (presence/absence of colour synaesthesia) x 2 (presence/absence of touch synaesthesia) ANOVA revealed a significant main effect of Touch Group ($F_{(1,40)}$ = 13.44, p = <.01). This was because synaesthetes who experience touch (either touch only or dual-synaesthetes) showed heightened tactile sensitivity (mean ± s.e.m = 0.79 ± 0.05 mm) compared to participants who do not experience synaesthetic touch (mean ± s.e.m = 1.25 ± 0.08 mm). No significant main effect of Colour Group or interaction was observed, indicating that the presence of synaesthetic touch was linked with heightened tactile sensitivity but not the presence of synaesthesia in general.

As with colour discrimination performance, tactile discrimination performance between all four groups (colour-synaesthetes; touch-synaesthetes; dual-synaesthetes; non-synaesthete controls) was compared using a one-way ANOVA. A significant main effect of group was observed [$F_{(3,38)}$ = 4.50, p = .008]. Post-hoc comparisons (corrected using Fisher's LSD) revealed that this was because synaesthetes who only experienced mirror-touch synaesthesia showed superior tactile discrimination relative to both colour-synaesthetes (p = < .05) and non-synaesthetic control subjects (p = < .05). Dual-synaesthetes also significantly outperformed both colour-synaesthetes (p = < .05) and non-synaesthetic control subjects (p = < .01). No significant differences were found between 'colour-only' synaesthetes and non-synaesthetic (p = .694) controls or between touch-synaesthetes and dual-synaesthetes (p = .891). Therefore the presence of synaesthesia for touch was related to enhancements in the perceptual processing of touch relative to the absence of synaesthesia for touch (Figure 3.2).

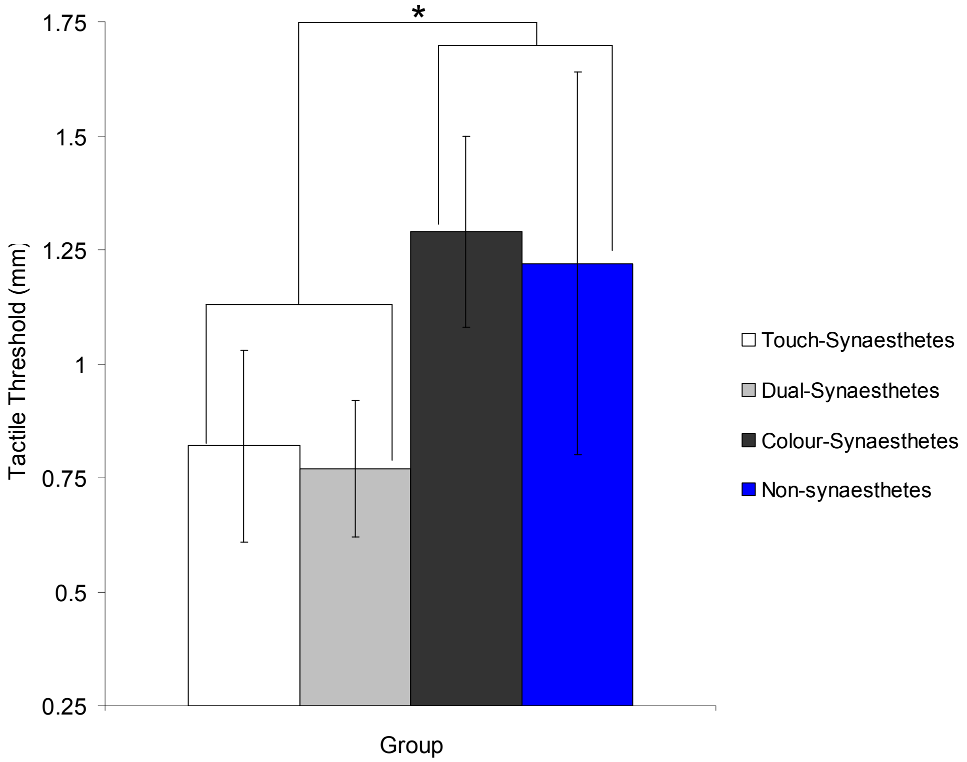


Figure 3.2 Synaesthetes who experience touch outperformed individuals who do not experience synaesthetic touch on a measure of tactile perception (a). This pattern of performance is shown by synaesthetes who experience touch only relative to non-synaesthetic and synaesthetic control subjects, and by synaesthetes who experience touch and colour relative to non-synaesthetic and synaesthetic control subjects. No differences in tactile perception were found between synaesthetes who experience colour only and non-synaesthete control subjects (b). Superior tactile sensitivity is indicated by a lower tactile threshold (mm). * = $p < .05$.

3.4 Discussion

This study extends previous reports of enhanced perceptual processing in grapheme-colour synaesthesia (Yaro and Ward, 2007) and aimed to clarify whether synaesthesia in other modalities has similar repercussions for perceptual processing of stimuli in that modality. Using a sample of synaesthetes who experience either colour, touch, or both touch and colour as evoked sensations, the findings first replicate previous reports that synaesthetes who experience colour show superior perceptual discrimination of colour relative to non-synaesthetic subjects. They extend this by showing:

i) synaesthetes who experience only touch show enhanced perceptual discrimination of touch but not of colour,

ii) synaesthetes who experience both a tactile and visual concurrent show enhanced perceptual processing of both touch and colour (although the robustness of differences in colour processing was less strong than for tactile processing),

iii) synaesthetes who experience only colour do not show enhanced sensory processing in modalities outside of vision.

These findings suggest that enhanced perceptual processing is a core property of synaesthesia, which is not limited to colour but occurs in each affected sensory modality.

There are two possible accounts for why synaesthetes should demonstrate an oversensitive concurrent perceptual system: 1) enhanced perceptual processing is a consequence of the additional synaesthetic percepts which are experienced in everyday life (i.e. enriched perceptual experience leads to enhanced perceptual processing) or 2) enhanced perceptual processing is related to differences in brain development as a function of synaesthesia (which may be either a cause or consequence of synaesthesia; i.e. widespread differences in cortical connectivity or mechanisms of cortical unmasking; Rouw and Scholte, 2007; Cohen Kadosh et al., 2009).

Under the first account, an oversensitive concurrent perceptual system would be explained as a proximal consequence of synaesthetic experience. For example, the presence of stable synaesthetic associations may impact on the internal structure of sensory representations. In the case of colour, it has been suggested that linguistic labels are necessary to categorize colours across a perceptual continuum (Davidoff, 2001) and cross-cultural differences in the number of colour labels has been shown to influence colour perception and memory (Robertson, Davies, and Davidoff, 2000). It may be the case that for some colour synaesthetes (i.e. grapheme-colour synaesthesia), the presence of stable associations with colour increases the number of colour terms and thereby impacts on the internal structure of colour space (Yaro and Ward, 2007). In accordance with this, Simner and colleagues (2005) report that grapheme-colour synaesthetes produce a greater depth of colour descriptions and use more colour terms than non-synaesthete control participants. It is unclear however, how this would extend to other variants and concurrent perceptual systems such as enhanced tactile acuity in mirror-touch synaesthesia.

Additionally, insights into the influence of enriched perceptual experience on sensory enhancement in the deprived brain would suggest that it is unlikely that extra synaesthetic percepts are the cause of superior perceptual processing (Pascual-Leone, Amedi, Fregni, and Merabet, 2005). For example, blind subjects have been shown to be superior to sighted subjects on the grating orientations test, however this superiority does not correlate with Braille reading experience or differ between Braille readers and blind non-readers (Goldreich and Kanics, 2003; Van Boven, Hamilton, Kauffman, Keenan, and Pascual-Leone, 2000). This indicates that mechanisms of cross-modal plasticity following visual deprivation (rather than increased tactile experiences) drives tactile acuity enhancement in the blind (Goldreich and Kanics, 2003). Consistent with this, in sighted-subjects visual deprivation induced by long-term blindfolding results in temporary enhancements of passive tactile acuity, but enriched tactile experience on the same finger does not (Kauffman, Théoret, Pascual-

Leone, 2002) – further implying that elevated sensory sensitivity may be linked to mechanisms of cross-modal plasticity rather than additional sensory experience.

Two mechanisms of cross-modal plasticity have been suggested to account for compensatory changes in the deprived brain: cortical unmasking of pre-existing connections and cortical reorganisation (e.g. Pascual-Leone et al., 2005; Wittenberg et al., 2004). Mechanisms of cortical unmasking (through processes such as disinhibition) involve the strengthening of existing within and between region anatomical pathways (i.e. functional but not structural differences), while mechanisms of cortical reorganisation involve the establishment of new local and widespread anatomical connections (i.e. structural differences). The role of these mechanisms on compensatory change is thought to reflect differences in the speed of plasticity, with unmasking representing a form of rapid change which if sustained leads to long lasting cortical changes such as the establishment of new anatomical connections (slow acting mechanism; Pascual-Leone et al., 2005). For example, in the case of temporary enhancements in tactile acuity following blindfolding, unmasking of existing connections may offer a fast-acting mechanism of cross-modal plasticity to maintain functional behaviour (i.e. perception of the environment through rapid enhancements in tactile processing). In comparison, in the case of enhanced tactile processing in the blind, sustained unmasking of existing connections may lead to new local and widespread anatomical pathways resulting in long lasting enhancements in tactile acuity which aid in daily life (Pascual-Leone et al., 2005).

There is growing evidence that synaesthesia may act upon the 'normal' architecture for cross-modal interactions (see Sagiv and Ward, 2006 for review) and parallels may be drawn between mechanisms of cross-modal plasticity following compensatory changes in the deprived brain and those which have been suggested to underlie synaesthetic experience (Cohen Kadosh and Walsh, 2006). A current area of debate is whether synaesthetic experience is a consequence of additional structural connectivity between brain regions (i.e. structural differences akin to cortical reorganisation following sensory deprivation), malfunctions in cortical inhibition (i.e. functional but not structural differences akin to cortical unmasking following sensory deprivation), or a combination of both (Bargary and Mitchell, 2008; Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001; Hubbard and Ramachandran, 2005; Rouw and Scholte, 2007; Smilek et al., 2001). Supporting evidence for structural connectivity accounts is provided by diffusion tensor imaging findings that grapheme-colour synaesthetes show increased structural connectivity in inferior-temporal, parietal and frontal brain regions when compared to non-synaesthetes (Rouw and Scholte, 2007). Evidence for inhibition accounts is provided by findings that synaesthetic-like experiences can be induced following hallucinogenic drugs (Aghajanian and Marek, 1999) and that grapheme-colour synaesthesia can be induced in non-synaesthetes (individuals without aberrant connectivity) using post-hypnotic suggestion (Cohen Kadosh et al., 2009). It is plausible that enhanced sensory perception in synaesthesia may reflect a combination of these mechanisms. Mechanisms of reduced inhibition may act by unmasking local anatomical pathways (akin to visual deprivation studies in sighted subjects; Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008), while altered cortical connectivity may lead to enhanced perceptual sensitivity through aberrant circuitry within the concurrent perceptual system (akin to sensory sensitivity enhancements in the blind). It will be interesting to determine if altered connectivity in synaesthesia (Rouw and Scholte, 2007) may reflect sustained unmasking of existing connections (e.g. Cohen Kadosh et al., 2009) and what implications this may have for veridical sensory processing.

In summary, this study extends previous findings that grapheme-colour synaesthetes show enhanced perceptual processing of colour (Yaro and Ward, 2007) to suggest that an oversensitive concurrent perceptual system is a core property of synaesthesia. Mirror-touch synaesthetes were shown to have enhanced tactile sensitivity only, synaesthetes who experience both mirror-touch and a form of colour synaesthesia were shown to demonstrate enhanced tactile and colour perception, and synaesthetes who only experience colour were shown to have enhanced perceptual processing of colour only. These findings imply that the presence of synaesthesia has repercussions for sensory processing for stimuli which do not themselves induce synaesthetic experience. It remains to be determined whether an oversensitive concurrent perceptual system is a cause or consequence of synaesthesia.

CHAPTER 4: MIRROR-TOUCH SYNAESTHESIA AND EMPATHY

In the preceding chapters I investigated the behavioural correlates and perceptual consequences of mirror-touch synaesthesia. Here I consider the implications of mirror-touch synaesthesia for general cognitive processing. Previous fMRI findings link mirror-touch synaesthesia to heightened activations in the mirror-touch system (the same neural system activated in non-synaesthetes when observing touch to others). It has been suggested that components of the mirror-touch system may act to facilitate processes such as empathy and emotion recognition because they provide the perceiver with a neurophysiological mechanism to simulate what it would "feel like" to be in the same situation. To examine this possibility, two experiments were conducted to investigate the influence of heightened sensorimotor simulation in mirror-touch synaesthesia on empathy. Experiment 1, 'Mirror-touch synaesthesia and empathy', demonstrates that mirror-touch synaesthesia, but not other variants of synaesthesia, is linked with heightened empathic abilities for specific components of empathy. Experiment 2, 'Empathy and personality', extends the findings from experiment 1 by demonstrating that differences in empathy are 'other' rather than 'self' orientated reactions.

4.1 Introduction

Empathy is a higher order psychological construct and is considered to have two main strands: (i) cognitive empathy – predicting and understanding another's mental state by using cognitive processes (i.e. role / perspective taking), and (ii) affective empathy – experiencing an appropriate emotional response as a consequence of another's state (Baron-Cohen and Wheelwright, 2004; Decety and Jackson, 2004; Preston and de Waal, 2002). Evolutionary perspectives suggest that there are several possible systems which mediate this division, including phylogentically early emotional contagion systems and more recently evolved cognitive perspective taking mechanisms (De Waal, 2007), with the former thought to play a crucial role in supporting the ability to empathize emotionally (e.g. I feel sad when I see someone else sad) and the later considered to be linked to more complex empathic cognitions including perspective taking and mentalizing.

Recent research has suggested that one neurophysiological mechanism which may mediate people's abilities to empathize and understand the emotions of others is shared affective neural systems in which common brain areas are activated during both experience and passive observation of other's experiences. Moreover, building on the discovery of mirror neurons in the monkey brain (Gallese, Fadiga, Fogassi, and Rizzolatti, 1996; Rizzolatti and Craighero, 2004), functional brain imaging has suggested the existence of mirror systems in humans not only for actions (e.g. Buccino et al., 2001), but also for sensations and emotions (e.g. disgust: Jabbi, Swart and Keysers, 2006; Wicker, Keysers¸ Plailly, Royet, Gallese, and Rizzolatti, 2003; touch: Blakemore, Bristow, Bird, Frith, and Ward, 2005; Ebisch, Perucci, Ferretti, Del Gratta, Luca Romani, and Gallese, 2008; Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004; pain: Avenanti, Beuti, Galati, and Aglitoi, 2005; Bufalari, Aprile, Avenanti, Di Russo, and Aglioti, 2007; Morrison, Lloyd, di Pellegrino, and Roberts, 2004; Singer, Seymour, O'Doherty, Kaube, Dolan, and Frith, 2004; emotion: Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003). These systems may be crucial for empathy because they enable the observer to simulate another's experience by activating the same brain areas that are active when the observer experiences the same emotion or state (Gallese, 2006; Gallese and Goldman, 1998; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007). Consistent with this, is evidence that increased activations in the auditory mirror system are correlated with high self reported empathy (Gazzola, Aziz-Zadeh, and Keysers, 2006); that increases in trait-cognitive empathy are correlated with increases in sensorimotor simulation when viewing others' pain (Avenanti, Minio-Paluello, Bufalari, and Aglioti, 2009); and that participants self reported empathy skills are positively correlated with levels of cortical mirroring of when witnessing disgust (Jabbi et al., 2006). Furthermore, there is a growing body of evidence suggesting that individuals with autistic spectrum disorder (ASD) have impaired activity in the action mirror system (Dapretto, Davies, Pfeifer, Scott, Sigman, Bookheimer, and Iacoboni, 2006; Oberman, Hubbard, McCleery, Altschuler, Ramachandran, and Pineda, 2005), which may lead to the deficits in imitation and empathy observed in ASD (Iacoboni and Dapretto, 2006; Oberman and Ramachandran, 2007; but see Southgate and Hamilton, 2008).

As discussed in preceding chapters, previous functional magnetic resonance imaging findings indicate that synaesthetic tactile experiences in mirror-touch synaesthesia are associated with hyperactivity in the same mirror-touch network that is evoked by observed touch in non-synaesthete controls in which no overt tactile experience is elicited (Blakemore et al., 2005). As such, mirror-touch synaesthesia may offer a unique opportunity to explore the role that the tactile mirror system has in empathy because it enables investigations into the relationship between heightened sensorimotor simulation in the mirror-touch system and empathic sensitivity.

To address this possibility two experiments were conducted. In experiment 1, the empathic abilities of ten mirror-touch synaesthetes were compared to a synaesthetic and non-synaesthetic control group. In experiment 2, potential factors which may contribute to heightened empathy were investigated by contrasting mirror-touch synaesthetes with non-synaesthetic participants on empathy and personality measures.

4.2 Experiment 1: Mirror-touch synaesthesia and empathy

Participants

Ten mirror-touch synaesthetes (6 females and 4 males, mean age ± Std. Error = 37.6 ± 5.59 years) and twenty non-synaesthetic controls matched for age and gender (12 females and 8 males, mean age ± Std. Error = 32.95 ± 3.24 years) took part in the study. All cases of mirror-touch synaesthesia were confirmed on the visual-tactile spatial congruity paradigm described previously (Banissy and Ward, 2007; also see Chapter 1 and Chapter 2 of this thesis for a description of the task).

In addition to this, twenty-five synaesthetes (22 females and 3 males, mean age ± Std. Error = 43.96 ± 3.38 years) experiencing other forms of synaesthesia (minimally grapheme-colour synaesthesia) but not mirror-touch synaesthesia took part. These synaesthetes acted as a synaesthetic control group and demonstrated test-retest consistency of ≥ 85% for letters, numbers and other verbal stimuli. The synaesthete control group were included to ensure that any differences in empathy were not due to a general feature of synaesthesia.

Materials and Procedure

All participants completed the Empathy Quotient (Baron-Cohen, Richler, Bisarya, Gurunathan, and Wheelwright, 2003; Baron-Cohen and Wheelwright, 2004). The EQ is a self report scale designed to empirically measure empathy. As noted previously, empathy is a higher order construct and has been theorised as having two main strands: (i) cognitive empathy – predicting and understanding another's mental state by using cognitive processes (i.e. role / perspective taking), and (ii) affective empathy – experiencing an appropriate emotional response as a consequence of another's state (Baron-Cohen and Wheelwright, 2004; Preston and de Waal, 2002). The EQ was developed to measure both cognitive and affective components of empathy, has been validated on both clinical and control groups (Baron-Cohen et al., 2003), and it has been shown to distinguish between these groups (Baron-Cohen et al., 2003; Baron-Cohen and Wheelwright, 2004). In addition to this, the EQ has been validated on measures of concurrent validity (Lawrence, Shaw, Baker, Baron-Cohen, and David, 2004) and has been shown to have high test-retest reliability over 12 months (Baron-Cohen et al., 2003). The scale is comprised of 40 test items and 20 filler items. All items are a series of statements (e.g. ‘I can tune into how someone feels rapidly and intuitively) and responses are given on a 4 point scale ranging from ‘strongly agree’ to ‘strongly disagree’. Responses score 1 or 2 points for an empathic response and 0 points for all other responses. Principal component analysis has indicated that the EQ is comprised of three main factors (i) cognitive empathy, (ii) emotional reactivity and (iii) social skills (Lawrence et al., 2004; Muncer and Ling, 2006). Confirmatory factor analysis has indicated that the EQ may be better conceived as comprising of this three factor structure rather than a 40 item unifactorial scale (Lawrence et al., 2004; Muncer and Ling, 2006).

Results and Discussion

The empathic ability of mirror-touch synaesthetes was compared with non-synaesthetic control participants and controls that report other types of synaesthesia but do not report mirror-touch synaesthesia. Results from non-synaesthetic controls and synaesthetes lacking mirror touch did not differ and were therefore combined. Empathy scores for each component of the EQ are summarised in Figure 4.1. Mirror-touch synaesthetes showed significantly higher scores on the emotional reactivity subscale of the EQ relative to controls [t(53) = 2.15, *p* = < .05]. This subscale is thought to reflect affective components of empathy, and instinctive empathic responses to others (Baron-Cohen and Wheelwright, 2004; Lawrence et al., 2004). There was also a non-significant trend for mirror-touch synaesthetes to outperform control subjects on the cognitive empathy (i.e. mentalizing / perspective taking) subscale [t(53) = 1.92, *p* = .061]. Scores on the social skills subscale did not approach significance [t(53) = 1.22, *p* = .227]. Therefore, mirror-touch synaesthetes showed heightened empathy on some, but not all aspects of empathy. This supports the notion that empathy is multi-faceted (Baron-Cohen and Wheelwright, 2004; Decety and Jackson, 2004; Lawrence et al., 2004; Muncer and Ling, 2006; Preston and de Waal, 2002) and implies that sensorimotor simulation may modulate some, but not all, aspects of this ability. Further, the evidence that enhanced empathy is not found in other types of synaesthesia suggests that heightened empathy relates specifically to mirror-touch synaesthesia (and the neural system which underpins this condition).

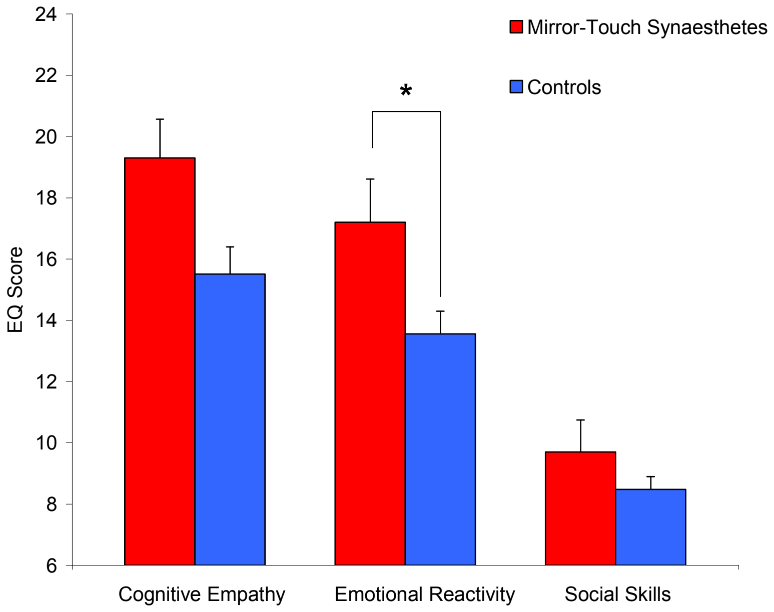


Figure 4.1 Mirror-touch synaesthetes showed significantly higher scores than controls on the emotional reactivity component, but not other components, of the Empathy Quotient (mean ± s.e.m). * = *p* < .05.

Previous functional magnetic imaging findings indicate that, in healthy adults, emotional empathy engages the cortical sensorimotor network (including the premotor cortex, primary somatosensory cortex and motor cortex) more than cognitive empathy (Nummenmaa, Hirvonen, Parkkola, and Hietanen, 2008). Further, neuropsychological findings have demonstrated a functional and anatomical double dissociation between deficits in cognitive empathy and emotional empathy, with emotional empathy being linked to lesions to the human mirror system and cognitive empathy being associated to lesions to the ventromedial prefrontal cortices (Shamay-Tsoory, Aharon-Peretz, and Perry, 2009). This functional coupling between emotional and cognitive empathy suggests that emotional empathy may be linked more closely to sensorimotor simulation of another's state and the evidence that mirror-touch synaesthetes only significantly differ from controls on levels of emotional reactivity is consistent with this.

Two qualifications are apposite: (a) it remains unclear whether heightened emotional reactivity reflects differences in the nature of the individual (i.e. more emotional or more distressed by emotional scenes as opposed to more empathic / concerned), and (b) evidence of a borderline significant difference on cognitive empathy suggests that differences in empathy may not be limited to emotional empathy per se. To further address these issues a second experiment was conducted.

4.3 Experiment 2: Empathy and personality in mirror-touch synaesthesia

While findings from experiment 1 indicate that mirror-touch synaesthesia is related to heightened emotional empathy, it remains unclear if the emotional reactivity component of the EQ reflects the nature of the individual (i.e. more emotional / more distressed) rather than emotional empathy per se (Muncer and Ling, 2006). Moreover, the emotional reactivity subscale of the EQ fails to consider the role of personal distress (an emotionally specific response to one's own state rather than an emotional response related to emotional empathy) and thus it is difficult to confirm whether responses on the emotional reactivity component are indeed other (e.g. feeling compassion or sorrow towards to another person) rather than self-oriented (e.g. feeling distress from an unpleasant scene rather than feeling sorrow or concern; c.f. Batson, 1991; Davis, 1994; Lamm, Batson, and Decety, 2007; Saarela, Hlushchuk, Williams, Schürmann, Kalso, and Hari, 2007). The implications of this distinction for behaviour are that other-oriented empathy may promote altruistic motivations to help another person, while self-orientated empathy may lead to egoistic motivations to reduce the personal distress felt by the observer and ultimately counteract positive empathic behaviours (e.g. helping behaviour; Batson, 1991; Eisenberg, 2000).

This study aimed to investigate this, by contrasting mirror-touch synaesthetes with age and gender matched non-synaesthetes on the EQ and an additional measure of empathy - the Interpersonal Reactivity Index (IRI; Davis, 1980). The IRI contains a component relating to 'personal distress' that is regarded as being self-oriented emotional reactivity and so is able to clarify if heightened emotional reactivity in mirror-touch synaesthetes is other rather than self-oriented. In addition, the relationship between individual differences in emotional reactivity (in both the synaesthetes and controls) and personality traits were investigated using the 'Big Five Inventory (BFI; John, Donahue, and Kentle, 1991). If emotional reactivity is self-oriented then a correlation with the neuroticism (or emotional stability) trait is expected, but not if it is other-oriented. A previous study found no relationship between empathy and emotional stability, but it did not divide empathy into component factors (Del Barrio, Aluja, and Garcia, 2004), thus my study is the first to consider the importance of personality on different facets of empathy as indexed by the EQ and IRI.

4.3.1 Methods

Participants

In the first part of the study, sixteen mirror-touch synaesthetes (mean age ± s.e.m = 35.5 ± 3.58 years) and sixteen age and gender matched non-synaesthete controls (mean age ± s.e.m = 35.69 ± 3.45 years) were compared. All cases of mirror-touch synaesthesia were confirmed on the visual-tactile spatial congruity paradigm designed to provide evidence for the authenticity of the condition (cf. Banissy and Ward, 2007; Chapter 1 and Chapter 2 this thesis). Of the sixteen synaesthetes, five took part in experiment 1.

For analysis of the relationship between empathy and personality, an additional 88 non-synaesthete control subjects were recruited. These controls were combined with mirror-touch synaesthetes and non-synaesthete controls from the first part of the study to provide a sample of 120 subjects (mean age ± s.e.m = 27.98 ± 2.78 years). The additional controls were included to provide a range of scores on the empathy and personality measures, with mirror-touch synaesthetes thought to reflect the top end of a spectrum on empathy scores.

Materials and procedure

All subjects completed the EQ, IRI, and BFI.

The EQ is a self report measure designed to empirically measure empathy and is described in experiment 1 of this chapter (pp. 78-79).

The IRI is a 28 item self-report empathy measure (Davis, 1980). It is comprised of four subscales; perspective taking, fantasizing, empathic concern and personal distress. Each subscale contains seven items which are measured on a five point Likert scale ranging from 0 (“Does not describe me well”) to 4 (“Describes me very well”). For each subscale, a minimum score of 0 or maximum score of 35 is possible. For the perspective taking, fantasizing and empathic concern subscales higher scores reflect heightened empathy. For the personal distress subscale higher scores are reflective of self-orientated emotional reactivity (Davis, 1994).

The BFI is a 44-item scale designed to measure components of the Big Five personality traits (extraversion, agreeableness, conscientiousness, neuroticism, and openness; John et al., 1991). Respondents are asked to indicate on a five point Likert scale the extent to which a series of statements related to each personality trait best describe their own characteristics. Responses are given from 1 ("Disagree strongly") to 5 ("Agree strongly"). Analysis of the reliability of the scale (John and Srivastava, 1999) indicates a coefficient alpha of 0.83 and the BFI shows good convergent validity with TDA (Goldberg, 1992) and NEO-PI personality measures (Costa and McCrae, 1985).

4.3.2 Results

Mirror-touch synaesthetes compared to non-synaesthete controls

The empathic abilities of mirror-touch synaesthetes and controls on each component of the EQ and IRI were compared. On the EQ (Figure 4.2), mirror-touch synaesthetes scored significantly higher than non-synaesthete controls on the emotional reactivity subscale [t (30) = 2.29, p = < .05]. Despite synaesthetes scoring higher than controls on the cognitive empathy (CE) and social skills (SS) subscales these did not approach significance [CE: t(30) = 1.20, p = .239; SS: t(30) = 1.37, p = .181]. This is consistent with findings from experiment 1 where mirror-touch synaesthetes differed significantly from controls on the emotional reactivity subscale, but not cognitive empathy or social skills subscale of the EQ.

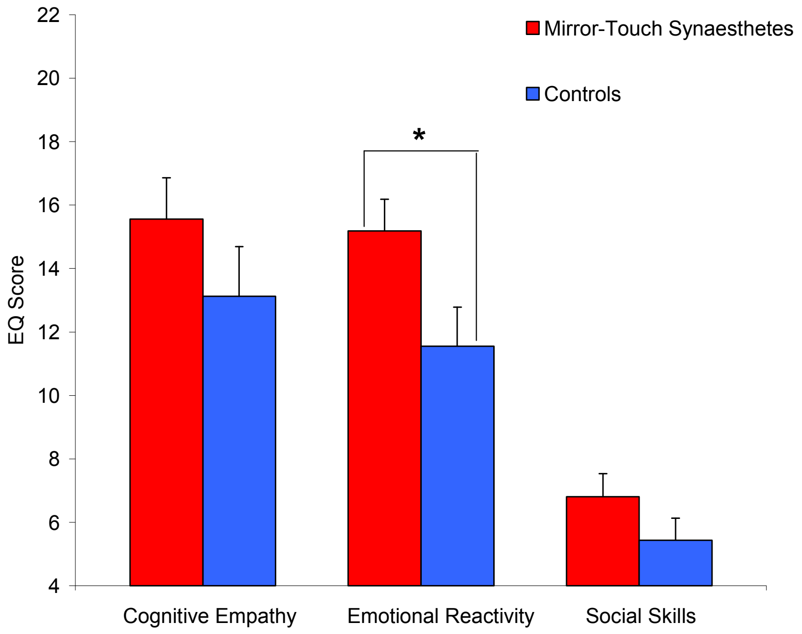


Figure 4.2 In experiment 2, mirror-touch synaesthetes showed significantly higher scores than controls on the emotional reactivity component, but not other components, of the Empathy Quotient (mean ± s.e.m). * = *p* < .05.

In addition, on the IRI mirror-touch synaesthetes showed significantly elevated scores on the fantasizing subscale [$t(30) = 2.35$, $p = < .05$], but not on the alternative subscales (Figure 4.3). Of note, is the comparable performance of synaesthetes and controls on the perspective taking subscale and higher scores of controls relative to synaesthetes on the personal distress subscale, which indicates that differences were not simply due to a tendency for synaesthetes to provided higher self-reported values overall (also see Figure 4.4).

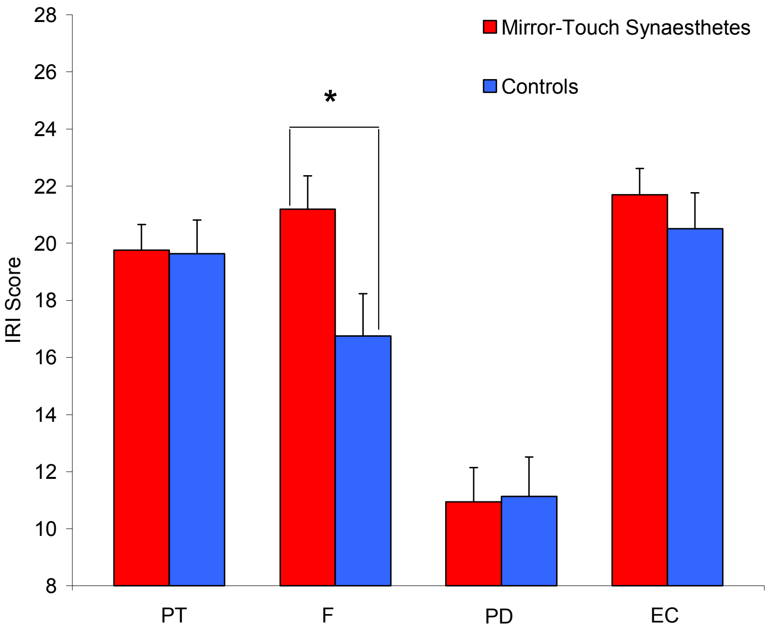


Figure 4.3 Mirror-touch synaesthetes showed significantly higher scores than controls on the fantasizing component, but not other components, of the Interpersonal Reactivity Index (mean ± s.e.m). * = $p < .05$. PT = Perspective Taking, F = Fantasizing, PD = Personal Distress, EC = Empathic Concern.

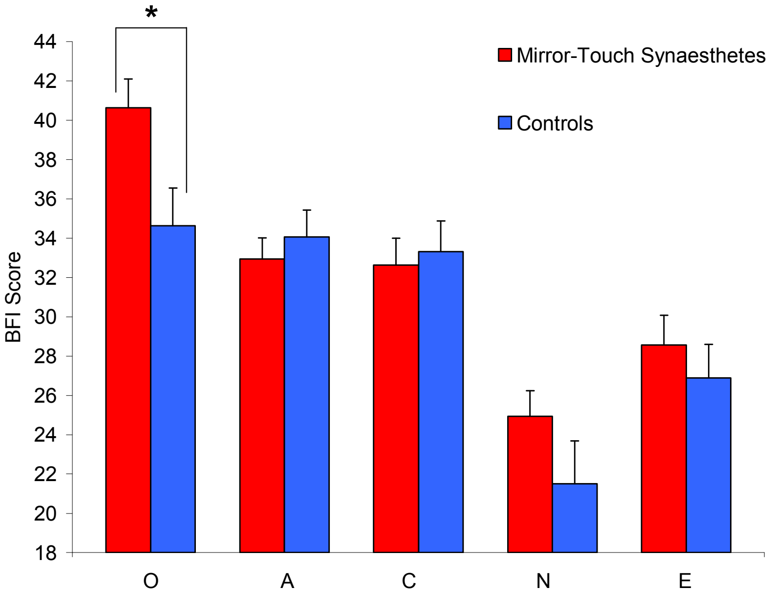


Figure 4.4 Mirror-touch synaesthetes showed significantly higher scores than controls on the Openness subscale, but not other components, of the BFI (mean ± s.e.m). * = $p < .05$. E = Extraversion, A = Agreeableness, C = Conscientiousness, N = Neuroticism, O = Openness.

Synaesthetes also differed from controls on the openness to experience trait of the BFI [t(30) = 2.62, *p* = .014], with synaesthetes demonstrating higher scores on this personality trait. No significant differences were found on the other BFI subscales (Figure 4.4).

Empathy and personality

Pearson's correlations were conducted to investigate the relationship between five components of personality (extraversion, agreeableness, conscientiousness, neuroticism and openness) with empathic abilities on each component of the EQ (cognitive empathy, emotional reactivity, social skills). This analysis revealed that the cognitive empathy subscale of the EQ showed a moderate correlation with extraversion [*n* = 120, *r* = .401, *p* = < .001], agreeableness [*n* = 120, *r* = .463, *p* = < .001], and conscientiousness [*n* = 120, *r* = .383, *p* = < .001]; but not neuroticism or openness traits. Similar associations were observed for the emotional reactivity subscale, which was associated with extraversion [*n* = 120, *r* = .292, *p* = < .01], agreeableness [*n* = 120, *r* = .455, *p* = < .001], conscientiousness [*n* = 120, *r* = .248, *p* = < .01] and openness [*n* = 120, *r* = .180, *p* = < .05]. Importantly, emotional reactivity was not correlated with neuroticism / emotional stability [*n* = 120, *r* = .016, *p* = .862]. The social skills subscale displayed a positive relationship with extraversion [*n* = 120, *r* = .337, *p* = < .001], agreeableness [*n* = 120, *r* = .336, *p* = < .001], and conscientiousness [*n* = 120, *r* = .324, *p* = < .001]; a negative relationship with neuroticism [*n* = 120, *r* = -.311, *p* = < .01]; but no relationship with openness.

Additionally, the relationship between IRI scores and personality were explored. This revealed a positive association between the perspective taking subscale and agreeableness [*n* = 120, *r* = .237, *p* = < .01]; the fantasizing subscale and openness [*n* = 120, *r* = .319, *p* = < .001]; the empathic concern subscale and extraversion [$n = 120$, $r = .185$, $p = < .05$], agreeableness [$n = 120$, $r = .524$, $p = < .001$], and conscientiousness [$n = 120$, $r = .201$, $p = < .05$]. The personal distress subscale was found to correlate negatively with extraversion [$n = 120$, $r = -.256$, $p = < .01$] and conscientiousness [$n = 120$, $r = -.283$, $p = < .01$], but positively with the neuroticism trait [$n = 120$, $r = .532$, $p = < .001$].

4.4 Discussion

Experiment 2 sought to examine findings of heightened emotional reactivity in mirror-touch synaesthesia documented in experiment 1. The study aimed to clarify if enhanced emotional reactivity was specific to enhanced other-orientated emotional empathy or to self related processes, and to investigate previous trends towards significantly higher levels of cognitive empathy in mirror-touch synaesthetes. Using a larger sample of mirror-touch synaesthetes and a new control group, the findings first replicate previous reports of heightened emotional reactivity, but not other components of empathy, in mirror-touch synaesthesia. They then confirm that heightened emotional reactivity in mirror-touch synaesthesia is not linked with heightened personal distress, indicating that heightened empathy in mirror-touch synaesthesia is indeed other rather than self-oriented. Further, the findings indicate that emotional reactivity does not reflect a less emotionally stable personality type – scores on emotional reactivity component of the EQ were not related to neuroticism / emotional stability personality trait.

Mirror-touch synaesthetes also differed from non-synaesthete controls on the fantasizing scale of the IRI. This subscale reflects an individual's ability to match another's feelings and behaviours onto their own. Previous findings indicate that increased scores on the fantasizing subscale of the IRI are related with heightened activations within the anterior insula and frontal operculum when witnessing others' gustatory emotions (Jabbi et al., 2006). In a previous brain imaging study on mirror-touch synaesthesia, the only brain region to differ between mirror-touch synaesthetes and non-synaesthetes when observing touch to others was the anterior insula (Blakemore et al., 2005). Shared representations within this brain region may be important for this component of empathy.

Finally, analysis of correlations between personality and measures of empathy provide important insights into the EQ and IRI measures. Evidence that heightened extraversion, agreeableness and conscientiousness are related with higher responses on all components of the EQ is consistent with findings implicating these personality traits in social cognition more generally; extraversion has been suggested to be a measure of social skills (John and Srivastava, 1999); agreeableness has been linked to altruistic behaviour (Barrick and Mount, 1991); and conscientiousness correlates negatively with psychoticism (Aluja, Garcia, and Garcia, 2002). Of note, is the lack of association between emotional reactivity and neuroticism, but presence of a strong positive correlation between the personal distress subscale of the IRI and neuroticism. This is consistent with the notion that the neuroticism personality trait would indicate self rather than other-oriented processes when correlated with empathy. Further to this, the openness trait appears specifically related to one’s ability to match another’s emotional state with one’s own (as indicated by the positive relationship between the openness subscale and emotional reactivity subscale of the EQ; and between the openness subscale and fantasizing subscale of the IRI) and this was the only personality trait where synaesthetes significantly differed from controls. Notably, it is difficult to determine the nature of the higher levels of openness to experience observed in mirror-touch synaesthetes relative to controls because the mirror-touch group included self-referred cases who have already demonstrated openness to experience by contacting unknown researchers for a study. Therefore, it is difficult to determine whether differences in the levels of openness to experience would extend to larger randomly recruited populations of mirror-touch synaesthetes (i.e. whether higher levels of openness to experience are more prominent in self-referred rather than randomly sampled populations of synaesthetes).

General Summary

In sum, the studies presented in this chapter indicate that mirror-touch synaesthetes show heightened levels of emotional, but not other components, of empathy. In experiment 1, mirror-touch synaesthetes scored significantly higher on emotional reactivity components of empathy, but not on social skills or cognitive empathy. A control group of synaesthetes who experience other types of synaesthesia but not mirror-touch did not differ from non-synaesthete controls, indicating that differences in empathy were specific to this subtype of synaesthete. Experiment 2 extended findings in experiment 1 to demonstrate that the heightened emotional reactivity observed in mirror-touch synaesthetes reflects other, rather than self-orientated, emotional reactions. Mirror-touch synaesthetes were also shown to differ from non-synaesthetes on an alternative measure to that used in experiment 1. On both measures synaesthetes showed heightened affective empathy (but not cognitive empathy), implying that sensorimotor simulation is important for some, but not all components of empathy. Given that mirror-touch synaesthesia has been linked to heightened sensorimotor simulation (Blakemore et al., 2005), these findings appear consistent with accounts of empathy that posit a role for sensorimotor simulation mechanisms (Gallese, 2006; Gallese and Goldman, 1998; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007) and are consistent with functional brain imaging

(Nummenmaa et al., 2008) and neuropsychological findings (Shamay-Tsoory et al., 2009) which indicate that emotional empathy may be linked more closely to sensorimotor simulation of another’s state.

CHAPTER 5: FACIAL EXPRESSION RECOGNITION IN MIRROR-TOUCH SYNAESTHESIA

The findings from chapter 4 indicate that mirror-touch synaesthesia is linked with heightened affective empathy. Simulation models of expression recognition contend that in order to understand another's facial expressions individuals map the perceived expression onto the same sensorimotor representations which are active during the experience of the perceived emotion. To investigate this view, the present study examines facial expression and identity recognition abilities in mirror-touch synaesthesia. Mirror-touch synaesthetes outperformed non-synaesthetic controls on measures of facial expression recognition, but not on control measures of face memory or face perception. These findings imply a role for sensorimotor simulation in the recognition of facial affect, but not facial identity.

5.1 Introduction

The ability to perceive a face is one of the most highly developed visual skills in humans, important not only for our ability to recognise the identity of others but also to facilitate social interaction. Neurocognitive models of face perception highlight the role of a number of face-specific and domain-general mechanisms in this process, and distinguish between those involved in the recognition of facial identity and those involved in the recognition of expressions at different stages of cortical processing (Bruce and Young, 1986; Calder and Young, 2005; Haxby, Hoffman, and Gobbini, 2000).

Simulation accounts of expression recognition contend that to understand another's facial emotion the observer simulates the sensorimotor response associated with generating the perceived facial expression (Adolphs, 2002; Adolphs, 2003; Gallese, Keysers, and Rizzolatti, 2004; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006). This is supported by evidence that electromyographic responses in expression relevant facial muscles are increased during subliminal exposure to emotional expressions (Dimberg, Thunberg, and Elmehed, 2000); that preventing the activation of expression relevant muscles impairs expression recognition (Oberman, Winkielman, and Ramachandran, 2007); and that perceiving another person's facial expressions recruits similar premotor and somatosensory representations as when the perceiver generates the same emotion or expression (Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003; Hennenlotter et al., 2005; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007; Winston, O'Doherty, and Dolan, 2003). Further, neuropsychological findings indicate that focal brain damage to right somatosensory cortices is associated with expression recognition deficits (Adolphs, Damasio, Tranel, Cooper, and Damasio, 2000), and transcranial magnetic stimulation findings demonstrate the necessity of the right somatosensory cortex for facial expression recognition abilities in healthy adults but not face identity recognition (Pitcher, Garrido, Walsh and Duchaine, 2008). These findings imply that purely visual face-processing mechanisms interact with sensorimotor representations to facilitate expression recognition. This thought to differ to facial identity recognition, in which there is no clear indication of how one could simulate another's identity (Calder and Young, 2005).

While much has been learnt from studies involving a disruption of simulation mechanisms, an alternative approach is to consider whether facilitation of these mechanisms promotes expression recognition. One example of facilitated sensorimotor simulation is the case of mirror-touch synaesthesia (Blakemore, Bristow, Bird, Frith, and Ward, 2005). As noted previously, in mirror-touch synaesthesia, simply observing touch to others elicits a conscious tactile sensation on the synaesthete's own body. Functional brain imaging indicates that this variant of synaesthesia is linked to heightened neural activity in a network of brain regions which are also activated in non-synaesthetic control subjects when observing touch to others (the mirror-touch system; Blakemore et al., 2005). The mirror-touch system is comprised of brain areas active during both the observation and passive experience of touch (including primary and secondary somatosensory cortices, and premotor cortex; Blakemore et al., 2005; Ebisch, Perucci, Ferretti, Del Gratta, Luca Romani, and Gallese, 2008; Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004). It has been suggested that brain systems with mirror properties may be crucial for social perception because they provide a probable neural mechanism to facilitate sensorimotor simulation of another's perceived state (Gallese, Keysers, and Rizzolatti, 2004; Keysers and Gazzola, 2006). In this sense, mirror-touch synaesthesia can be viewed as a case of heightened sensorimotor simulation, which may be able to inform on the role of sensorimotor simulation mechanisms in social cognition. Consistent with this, in chapter 4 I report that mirror-touch synaesthetes show heightened emotional empathy compared to control subjects. Enhanced empathy was not found in other types of synaesthesia, suggesting that it relates specifically to this variety of synaesthesia.

This study sought to establish whether this type of synaesthetes differed in another aspect of social perception, namely facial expression recognition. To do so, the performance of mirror-touch synaesthetes and non-synaesthetic control subjects on tasks of facial expression recognition, identity recognition and identity perception were compared. Based upon the hypothesis that mirror-touch synaesthetes have heightened sensorimotor simulations mechanisms it was predicted that synaesthetes would show superior performance on expression recognition tasks due to heightened sensorimotor simulation mechanisms, but not on the identity recognition or face perception control tasks that are less dependent on simulation.

5.2 Method

Participants

Eight mirror-touch synaesthetes (6 female and 2 male; mean age ± s.d = 45.6 ± 11.7 years) and twenty non-synaesthetic control subjects (15 female and 5 male; mean age ± s.d = 35.6 ± 13.6 years) took part in the study. All cases of mirror-touch synaesthesia were confirmed using a previously developed visual-tactile congruity paradigm designed to provide evidence for the authenticity of the condition (Banissy and Ward, 2007; also see Chapters 1 and 2 of this thesis for a description of the task used).

Materials and Procedure

Participants completed four tasks in a counterbalanced order. These tasks are detailed below.

Films Facial Expression Recognition

This task investigated participants' abilities to recognize the emotional expressions of others. In each trial participants were presented with an adjective describing an emotional state followed by three images (each image shown for 500 msec, with a 500msec ISI) of the same actor or actress displaying different facial expressions. Participants were asked to indicate which of the three images best portrayed the target emotional adjective. There was no fixed inter-trial interval as participants began each trial with a key press (i.e. the task was self-paced).

In order to portray subtle facial expressions, expression stimuli were captured from films (Figure 5.1a). Fifty-eight target images (preceded by three practice trials) from 15 films were used. All films were from a non-English speaking country to decrease the probability that participants had seen them or were familiar with the actors. Target and distracter stimuli were selected based on four pilot studies (see Garrido et al., in press for description). Each stimulus was shown once during the test and trials were presented in a pseudo-random order over two blocks (29 trials per block).

Cambridge Face Memory Test Long Form (CFMT+)

To test face recognition the performance of synaesthetes and non-synaesthetes on the CFMT+ was compared (Russell, Duchaine, and Nakayama, 2009). The task is an adapted version of the Cambridge Face Memory Test (Duchaine and Nakayama, 2006; Figure 5.1b) and was designed to distinguish normal from super-normal ability at recognising faces (Russell et al., 2009). During the task subjects learn to recognize six unfamiliar male faces from three different views (left 1/3 profile, frontal, right 1/3 profile) and are then tested on their ability to recognise these faces in a three-alternative forced-choice task. The test is comprised of four sections, each more difficult than the previous. The first three sections are taken from the original CFMT (Duchaine and Nakayama, 2006) and the final section forms the longer CFMT+ (Russell et al., 2009).

The test begins by testing recognition with the same images that were used during training (i.e. participants are are asked to memorise an unfamiliar male face from three different views and are then tested on their memory for the trained face). In the first phase each training image is shown for three seconds and immediately followed by three trials per face, resulting in eighteen trials overall. This relatively easy introduction is followed by a further training phase in which participants are shown six frontal views of the faces for twenty seconds. The participants’ memory for each face is then assessed using novel images that show the target faces from un-trained views and lighting conditions (thirty trials). Following a further twenty second training phase in which participants are shown six frontal views of the face, a third section consisting of novel images with visual noise added (twenty-four trials) is completed. In the CFMT+, this is followed by a final section containing thirty very difficult trials in which distracter images repeat much more frequently, targets and distracters contain more visual noise than the images in the third section, cropped (i.e. only showing internal features) and uncropped images (i.e. showing hair, ears, and necks) are used, and images showing the targets and distracters making emotional expressions are included. An inter-trial interval of 1 second is used throughout. The percentage of correct responses for each section and overall are measured. Feedback is not provided during the test.

Cambridge Face Perception Test (CFPT)

To investigate face perception the CFPT was administered (Duchaine, Germine, and Nakayama, 2007). This test assesses the ability to perceive differences between facial identities. Memory demands are minimal because faces are presented simultaneously. During the task, subjects are shown a target face (from a ¾ viewpoint) and six faces (from a frontal view) morphed between the target and distracter in varying proportions (88%, 76%, 64%, 52%, 40%, 28%) so that they vary systematically in their similarity to the target face (Figure 5.1c). Subjects are asked to sort the six faces by similarity to the target face and are given one minute to do so. Participants sorted the faces by clicking on the face which they wished to move and then indicating where the face should be by clicking in the area between two faces. The desired face was then moved to the chosen location by the program. At the end of each trial participants then clicked an option on screen to begin the next trial (i.e. the task was self-paced). The task involves eight upright and eight inverted trials that alternate in a fixed pseudo-random order. This allows investigation of the inversion effect for face perception. Performance is measured by an error score. This is calculated by summing the deviations from the correct position for each face, with one error reflecting each position that a face must be moved in order to be in the correct location. For example, if a face was one position from the correct location than this leads to an error score of one. If it is three positions away this is an error score of three.

Same-Different Expression and Identity Matching Task

This experiment investigated participants' abilities to match another's facial identity or facial expressions under identical experimental conditions.

In the expression matching task, participants were presented with a "sample" face (250 msec) followed by a fixation cross (1000 msec), and a "target" face (250 msec). Participants were asked to indicate whether the target facial expression matched, or was different to, the sample facial expression. On half of the trials, the target and sample face expressed the same emotion and half the sample-target pairs showed different emotions (Figure 5.1d). A total of 72 trials (split between 2 blocks) were completed. Each image showed one of six female models making one of six basic facial expressions: anger, disgust, fear, happiness, sadness or surprise. Each stimulus was a greyscale image taken from the Ekman and Friesen (1976) facial affect series. Stimuli were cropped with the same contour to cover the hair and neck using Adobe Photoshop. In the expression task, identity always changed between sample-target pairs and each expression was presented an equal number of times.

In the identity matching task, the same stimuli and procedure were used. Participants were asked to indicate whether the sample and target face were the same or a different person. Half of the trials showed pairs with the same identity and half with a different identity. Expression always changed between the sample and target face, and the six models were presented an equal number of times.

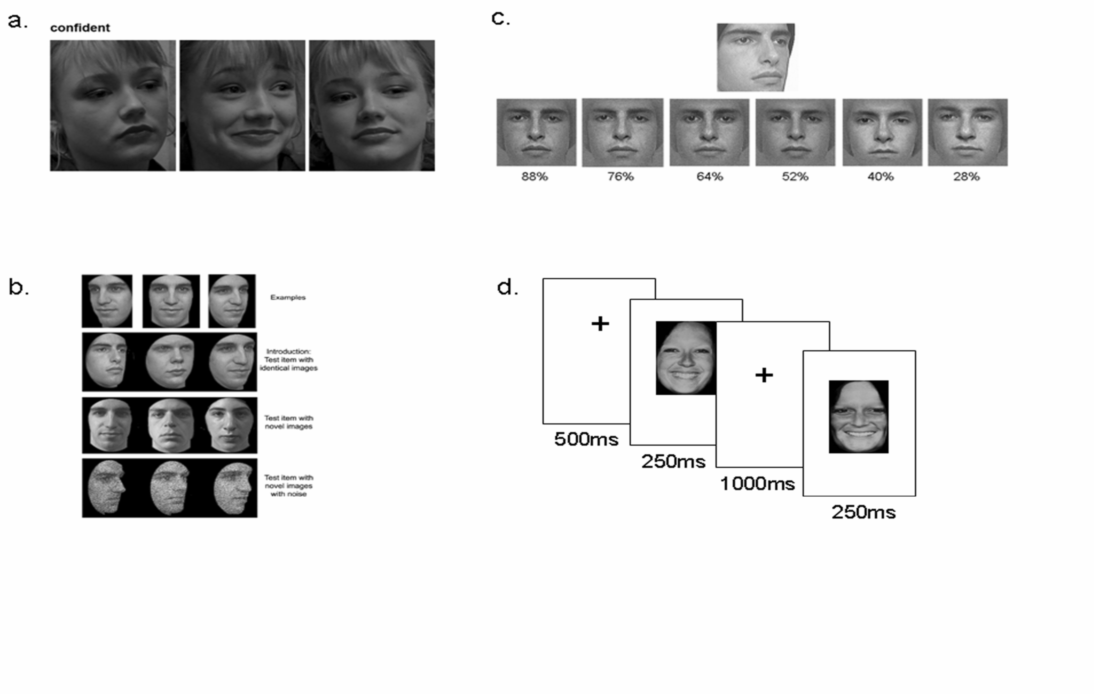


Figure 5.1 Summary of the tasks used. (a) Films Facial Expression Task. This task investigated participants' abilities to categorize the emotional expressions of others. Participants were presented with a target adjective describing an emotional state followed by three images shown consecutively for 500 msec each. Participants were asked which of the three images best portrayed the target emotion. In the actual task colour stimuli were used. (b) Cambridge Face Memory Test Long Form. This task investigated participants' abilities to memorize facial identity and was derived from the Cambridge Face Memory Test (shown in figure). During the task participants memorized six unfamiliar male faces. They were then tested on their ability to recognize the faces in a three-alternative-forced-choice paradigm. The task involves four sections (for stimuli from the final section see Russell et al., 2009), each more difficult than the preceding section. (c) Cambridge Face Perception Test. This task investigated participants' abilities to perceive faces in the absence of memory. Participants were shown a target face and six faces morphed between the target and a distracter face. Participants sorted the six faces by similarity to the target face. Faces were presented upright and inverted in a fixed pseudo-random order. (d) Same-Different Expression-Identity Matching Task. This task investigated participants' abilities to match another's facial identity or facial expressions. Participants were presented with a sample face followed by a fixation cross, and then a target face. In the expression matching task participants indicated whether the expression in the target face matched the expression in the sample face. In the identity matching task participants indicated whether the identity of the target face and the prime face matched.

5.3 Results

Films Facial Expression Recognition

Accuracy and reaction time performance were compared separately using a one way between subjects ANCOVA. Participant age was used a covariate on all analyses because of slight trend for synaesthetes to differ from controls on age [$t_{26} = 1.84$, $p = .078$]. One control subject was withdrawn from analysis due to difficulties in understanding the meaning of expression adjectives and performing more than three standard deviations below the control group mean on accuracy and reaction time measures.

Synaesthetes showed superior abilities at recognizing the emotional expressions of others (Figure 5.2). Analysis of accuracy performance revealed that mirror-touch synaesthetes outperformed control subjects on expression recognition [$F_{1,24} = 16.38$, $p = < .001$] (Figure 5.2a). This difference was not due to a speed-accuracy trade off as no significant effect of group (synaesthete or control) was found for reaction time performance, and in fact synaesthetes tended to perform faster than controls [$F_{1,24} = .962$, $p = .336$] (Figure 5.2b). These findings suggest that mirror-touch synaesthetes show superior facial expression recognition, which may be due to heightened sensorimotor simulation mechanisms.

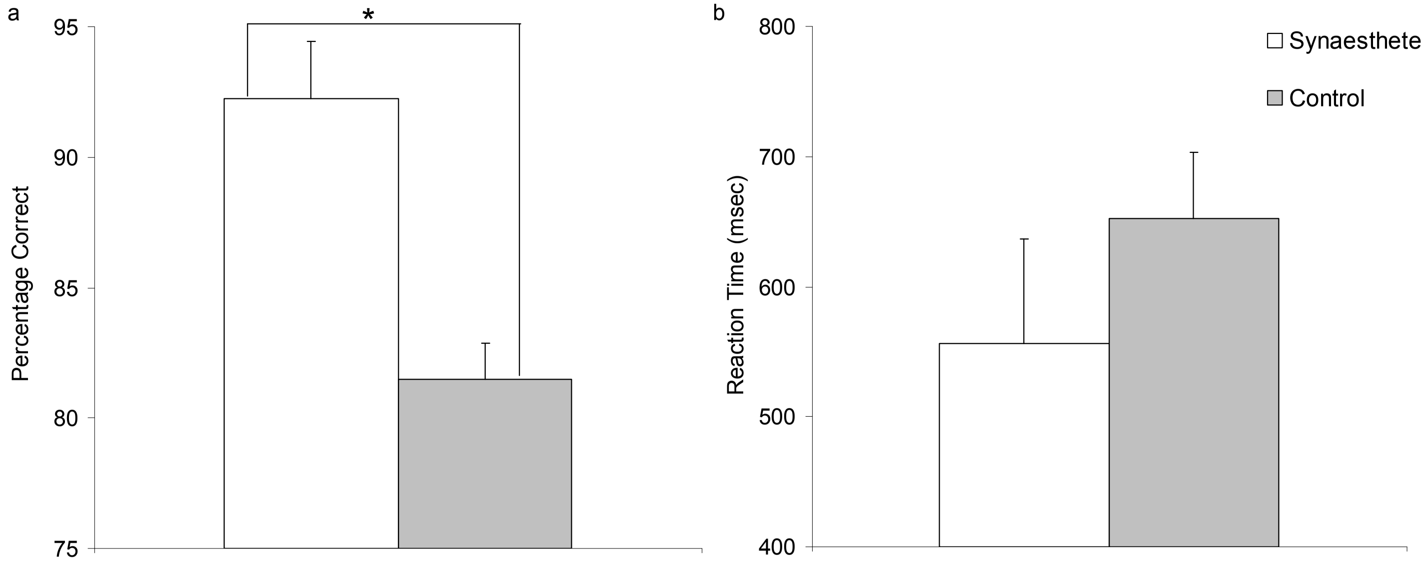


Figure 5.2 Mean accuracy (a) and reaction time performances (b) of synaesthetes and controls on the films facial expression task (± s.e.m). Synaesthetes were significantly more accurate at categorizing the emotional facial expressions of others (a). This was not due to a speed accuracy trade off as no significant differences were found for reaction time and synaesthetes showed a trend to be faster than control subjects (b).

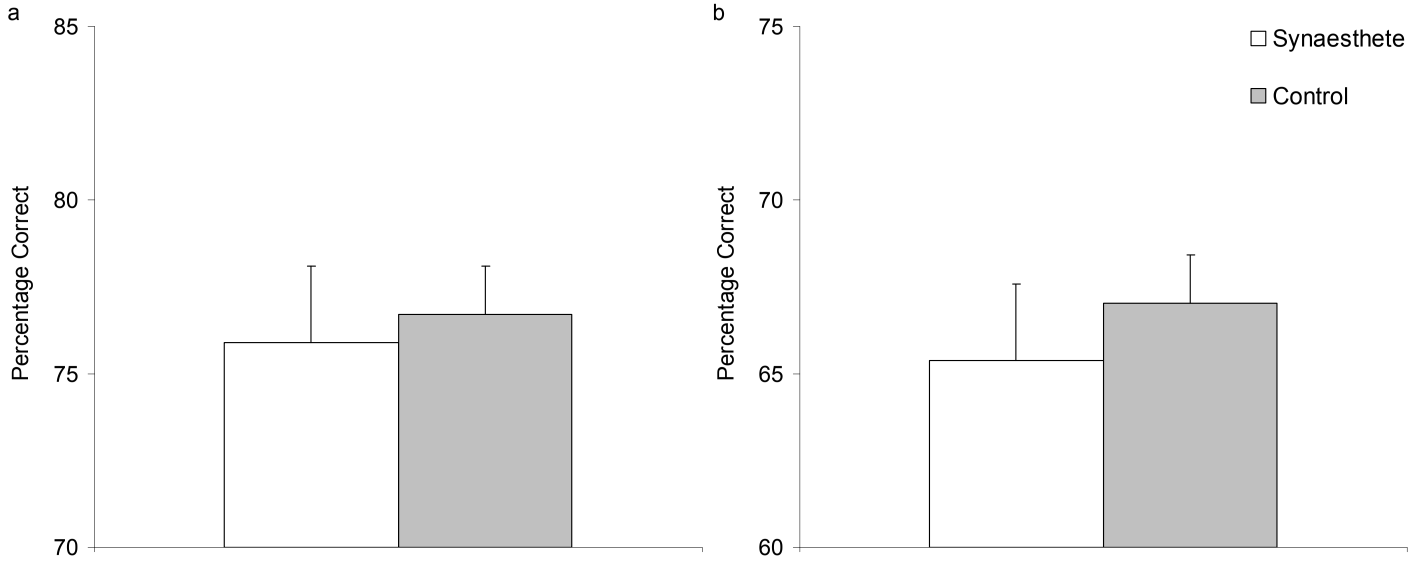


Figure 5.3 Mean accuracy performances (± s.e.m) on the CFMT (a) and CFMT+ (b) for synaesthetes and controls. The performance of synaesthetes and controls did not significantly differ on the CFMT (first three sections of task) or CFMT+.

Cambridge Face Memory Test Long Form

Accuracy performance from the Cambridge Face Memory Test (first three sections) and Cambridge Face Memory Test Long Form are shown in figure 5.3. No significant differences were observed between synaesthetes and controls on either the CFMT [$F_{1,25} = .023$, $p = .880$] (Figure 5.3a) or the CFMT + [$F_{1,25} = .095$, $p = .761$] (Figure 5.3b). Therefore unlike facial expression recognition, synaesthetes and controls did not differ in their ability to memorize facial identity.

Cambridge Face Perception Test

Error scores on the eight upright and eight inverted trials were summed to determine the total number of upright and inverted errors. A 2 (Group) x 2 (Trial Type) ANCOVA revealed a significant effect of trial type [$F_{1,25} = 5.81$, $p = .024$] which was due to an inversion effect, whereby overall participants were less accurate on inverted (mean ± s.e.m = 70 ± 3) compared with upright trials (mean ± s.e.m = 41.5 ± 3.21). Importantly, this effect did not interact with group [$F_{1,25} = .37$, $p = .549$] and no main effect of group was found [$F_{1,25} = .253$, $p = .619$] (Figure 5.4). Therefore, unlike expression recognition, synaesthetes and controls did not significantly differ in their abilities to detect another's facial identity.

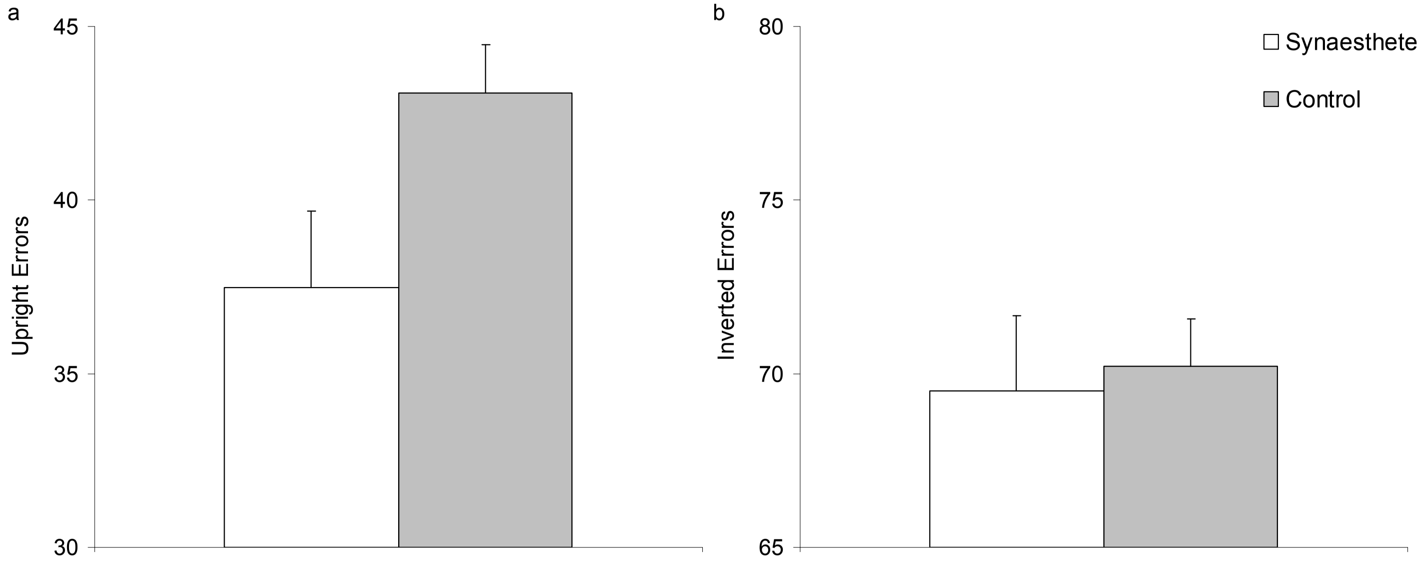


Figure 5.4 Mean error score (± s.e.m) for synaesthetes and controls on upright (a) and inverted (b) trials of the CFPT. No significant differences were found between the performance of synaesthetes and controls on a measure of facial identity perception. Error scores are based on the deviation from the expected correct ordering of the correct location of the target face. Superior performance is reflected in a lower error score.

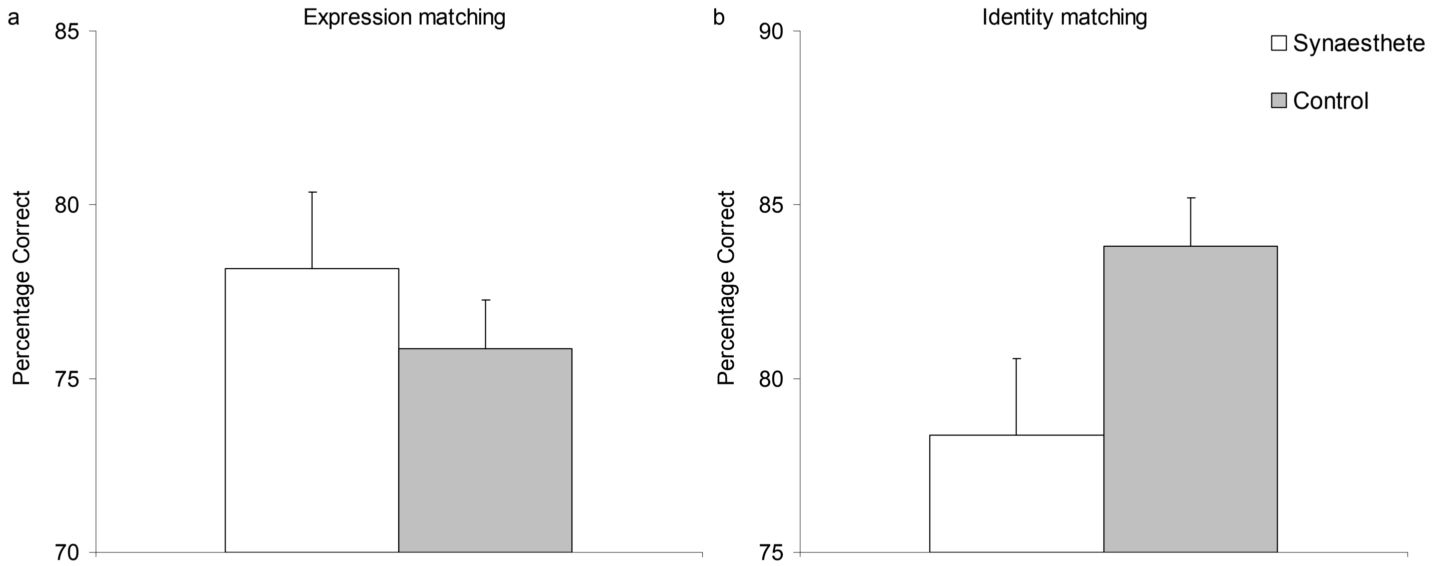


Figure 5.5 Mean accuracy performances (± s.e.m) on the expression matching (a) and identity matching (b) task for synaesthetes and controls. A 2 (Task) x 2 (Group) ANCOVA revealed a significant task x group interaction. On the expression task, there was a trend for synaesthetes to outperform controls whereas on the identity task, there was a trend for controls to outperform synaesthetes. Within-group comparisons between the tasks revealed that controls were significantly more accurate in the identity compared to the expression task. Synaesthetes did not show this bias towards identity matching - expression and identity matching performances were comparable.

Same-Different Expression and Identity Matching Task

A 2 (Group) x 2 (Task) mixed ANCOVA was conducted. Participant age was used as a covariate. No main effect of task or group was found. No relationship between task and age was observed. There was however a significant interaction between task and group [$F_{1,25} = 4.507$, $p = .044$]. Controls were more accurate, and therefore showed an advantage, on the identity matching task relative to the emotion matching task [$F_{1,18} = 5.10$, $p = .037$]. Synaesthetes did not show this pattern - analysis of within-subject effects revealed no significant difference between the two tasks for the synaesthetic group [$F_{1,6} = .759$, $p = .417$]. There was also a non-significant trend for synaesthetes to outperform controls on the expression matching task (Figure 5.5a), but for controls to outperform synaesthetes on the identity matching task (Figure 5.5b).

5.4 GENERAL DISCUSSION

This study investigated expression and identity face processing in mirror-touch synaesthetes and non-synaesthete control participants. It was predicted that heightened sensorimotor simulation mechanisms would result in superior expression recognition, but would not affect the identity recognition abilities of mirror-touch synaesthetes. Consistent with these predictions, mirror-touch synaesthetes were superior when recognizing the facial expressions, but not facial identities of others. These findings are consistent with simulation accounts of expression recognition which suggest that in order to understand another's emotional expressions individuals must simulate the sensorimotor response associated with generating the perceived facial expression (Adolphs, 2002; Adolphs, 2003; Gallese, Keysers, and Rizzolatti, G, 2004; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006).

A variety of sources indicate that recognizing another's identity and expressions relies upon multiple stages of representation, including purely visual, multimodal, expression-general and expression-specific mechanisms (e.g. Adolphs et al., 2000; Anderson, Spencer, Fulbright, and Phelps, 2000; Calder, Lawrence, and Young, 2001; Calder, Keane, Lawrence, and Manes, 2004; Lawrence, Calder, McGowan, and Grasby, 2002; Lewis et al., 2003; Keane, Calder, Hodges, and Young, 2002; Pitcher et al., 2008; Sprengelmeyer et al., 1996). Simulation accounts of expression recognition contend that one mechanism involved in expression, but not identity, recognition is an internal sensorimotor re-enactment of the perceived expression (Adolphs, 2002; Adolphs, 2003; Gallese, Keysers, and Rizzolatti, 2004; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006). Functional brain imaging (Carr et al., 2003; Hennenlotter et al., 2005; Montgomery and Haxby, 2008; van der Gaag, et al., 2007; Winston et al., 2003), neuropsychological (Adolphs et al., 2000), and transcranial magnetic stimulation studies (Pitcher et al., 2008) suggest a key role for somatosensory resources in expression recognition. The findings that individuals who show increased levels of somatosensory simulation (mirror-touch synaesthetes) demonstrate superior expression, but not identity perception, are consistent with this view. The task specific nature of the findings also indicate that the superior performance shown by mirror-touch synaesthetes on the expression recognition tasks are not linked to heightened motivation on the part of the synaesthetic subjects.

The experiments in chapter 4 documented that mirror-touch synaesthetes show heightened emotional reactivity compared to controls, but do not differ on other components of empathy. The findings from the current investigation indicate that mirror-touch synaesthesia is not only linked with some components of empathy, but also with superior emotion recognition. It remains to be established whether heightened emotion sensitivity displayed by mirror-touch synaesthetes is a cause or consequence of this type of synaesthetic experience. While it is assumed that mirror-touch synaesthetes form part of the synaesthetic population, and are therefore a unique group of subjects, the principles which bias what type of synaesthesia will or will not be developed are a matter of debate (Bargary and Mitchell, 2008; Cohen Kadosh, Henik, and Walsh, 2009; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001; Hubbard and Ramachandran, 2005; Ramachandran and Hubbard, 2001; Rouw and Scholte, 2007; Sagiv and Ward, 2006). Conceptually there are two possibilities: i) mirror-touch synaesthetes reflect the top end of a spectrum along which emotion sensitivity ranges (e.g. the 'normal' architecture for multi-sensory interactions) and this biases them towards interpersonal synaesthetic experience, or ii) mirror-touch synaesthetes are a unique population whose extra sensory experiences predispose superior emotion sensitivity.

In sum, this study demonstrates that mirror-touch synaesthesia is associated with superior facial expression recognition abilities. The observed superiority in face processing is restricted to expression recognition. Mirror-touch synaesthetes show enhanced emotional expression abilities. They did not differ from controls on identity perception measures. Given that mirror-touch synaesthesia has been linked to heightened somatosensory simulation these findings are consistent with simulation based accounts of expression recognition and indicate that somatosensory resources are an important facet in our ability to recognise the emotions of others.

CHAPTER 6: METHODOLOGICAL INTRODUCTION TO TMS

This chapter outlines the methodological principles for using transcranial magnetic stimulation (TMS) to disrupt normal cognitive functioning. The main principles, ethical considerations, spatial and temporal constraints, and types of TMS are discussed. In chapters 7 and 8 continuous theta burst TMS was performed to investigate the role of sensorimotor simulation in expression recognition. This TMS paradigm is introduced here and it's spatial and temporal effects are discussed.

6.1 INTRODUCTION

Transcranial magnetic stimulation (TMS) is a non-invasive experimental technique that is capable of suppressing or facilitating activity in the brain. The effect of this modulation of neural activity can be measured using a variety of standard behavioural (e.g. reaction time, accuracy, thresholds) and physiological (e.g. evoked potentials, functional brain imaging) measures; is temporally discrete (c.f. Walsh and Cowey, 2000); and shows good spatial specificity (e.g. Pitcher, Charles, Devlin, Walsh, and Duchaine, 2009). The technique provides a unique tool to the cognitive neuroscientist because it permits the opportunity to assess the causality of a particular brain region to a given cognitive task. For example, one can use TMS to disorganize neural activity in a given brain region and investigate the effects of this disruption on functionally specific cognitive tasks (e.g. motion priming and human V5 / MT stimulation – Campana, Cowey, and Walsh, 2002; face processing and Occipital Face Area stimulation – Pitcher, Walsh, Yovel, and Duchaine, 2007). In this sense, TMS is similar to both human (e.g. Milner, 1966; Shallice, 1988) and animal (e.g. Cowey and Gross, 1970; Walsh and Butler, 1996) lesion studies in which one is able to make inferences about the necessity of specific brain areas based upon impairment to cognitive functioning.

There are also important differences between lesion and TMS studies, which lead to a number of benefits over patient-based research. Firstly, the nature of lesion studies means that the experimenter is required to make inferences about the normal architecture based on an abnormal system. This has a number of caveats including the influence of mechanisms of compensatory plasticity in the abnormal system, which may lead to changes in function or task performance. For example, it is often months after brain injury that the experimenter is able to examine patient performance systematically and it is difficult to disentangle whether one is measuring the removal of a region or the ability of other brain regions to compensate the function being investigated (Lomber, 1999; Robertson and Murre, 1999). Further, brain lesions are rarely spatially discrete and removal of a brain area may also incur damage at distal sites (e.g. via severed vessels, ablated white matter; Robertson and Murre, 1999; Walsh and Pascual-Leone, 2003). In contrast to this, TMS permits investigation of spatially specific brain regions in normal subjects and overcomes problems of neural compensation / reorganization because the main effects occur in a discrete temporal window (lasting a few tens of milliseconds to minutes depending on the type of stimulation used). In addition, because behavioural performance can be measured within-subjects (during both the application and the absence of stimulation), it is possible for subjects to act as their own control group, thereby strengthening the validity of the conclusions that can be drawn from a TMS experiment.

To consider the method further, this chapter discusses the principles, ethical aspects, spatial resolution, temporal constraints, and alternative TMS paradigms.

6.2 What is TMS?

Attempts to modulate human brain function using magnetic fields can be traced back to the late 19th century and developed over the next 100 years (c.f. Walsh and Pascual-Leone, 2003). However, these attempts rarely systematically measured the effects of magnetic stimulation and it was not until the 1980s that TMS (as we know it) was first introduced as a tool for cognitive neuroscience - Barker and colleagues (1985) reported the first successful attempts to disrupt normal cortical functioning when they applied magnetic stimulation over the motor cortex in human subjects and recorded the resulting muscle twitches via motor evoked potentials (MEPs).

The technique builds upon Faraday's observations of electromagnetic induction (1831), in which electric current passed along one wire coil (coil A) generates a magnetic field that induces electrical current in another wire coil (coil B). In TMS, rapidly changing electrical current is passed through a coil (i.e. coil A in Faraday example) located on the participant's scalp to generate a brief magnetic field which passes through the skull and induces electrical fields in the underlying cortex (i.e. coil B in Faraday example). The induced current alters the electrical state inside and outside of nerve axons, leading to membrane depolarisation and the initiation of action potentials (Nagarjan, Durand, and Warman, 1993). Thus, the electrical field induced by the TMS coil causes changes in the resting potential of the underlying neurons and effectively disorganises neural processing in a stimulated cortical region.

The duration of this disorganisation of neural processing is linked to the size of the induced current, which is related to the amplitude and the rate of change of the current passing through the TMS coil. Typically the current in the coil is large, up to 8 kiloamperes (kA), with a swift rise time of roughly 200 milliseconds (ms) and an overall duration of roughly 1 ms (Figure 6.1). The extent to which the resulting TMS pulse disrupts neural processing in the targeted area depends on the orientation of the coil and the orientation of the underlying nerve fibres (Amassian, Eberle, Maccabee, and Cracco, 1992). If the induced field is uniform across the cell membrane then no current will be induced. The TMS effects are optimised when the electric field is tangential to the orientation of the nerve fibre either due to the electric field orientation being perpendicular to a straight axon or an axon bending relative to the orientation of the induced field (Figure 6.2).

Two types of coils are typically used in TMS studies. They are the figure-of-eight and circular coils (Figure 6.3). All of the studies reported in this thesis use a figure-of-eight coil, which has been shown to produce the most focal effects of TMS (Ueno, Tashiro, and Harada, 1988). In the figure-of-eight coil, current flows in opposite directions around each of the windings and converges on the centre point of the coil where the electrical currents summate. This leads to focal neural stimulation with the largest effect occurring in the cortex situated directly under the centre-point of the coil. Because the outer-windings of the coil are away from the surface of the scalp they are unlikely to induce an additional disruptive magnetic field. The stimulation effects dissipate gradually as distance from the maximal point increases (Figure 6.3).

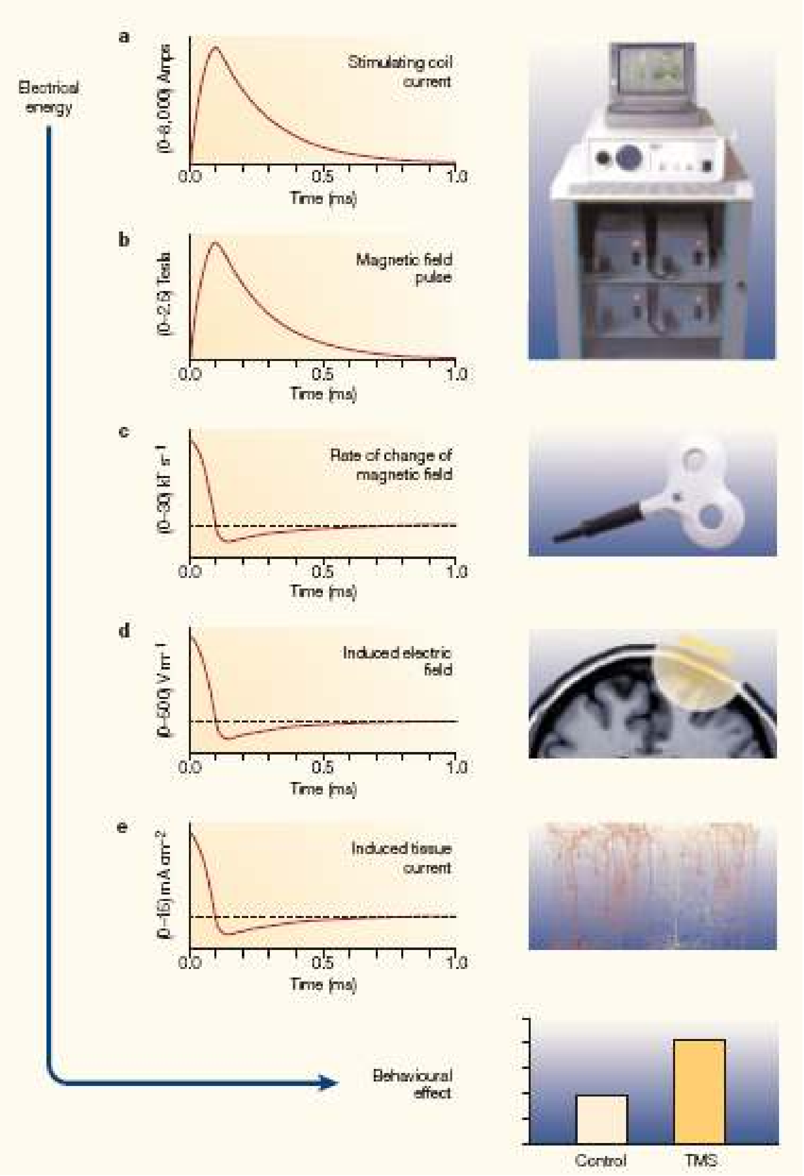


Figure 6.1 The sequences of events for a transcranial magnetic stimulation pulse (taken with permission from Walsh and Cowey, 2000). (a) A capacitor generates an electric current (up to 8kA). (b) This discharges into the TMS coil generating a magnetic pulse of up to 2 T. (c) The pulse has a rise time of roughly 200ms and lasts for 1ms, which changes rapidly due to its intense and brief nature. (d) The magnetic field generates an electrical field. (e) The magnetic field causes neural activity or changes in the resting potential of the underlying neurons. Note that monophasic pulses are shown in the figure (but biphasic pulses are used for repetitive TMS).

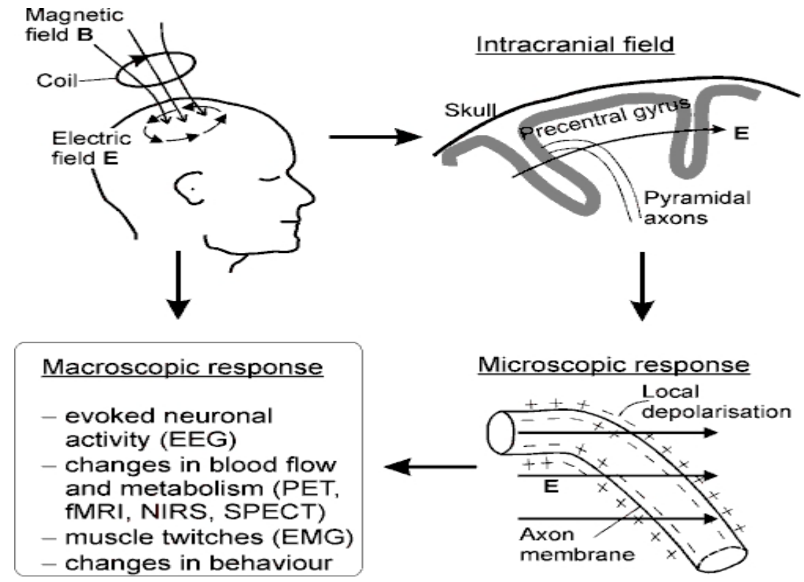


Figure 6.2 The effects of fibre orientation and electric field orientation for the application of a TMS pulse.

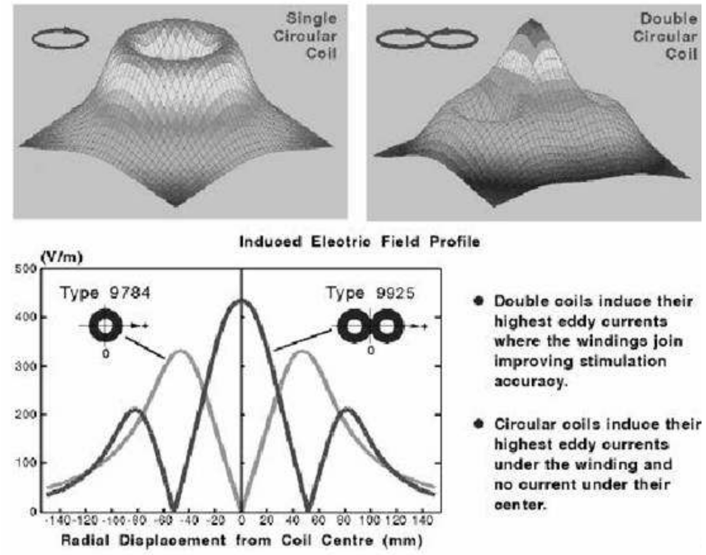


Figure 6.3 TMS-induced electrical fields produced by circular (top left) and figure-of-eight (top right) shaped coils. Maximal intensity with a circular coil is located directly under the winding, but with a figure-of-eight coil it is at the intersection of the two windings. The intensity of the induced current dissipates with a radial distance from the area of maximum intensity (diagram taken from the Magstim Guide to Magnetic Stimulation).

6.3 The spatial resolution of TMS

Figure 6.4 illustrates the spatial and temporal specificity of TMS in relation to other experiment methodologies.

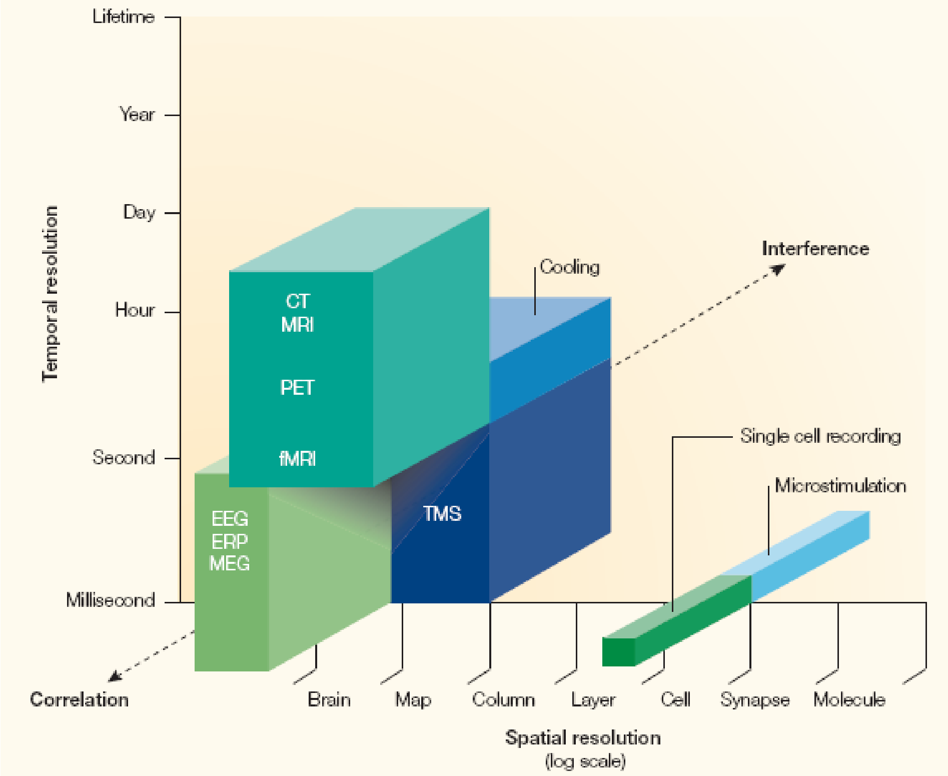


Figure 6.4 The spatial and temporal resolution of TMS compared with other experimental techniques. TMS benefits from high spatial and temporal resolution and is capable of interfering with brain function (taken with permission from Walsh and Cowey, 2000).

As noted in the last section, the magnetic field induced by TMS dissipates gradually as distance from the maximal point of stimulation decreases. This raises a concern of how confident one can be in the spatial and functional specificity of TMS. Put another way, how can one be sure that the effects observed in a TMS study are due to stimulation of the target region or due to more widespread dissipating effects of the induced magnetic field. The answer to this lies in a number of converging lines of evidence which demonstrate that while in theory, the magnetic field induced by TMS is infinite (with the induced electrical field decreasing from the centre of the stimulation focal point), in practice the size of the electrical field capable of disrupting normal neuronal activity is limited (i.e. it is anatomically and functionally specific). For example, TMS of the motor cortex results in visible and measurable (via MEPs) motor twitches in the muscles. This effect however is neither random nor non-specific – TMS to the motor cortex has been shown to evoke muscular twitches from selective muscle groups in a manner compatible with the functional layout of the motor homunculus, with stimulation at target sites varying from 0.5 to 1 centimetres apart leading to selective activation of each muscle type (Singh, Hamdy, Aziz, and Thompson, 1997; Wassermann, McShane, Hallet, and Cohen, 1992). The functional focality of the method is further demonstrated in the visual domain, where a similar spatial resolution (less than 1 cm on the scalp) has been reported through the study of the physiological effects induced by TMS stimulation of the primary visual cortex (V1; c.f. Walsh and Cowey, 2000). Moreover, stimulation to V1 leads to the generation of phosphenes, which are spatially distributed in a manner that corresponds with the retinotopic organisation of V1 (Kammer, 1999).

Outside of the primary motor and sensory areas, the effective spatial resolution[3] of TMS has regularly been demonstrated by functional dissociations following TMS to spatially discrete regions of the cortex. For example, in the same subjects, TMS targeted at the right occipital face area (thought to be functionally specialised for face processing) has been shown to impair face but not body or object recognition, while stimulation at a region of lateral occipital cortex (LO; thought to be functionally specialised for object processing) has been shown to impair object but not face or body recognition, whilst stimulation at the right extra-striate body area

---

[3] It is of note, that TMS does not only stimulate the neuron in a 1cm region, rather, it is that this represents the *physiologically effective* resolution of TMS.

(EBA; thought to be functionally specialised for body processing) has been shown to impair body but not face or object recognition (Pitcher et al., 2009) – this dissociation is particularly striking given the anatomical adjacency between these regions. Functional dissociations such as the triple dissociation described above demonstrate the functional focality of TMS and have been regularly observed across a variety of domains (e.g. Ashbridge, Walsh, and Cowey, 1997; Stewart, Walsh, Frith, and Rothwell, 2001).

A further approach to assess the spatial specificity of TMS is to combine the approach with methods such as fMRI, MEG or PET. To date, studies that have combined these methodologies have demonstrated a good correspondence between TMS defined functional regions and the areas revealed with high spatial resolution brain imaging techniques (Bestmann, Baudewig, Siebner, Rothwell, and Frahm, 2004; Bohning, Shastri, McConnell, Nahas, Lorberbaum, and Roberts, 1999; Ruff et al., 2006; Siebner et al., 1998; Terao et al., 1998).

In sum, while the effects of TMS will dissipate from the targeted region to other cortical areas, the functionally effective resolution is much more discrete (approximately 1cm). This has been demonstrated across a variety of studies by systematically measuring the effect on behaviour as the coil is moved away from an optimal stimulation site (e.g. by stimulating adjacent areas of cortex [Figure 6.5] which demonstrate functionally different characteristics or examining direct physiological effects).

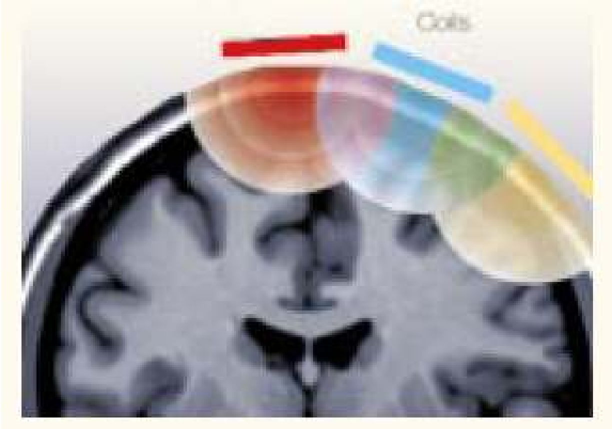


Figure 6.5 Functional dissociation method that can be employed using TMS (taken with permission from Walsh and Cowey, 2000). Using TMS one can infer the importance of a targeted region of stimulation for a particular function. Stimulation to an adjacent or functionally alternative region enables refined inferences to be made, including functional-anatomical attributions. The ‘coils’ and induced fields in this figure are illustrative of the methodological rationale and do not represent real configurations and effects.

6.4 Offline and online TMS: The temporal resolution of TMS

When considering the temporal effects of TMS a distinction needs to be drawn between offline and online paradigms. Online paradigms involve stimulation concurrent with behavioural performance (i.e. when a participant is doing a task) and have short-lasting effects (e.g. 1 msec per pulse), while offline paradigms take place prior to task performance and have more long-lasting effects during an experimental session (e.g. 20-60 minutes of altered brain activity).

For online TMS experiments, a typical single pulse of TMS is very brief, around 1ms. An important consideration for online TMS experiments is when is the most appropriate time window for neural disruption to produce behavioural impairment. A number of approaches have been developed to address this, including delivering single (Amassian, Cracco, Maccabee, Cracco, Rudell, and Eberle, 1993) or paired-pulses (Juan and Walsh, 2003; O’Shea, Muggleton, Cowey, and Walsh, 2004) of TMS to the target region at different time points after stimulus onset or the start of trial. The later has the advantage of reducing the number of temporal conditions in a TMS timing experiment.

It is also possible that the disruption induced by multiple pulses of TMS will summate, therefore inducing larger behavioural impairments. The potential for summation of the disruptive effect has been further exploited by repetitive TMS (rTMS) protocols. For example, Rushworth and colleagues (2001) delivered TMS at a frequency of 10 Hz for 500 ms and showed dissociations between parietal regions (supramarginal gyrus and angular gyrus) for mediating modality-specific attentional processes. To date there is no corroborating physiological evidence that the five pulses of TMS actually do summate, but despite this the approach has proven to be a robust online TMS protocol for demonstrating function-specific involvement of a wide variety of cortical areas across a number of domains (e.g. Beck, Muggleton, Walsh, and Lavie, 2006; Bjoertomt, Cowey, and Walsh, 2002; Campana et al., 2002; Lavidor and Walsh, 2003; Pitcher et al., 2008; Pitcher et al., 2009; Wig, Grafton, Demos, and Kelley, 2005).

In contrast to online TMS paradigms which rely upon observing effects in very short-lasting temporal windows, a recently introduced paradigm of offline continuous theta-burst stimulation (cTBS) provides a more long lasting window for one to examine changes in cortical function on behaviour. cTBS is a form of rTMS based on the burst patterns used to induce long lasting changes in synaptic effectiveness in animal experiments. The approach uses high frequency stimulation bursts (3 pulses at 50Hz), which are repeated at intervals of 200 milliseconds (i.e. 5Hz). In the motor system cTBS to M1 suppresses the excitability of motor cortical circuits for 20-60 minutes depending on the cTBS parameters used (Di Lazzoro et al., 2005; Di Lazzoro et al., 2008; Huang, Edwards, Rounis, Bhatia, and Rothwell, 2005;

Huang et al., 2009; Stefan, Gentner, Zeler, Dang, and Classen, 2008). In paradigms in which 20 seconds of cTBS (300 TMS pulses) is applied to the motor cortex, MEP amplitude is reduced for approximately 20-30 minutes; in paradigms in which 40 seconds of cTBS (600 TMS pulses) is applied MEP amplitude is reduced for considerably longer (up to one hour; Huang et al., 2005). This rapid method of suppressing cortical activity offers a unique opportunity to examine the functional role of a given brain region on behaviour in a relatively large time window. It also overcomes a number of potential confounds related to online stimulation, including the peripheral and proprioceptive effects of online TMS (e.g. muscular twitching; Terao et al. 1997) that may impact on task performance. The potential for this paradigm to be used to study cognitive processing has recently been fulfilled in several domains. Firstly, Vallesi and colleagues (2007) used cTBS to show a critical role for the right dorsolateral prefrontal cortex, but not left dorsolateral prefrontal cortex or right angular gyrus, in temporal processing. More recently, Kalla and colleagues used cTBS targeted at the dorsolateral prefrontal cortex to demonstrate the necessity of this brain region, but not the vertex or MT/V5 (TMS to MT / V5 facilitated processing), in conjunction visual search (Kalla, Muggleton, Cowey, and Walsh, 2009). The studies reported in chapters 7 and 8 used cTBS to investigate the role of sensorimotor cortices in expression recognition from visual and auditory cues.

6.5 The safety of TMS as an experimental tool

The primary concern in any TMS experiment is the health and safety of the subjects (c.f. Wasserrmann, 1998 for detailed safety guidelines). The main ethical concern in the use of TMS is the possible side effects of this method. TMS is sometimes associated with minor discomfort, muscular pain, and occasionally mild headache. These are all treatable with simple pain killers such as aspirin, and any discomfort can mostly be alleviated by repositioning the TMS coil. All volunteers should be informed of these possible effects and they should be minimised in each individual. As with all studies, participants should be informed that they can withdraw from the experiment at any time, without having to give a reason why. Sessions in which subjects are perceived to be uncomfortable but do not report this should also be terminated by the experimenter. The concern most commonly associated with TMS is that in rare circumstances TMS has induced seizures. These are most likely to occur in individuals already susceptible to seizures (i.e. with a history of epilepsy) and those taking neuroleptic medication (Stewart, Ellison, Walsh, and Cowey, 2001). For the studies reported in this PhD, only healthy adult subjects (aged from 18-50 years), with no psychiatric or neurological history and no family history of seizures took part in the proposed research. All safety guidelines regarding the use of TMS (Wassermann, 1998) were followed and all the experiments reported in the thesis were approved by the local ethics committee at University College London.

CHAPTER 7: THE ROLE OF SENSORIMOTOR SIMULATION IN AUDITORY EMOTION DISCRIMINATION

Functional neuroimaging studies indicate that activity in primary somatosensory and premotor cortex is evoked during the perception of emotion. In the visual domain, right somatosensory cortex activity has been shown to be critical for facial emotion recognition. However, the importance of these representations in modalities outside of vision remains unknown. This study used continuous theta-burst transcranial magnetic stimulation (cTBS) to investigate whether neural activity in the right primary somatosensory cortex (rSI) and right lateral premotor cortex (rPM) is central to non-verbal auditory emotion recognition. Two groups of participants completed same-different tasks on auditory stimuli, discriminating between either the emotion expressed or the speakers' identities, prior to and following cTBS targeted at rSI, rPM or the vertex (control site). A task-selective deficit in auditory emotion discrimination was observed. Stimulation to rSI and rPM resulted in a disruption of participants' abilities to discriminate emotion, but not identity, from vocal signals.

7.1 Introduction

Our ability to recognise the emotions of others is a crucial feature of human social cognition. The neurocognitive processes which underpin this have recently been described as being achieved through simulation processes (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, 2004; Goldman and Sripada, 2005; Keysers and Gazzola, 2006). These models suggest that understanding another's emotions requires individuals to map the observed state onto their own representations which are active during the experience of the perceived emotion. The discovery of mirror neurons in the primate brain (Gallese, Fadiga, Fogassi, and Rizzolatti, 1996), and evidence of not only a 'classical' action mirror system (Buccino et al., 2001; Fadiga, Fogassi, Pavesi, and Rizzolatti, 1996; Gazzola, Aziz-Zadeh, and Keysers, 2006), but also 'extended' mirror systems in the human brain (involved in mirroring sensation and emotion; Avenanti, Bueti, Galati, and Aglioti, 2005; Blakemore, Bristow, Bird, Frith, and Ward, 2005; Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003; Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004;

Singer, Seymour, O'Doherty, Kaube, Dolan, and Frith, 2004; Wicker, Keysers¸ Plailly, Royet, Gallese, and Rizzolatti, 2003) has provided a candidate neurophysiological mechanism for such shared representations in emotion recognition. These brain regions may, in part, aid emotion recognition because they enable the observer to match the observed emotion within cortical areas active during the observer's own experience of the perceived emotion (Carr et al., 2003; Hennenlotter et al., 2005; Jabbi, Swart and Keysers, 2007; Leslie, Johnsen-Frey, and Grafton, 2004; van der Gaag, Minderaa, and Keysers, 2007). Consistent with this, functional brain imaging studies indicate that components of classical and extended mirror systems (including premotor cortex and primary somatosensory cortex) are recruited when perceiving others' facial emotions (Hennenlotter et al., 2005; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007); that primary somatosensory cortex is activated when judging another's facial emotion (Winston, O'Doherty, and Dolan, 2003); and that the auditory-motor mirror system is activated during the perception of non-vocal emotion expressions (e.g. hearing somebody laughing; Warren et al., 2006). Further, in chapters 4 and 5 I show that facilitated sensorimotor simulation (in mirror-touch synaesthesia) is linked to heightened emotional empathy and emotional expression recognition. In attempt to assess what impact suppressing sensorimotor activity has on the expression recognition abilities of healthy adults, here (and in chapter 8) I use TMS in non-synaesthetes to assess whether sensorimotor activity plays a central role in our ability to recognize the emotions of others.

In the visual domain, there is growing evidence that sensorimotor activity plays a causal role in facial emotion recognition. Neuropsychological findings indicate that deficits in the recognition of facial affect are related to damage within right hemisphere somatosensory-related cortices (Adolphs, Damasio, Tranel, Cooper, and Damasio, 2000) and transcranial magnetic stimulation (TMS) findings in healthy adults are consistent with this (Pitcher, Garrido, Walsh and Duchaine, 2008). In the study by Pitcher and colleagues (2008), rTMS targeted at right primary somatosensory cortex resulted in a disruption of participants' abilities to discriminate the facial expressions, but not facial identities, of others. It remains unclear if neural activity within these systems is necessary for the recognition of affect from alternative modalities. Moreover, if sensorimotor resources are vital for global processing of emotion then these resources should also be central for emotion recognition abilities of healthy adults in modalities outside of visual perception. An example of this would be in the auditory domain. Primates are highly sensitive to vocal cues and the affective contents of vocal signals are reliably recognised by humans (Bryant and Barett, 2007; Sauter and Scott, 2007; Schröder, 2003). An fMRI study indicates that adult human listeners activate the sensorimotor cortices when listening to emotional vocalisations of others (Warren et al., 2006), however whether this activity is necessary for affect recognition remains unknown. To address this, the studies presented in this chapter use continuous theta burst TMS (cTBS; Di Lazzaro et al., 2005; Huang, Edwards, Rounis, Bhatia, and Rothwell, 2005; Vallesi, Shallice, and Walsh, 2007; Kalla, Muggleton, Cowey, and Walsh, 2009), an offline (i.e. conducted while the participant is at rest) TMS paradigm following which neural activity may be suppressed for several minutes (Di Lazzaro et al., 2005; Huang et al., 2005), to examine whether neural activity in the right lateral premotor (rPM) and right primary somatosensory cortex (rSI) is involved in discriminating affect from vocal signals. Right hemisphere representations were selected based on previous fMRI, neuropsychological and TMS findings demonstrating the importance of right hemisphere activity in affect recognition (e.g. Adolphs et al., 2000; Mitchell and Crow, 2005; Pitcher et al., 2008; Pourtois et al., 2004; Van Lancker and Fromkin, 1973).

Two experiments were conducted. Experiment 1 sought to establish the effects of cTBS targeted at rPM, rSI, or the vertex (cTBS control site) on participants' abilities to complete a same-different auditory emotion recognition task (Figure 7.1; Figure 7.2). Non-verbal emotional vocalisations (such as laughter or screams) were used. These vocalisations are reliably recognised by human listeners (Sauter and Scott, 2007; see also Meyer, Zysset, von Cramon, and Alter, K, 2005; Schröder, 2003) and can be considered to be closer to emotional facial expressions than emotional speech because they do not contain the segmental structure of emotionally inflected or nonsense speech (Dietrich, Szameitat, Ackermann, and Alter, 2006; Scott, Sauter, and McGettigan, in press; Scott, Young, Calder, Hellawell, Aggleton, and Johnsen, 1997). In experiment 2, identical stimuli and cTBS parameters were used, but a new group of participants were instructed to complete a same-different auditory identity discrimination task. This enabled examination of any non-specific effects of cTBS and whether the effects observed in experiment 1 were selective to affective processing. Based on simulation accounts of emotion recognition it was predicted that cTBS targeted at rPM and rSI would result in a disruption of participants' ability to discriminate the auditory emotions, but not identity, of others.

7.2 Methods

Participants

Twenty healthy naïve adult participants, 11 female and 9 male (aged 20 to 35years), took part in the study. All were right handed, had normal or corrected-to-normal vision, and gave informed consent in accordance with the ethics committee of

University College London. Ten participants took part in each experiment (Experiment 1: 6 female and 4 male aged 20 to 30 years; Experiment 2: 5 female and 5 male aged 20 to 35 years).

Materials

Identical stimuli were used in experiments 1 and 2. Stimuli were one of four categories of non-verbal auditory emotions (amusement, sadness, fear, or disgust). These stimuli were adapted from a previously validated set of non-verbal vocalisations (Sauter, PhD thesis, University of London, 2006; Sauter and Scott, 2007; Sauter and Eimer, in press; Warren et al., 2006) and two of these emotions (amusement and fear) were adapted (trimmed to 500msec) from stimuli used in a previous fMRI study investigating the role of sensorimotor resources in non-verbal auditory emotion perception (Warren et al., 2006). Ten stimuli, produced by four different actors (two male / two female), per emotion type were used. All were 500 milliseconds in duration and were presented aurally via headphones.

Procedure

Both experiments consisted of three testing sessions conducted over three non-consecutive days. At each testing session one of the three brain regions was stimulated (rSI, rPM or Vertex). The order of site of stimulation was pseudo-randomised between participants in an ABC-BCA-CAB fashion. Participants completed the experimental task twice within each session, one run prior to cTBS (baseline performance) and the other following cTBS.

In experiment 1, the task comprised of 120 trials (preceded by 20 practice trials) divided between two blocks of 60 trials. Each trial began with the presentation of a fixation cross (1500 ms) followed by the presentation of the prime stimulus. 500

milliseconds after the offset of the prime stimulus a second emotion was presented aurally. Concurrent with the presentation of the second emotion, participants were asked to indicate if the second non-verbal emotion was the same or different from the first using a key press (Figure 7.1). The need for speed and accuracy were emphasised. Each block lasted approximately 10-15 minutes.

In experiment 2, the same stimuli and paradigm were used, but participants were instructed to indicate if the prime and target emotions were expressed by the same or different person.

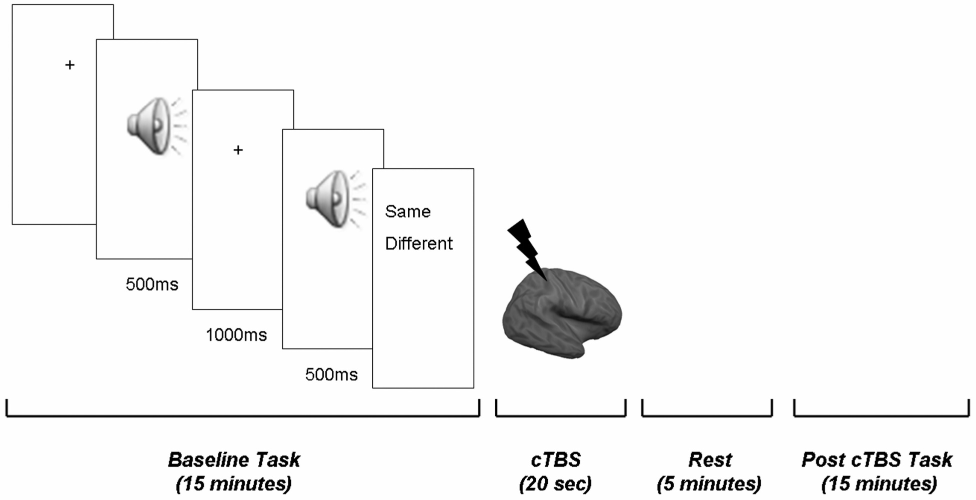


Figure 7.1 Summary of cTBS and task protocol. Participants completed a same-different auditory emotion (Experiment 1) or identity (Experiment 2) matching task. Both experiments consisted of three testing sessions conducted over three non-consecutive days. At each testing session one of the three brain regions was stimulated (rSI, rPM or the vertex). In each session, the task was completed prior to and 5 minutes following cTBS to each site. The 5 minute rest period was based on the observed time course of effects seen in the motor cortex. During the task, trials began with a fixation cross followed by the presentation of a prime emotion via headphones. Non-verbal auditory emotions of amusement, sadness, fear or disgust were used. After 500 milliseconds a second emotional expression was presented which was either the same or different from the target. In experiment 1, participants were asked to indicate whether the emotional expression was the same or different to the prime using a key press. In experiment 2, a new group of participants were asked to indicate whether the emotional expressions were produced by the same or different person. The need for speed and accuracy were emphasised.

TMS parameters and coregistration

TMS was delivered via a figure of eight coil with a 70mm diameter using a Magstim Super Rapid Stimulator (Magstim, UK). An offline cTBS paradigm was used, which consisted of a burst of 3 pulses at 50Hz repeated at intervals of 200ms for 20 seconds, resulting in a total of 300 pulses. This paradigm was used to prevent any influence of online auditory and proprioceptive effects of TMS on task performance

(Terao et al., 1997). Based upon previous findings (Di Lazzaro et al., 2005; Huang et al., 2005; ; Kalla et al., 2009; Valessi et al., 2007) the time window of reduced excitability following theta burst stimulation was expected to last between 20-30 minutes and a 5 minute rest period after stimulation offset was implemented for each site stimulated.

TMS machine output was set to 80% of each participant's motor threshold with an upper limit of 50% of machine output. Motor threshold was defined using visible motor twitch of the contralateral first dorsal interosseus following single pulse TMS delivered to the best scalp position over motor cortex. Motor threshold was calculated using a modified binary search paradigm (MOBS [Tyrell and Owens, 1988; see also Thilo, Santoro, Walsh and Blakemore, 2004 for example use). For each subject, motor threshold was calculated following pre-cTBS baseline and prior to coregistration.

Locations for cTBS were identified using Brainsight TMS-magnetic resonance coregistration system (Rogue Research, Montreal, Canada). FSL software (FMRIB, Oxford) was used to transform coordinates for each site to each subject's individual MRI scan (Figure 7.2). Coordinates for rSI (27, -27, 69) were taken from Blakemore and colleagues (2005) and were averages for twelve neurologically normal participants in an fMRI study following touch to their own face. The coordinates for rPM (54, -2, 44) were the averages of neurologically normal participants in an fMRI study of non-verbal auditory emotion processing (Warren et al., 2006). The vertex was identified as the point midway between the inion and the nasion, equidistant from the left and right intertragal notches.

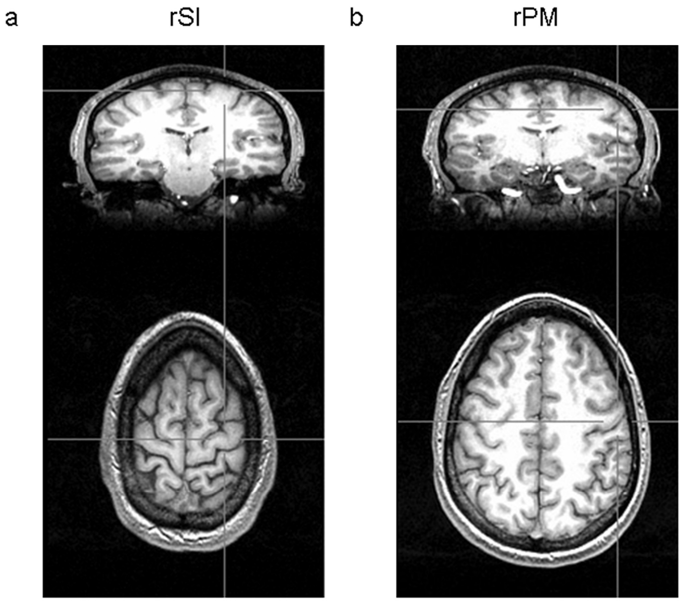


Figure 7.2 Summary of TBS sites stimulated, rSI (a), rPM (b). Locations of TMS were determined using the Brainsight coregistration system. The co-ordinates for rSI (27, -27, 69) were taken from a study on the tactile mirror-system (Blakemore et al., 2005), the co-ordinates for rPM (54 -2 44) were taken from a study on the role of sensorimotor resources in auditory emotion recognition (Warren et al., 2006). cTBS parameters were used to stimulate each site. To ensure that any differences observed were not due to non-specific effects of cTBS, the vertex was stimulated as a TMS control site.

7.3 Results

Reaction times were trimmed prior to analysis (± 3 standard deviations and all errors removed) and were corrected for accuracy (mean RT divided by percentage of correct).

The role of r SI and rPM in recognizing emotions and identity from auditory cues

Baseline performance did not differ significantly across sites in either task (Emotion task group: F(2,18) = 1.64, n.sig; Identity task group: F(2,18) = .815, n.sig). To assess the effects across tasks and across sites, the difference between the post cTBS and pre-cTBS baseline reaction times (i.e. baseline RT corrected for accuracy minus post cTBS RT corrected for accuracy) was compared for each site stimulated. A 2 (Task Group) x 3 (TMS Site) mixed ANOVA was then conducted to determine the effects of cTBS on participants' abilities to recognize identity and emotion from auditory signals. The overall main effect of TMS Site was not significant [F(2,36) = .361, p = .699], however a significant Task Group x TMS Site interaction was found [F(2, 36) = 3.43, p = < .05]. This was because the effects of cTBS significantly differed across sites on the emotion [F(2, 18) = 4.78, p = < .05], but not on the identity task [F(2, 18) = .574, *p* = .573] (Figure 7.3). The main effect of TMS Site on the emotion task was due to significant impairments following cTBS targeted at rPM compared to the vertex (*p* = < .05) and following cTBS targeted at rSI relative to the vertex (*p* = < .05). Therefore, cTBS stimulation of rSI and rPM disrupted participants' abilities to discriminate between the auditory emotions, but not the vocal identities, of others - indicating that neural activity within these brain regions is important for the emotion discrimination abilities of healthy adults.

Between-group comparisons also revealed a main effect of Task Group [F(1, 18) = 12.81, p = < .005]. This task-specific dissociation was modulated by site of stimulation, with cTBS targeted at rSI (*p* = < .01) and rPM (*p* = < .01) resulting in a different pattern of performance between the emotion and identity tasks (Figure 7.3). This pattern of effects was not found following stimulation at the vertex (cTBS control site), where there was a trend for facilitation in both tasks (*p* = .841). Thus, the cTBS impairments observed at rSI and rPM in the emotion task are not due to general impairments in processing following cTBS, but reflect a task specific impairment on emotion discrimination performance.

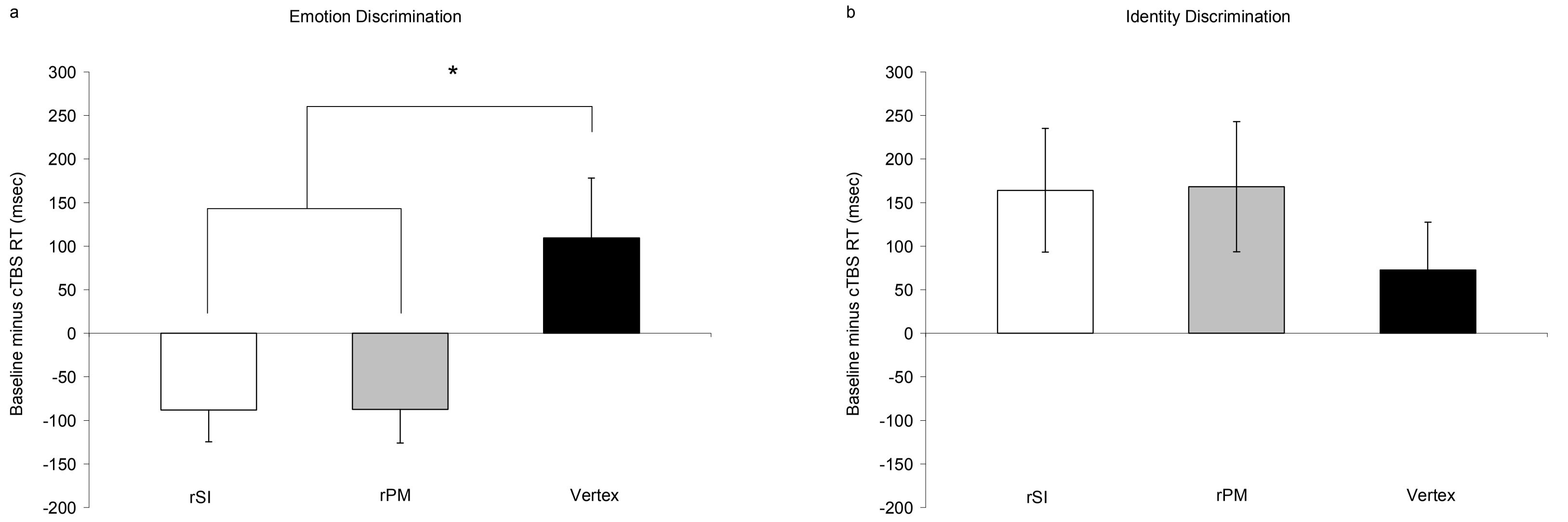


Figure 7.3 Magnitude of disruption or facilitation (mean ± s.e.m) in milliseconds following cTBS targeted at rSI, rPM and the vertex across task groups. In order to determine if the magnitude of impairment following cTBS stimulation differed across the sites and tasks, the difference between the post cTBS and pre-cTBS baseline reaction times (± 3 standard deviations and all errors removed; and corrected for accuracy) were calculated for each condition (i.e. baseline RT/Accuracy minus post cTBS RT/Accuracy for each site stimulated across tasks). A disruption in reaction times following stimulation is shown by a negative value and facilitation by a positive value. (a) For the emotion discrimination task, participants (n = 10) were impaired in their abilities to discriminate between the auditory emotions of others following stimulation to rSI and rPM compared to stimulation at the vertex (cTBS control site). (b) This was not found to be the case when participants (n = 10) had to discriminate auditory identity in the experiment - the effects of cTBS targeted at rSI, rPM and the vertex did not significantly differ between the sites stimulated, and there was a trend for facilitation at all sites. Between-group comparisons also revealed that the disruption in performance on the emotion-discrimination task following cTBS to rSI and rPM was significantly different to the facilitation shown in the identity task. No significant difference between the emotion discrimination and identity discrimination task performance was found following cTBS at the vertex. * = *P* <.05.

Are some emotions affected more than others?

To clarify whether the overall disruption of auditory emotion discrimination observed at rSI and rPM in experiment 1 was linked to a greater impairment for specific emotions or was expression-general, the effects of cTBS (corrected baseline RT minus corrected post cTBS RT) for each emotion type (amusement, disgust, fear, sadness) in the emotion task group were compared using a 3 (TMS Site) x 4 (Emotion-Type) repeated measures ANOVA. This revealed a main effect of TMS Site, [F(2, 18) = 4.97, *p* = <.05], due to the overall impairment in auditory expression matching following cTBS targeted at rSI and rPM relative to the vertex noted previously, but no significant interaction [F(6, 54) = 1.32, *p* = .266] or main effect of emotion-type [F(3, 27) = .812, *p* = .498]. Therefore the overall impairment in emotion discrimination following cTBS to rSI and rPM was not modulated by emotion-type.

7.4 Discussion

The current study investigated whether neural activity in rSI and rPM was important for discriminating affect from non-verbal vocal signals. Using neuronavigation procedures to co-register targeted sites onto each participant's structural MRI scan, stimulation targeted at rSI and rPM led to a significant disruption in the ability to discriminate the auditory emotions, but not identities, of others (Figure 7.3). This pattern was not found following cTBS at the vertex, indicating that the differences observed were not due to non-specific effects of cTBS. Therefore consistent with predictions, rSI and rPM stimulation reduced the ability to discriminate the auditory emotions, but not identities, of others.

These findings extend upon research demonstrating the involvement of right somatosensory cortex representations in facial affect recognition (Adolphs et al., 2000; Pitcher et al., 2008) to suggest that activity in rSI is central to the perception of emotion across different modalities. Further, in recent years a number of functional brain imaging studies have documented the role of premotor cortex activity in the mirroring of actions and emotions of others (Dapretto et al., 2006; Hennenlotter et al., 2005; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007; Warren et al., 2006). Using stimuli adapted from one such study (Warren et al., 2006), the findings show that neural activity in rPM plays a central role in non-verbal auditory emotion discrimination in healthy adults. These findings are consistent with simulation-based accounts of emotion processing, which contend that perceived emotions are mapped onto an individual's own somatosensory and motor representations to facilitate emotion recognition (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, 2004; Goldman and Sripada, 2005; Keysers and Gazzola, 2006).

The task specific nature of the findings further supports the role of rSI and rPM activity as a substrate for a mechanism that facilitates emotion processing. Under equivalent conditions to experiment 1, cTBS targeted at rSI and rPM did not impair participants' ability to discriminate another's identity, indicating that the changes in reaction time are not simply due to a general reduction in reaction times following cTBS stimulation of these regions or more widespread suppression of neural activity. In contrast to a disruption in emotion discrimination abilities, there was a trend for facilitation when participants were asked to discriminate the identity of others. This facilitation is non-specific because it is seen over all sites stimulated in the identity task, and does not differ significantly between sites. The nature of the effect may reflect practice in the post-cTBS blocks or intersensory facilitation following cTBS (Marzi et al., 1998; Walsh and Pascual-Leone, 2003).

The findings are also compatible with recent TMS findings documenting the necessity of the right fronto-parietal operculum in emotional prosody (van Rijn, Aleman, van Diessen, Berckmoes, Vingerhoets, and Kahn, 2005; Hoekert, Bais, Kahn, and Aleman, 2008). They extend upon them by examining the role of somatosensory and motor cortices in non-verbal auditory emotion processing. These kind of auditory signals differ from emotionally inflected speech because they do not have the segmented structure of speech and provide relatively “pure” vocal expressions of emotion (Scott et al., 1997; Scott, Sauter, and McGettigan, in press; Dietrich, Szameitat, Ackermann, and Alter, 2006). This enables a closer parallel to previous studies examining the necessity of cortical resources in the processing of emotional facial expressions (Adolphs et al., 2000; Pitcher et al., 2008). In addition, the findings demonstrate the importance of motor resources in auditory emotion discrimination and show a functional dissociation for the role of sensorimotor simulation in discriminating speaker emotion, but not speaker identity, from vocal signals.

There is growing evidence that the ability to detect affect from voice relies upon similar neural mechanisms which are recruited for visual social signals. For example, in the visual domain, event related potential (ERP) studies have demonstrated enhanced frontal positivity for emotional compared to neutral faces 150 msec after stimulus onset (Ashley, Vuilleumier, and Swick, 2004; Eimer and Holmes, 2002; Eimer and Holmes, 2007; Eimer, Holmes, and McGlone, 2003; Holmes, Vuilleumier, and Eimer, 2003). This mechanism also extends to the auditory domain, in which non-verbal auditory emotions compared with spectrally rotated neutral sounds result in an early fronto-central positivity which is similar in timing, polarity and scalp distribution to ERP markers of emotional face processing (Sauter and

Eimer, in press). The findings presented here add to this by demonstrating that activity in rSI is implicated in not only facial (Adolphs et al., 2000; Pitcher et al., 2008), but also auditory emotion perception and imply that sensorimotor resources may sub-serve an emotion-general processing mechanism in healthy adults (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, 2004; Goldman and Sripada, 2005; Keysers and Gazzola, 2006).

In the current study I focussed on right hemisphere representations based on previous fMRI, neuropsychological and TMS findings demonstrating the importance of right hemisphere activity in affect recognition (Adolphs et al., 2000; Mitchell and Crow, 2005; Pitcher et al., 2008; Pourtois et al., 2004; Van Lancker and Fromkin, 1973). There is some fMRI evidence that viewing static and dynamic facial expressions evokes activity in bilateral primary somatosensory cortex and premotor cortex (Montgomery and Haxby, 2008; van der Gaag et al., 2007). Further, in the auditory domain, listening to non-vocal emotional expressions leads to bilateral activations of the lateral premotor cortex (Warren et al., 2006). The lateralization of these effects shall be addressed with further studies.

In sum, this study extends previous findings that rSI activity is important in facial emotion recognition (Adolphs et al., 2000; Pitcher et al., 2008), by demonstrating that neural activity in rSI is involved in emotion processing across modalities. The findings also demonstrate that rPM activity reported in previous fMRI studies is central to non-verbal auditory emotion discrimination. These resources are not specifically required for discriminating the identity of others and appear to play a specific role in facilitating emotion discrimination in healthy adults.

CHAPTER 8: THE ROLE OF SENSORIMOTOR SIMULATION IN FACIAL EXPRESSION RECOGNITION

The findings in chapter 7, demonstrated that the right primary somatosensory cortex and right premotor cortex play a critical role in discriminating between the non-verbal auditory emotions of others. Recent findings indicate that neural activity in right primary somatosensory cortex is also necessary for the recognition of facial expressions in healthy adults, but it remains unclear whether neural activity in cortical regions involved in other aspects of sensorimotor simulation (e.g. simulation of motor as opposed to somatic consequences of the perceived emotion) are also central to the facial expression recognition abilities of healthy adults. Further, in the face processing literature, whether neural activity in different components of the sensorimotor simulation network are central for recognizing all expressions (i.e. an expression-general mechanism) or for subsets of expressions remains a point of debate (i.e. an expression-specific mechanism). Using continuous theta burst transcranial magnetic stimulation (cTBS) in neurologically normal subjects, this study sought to establish whether sensorimotor neural activity is critical for the facial expression recognition abilities for some, or all, basic facial expressions. cTBS was targeted at right primary somatosensory cortex (rSI), right inferior frontal gyrus (rIFG) or right V5 / MT (control site) while participants completed a four-forced-choice expression categorization task. cTBS to rSI, but not rIFG or right V5 / MT (control site), significantly disrupted participants abilities to correctly categorize happy and sad facial expressions, but not disgust or neutral facial expressions. These findings are consistent with sensorimotor simulation models of expression recognition which suggest that in order to understand another's facial expressions individuals must map the perceived expression onto the same sensorimotor representations which are active during the experience of the perceived emotion.

8.1 Introduction

As noted previously, perceiving and correctly interpreting the expressions of others is a vital component of social interaction. The processes which facilitate this skill have often been described through mechanisms of simulation (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, G, 2004; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006). These simulation-models of expression recognition contend that in order to understand another's expression one must match the perceived state onto the sensorimotor responses associated with experiencing the expression. Supporting this contention, in the visual domain, subliminal exposure to emotional facial expressions leads to increased responses in expression relevant facial muscles of the observer (Dimberg, Thunberg, and Elmehed, 2000); blocking expression relevant facial muscles results in deficits in the observer's ability to correctly categorize the expressions of others (Oberman, Winkielman, and Ramachandran, 2007); perceiving another person's facial expressions correlates with increased activity in similar motor (e.g. inferior frontal gyrus and premotor cortex of the human mirror system) and somatosensory representations (e.g. primary and secondary somatosensory cortex) as when the perceiver generates the same emotion or expression (Hennenlotter et al., 2005; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007); transiently disrupting neural activity in the somatosensory cortex disrupts the observer's expression recognition abilities (Pitcher, Garrido, Walsh and Duchaine, 2008; Pourtois et al., 2004); and brain damage to somatosensory-related cortices results in facial expression recognition deficits (Adolphs, Damasio, Tranel, Cooper, and Damasio, 2000).

While these findings converge on a key role for sensorimotor simulation in facial expression recognition, a number of unanswered questions remain. For example, recent findings indicate that right somatosensory-related cortices play a pivotal role in facial expression recognition (Adolphs et al., 2000; Pitcher et al., 2008; Pourtois et al., 2004), but the extent to which neural activity in cortical regions involved in other aspects of sensorimotor simulation (e.g. simulation of motor as opposed to somatic consequences of the perceived emotion) are also critical for facial expression recognition remains unclear. Functional brain imaging indicates a role of neural activity in both somatosensory and motor regions of the cortex in expression recognition (Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003; Hennenlotter et al., 2005; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007; Winston, O'Doherty, and Dolan, 2003), but these data alone cannot imply causation about the role of motor resources for expression recognition. Motor mirror system activation involving the inferior frontal gyrus (IFG; BAs 44, 45) has been shown to occur in a number of studies investigating facial expression recognition or evaluation (Carr et al., 2001; Dapretto et al., 2006; Hennenlotter et al., 2006; Kesler-West et al., 2001; Seitz et al., 2008); emotional empathy (Jabbi, Swart, and Keysers, 2007; Schulte-Ruther, Markowitsch, Fink and Piefke, 2007); and emotion recognition more generally (Wildgruber et al., 2005). Neuropsychological findings indicate that the IFG is necessary for recognizing emotions from the eyes (Shamay-Tsoory, Aharon-Peretz, and Perry, 2009), but the ability to recognize expressions from the whole-face was not tested. Adolphs and colleagues (2002) also report deficits in facial emotion recognition following damage to the frontal operculum (including BA44), but the lack of region specificity limits the conclusions which one can draw on the role of the IFG in facial expression recognition in healthy adults. Therefore whether the IFG is critical to facial expression recognition in healthy adults remains unknown.

There is also a discrepancy in the literature on whether sensorimotor resources are critical for recognizing all or only some distinct facial expressions. fMRI indicates that changes in neural activity in both motor (including premotor cortex and IFG) and somatosensory (including SI and SII) cortices are related to perceiving a range of facial expressions (Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007). Neuropsychological findings are consistent with a role for somatosensory-related cortices in expression general processing (Adolphs et al., 2000), but whether neural activity in the somatosensory cortex of healthy adults is necessary for all or only some distinct facial expressions is a matter of debate. To date only two transcranial magnetic stimulation studies have addressed the necessity of the right somatosensory cortex in healthy adults. In one study, two emotional expressions (fear and happiness) and single pulse TMS over right somatosensory cortex were used to investigate the necessity of this brain region for emotion recognition in healthy adults. These authors observed an expression-selective TMS-related interference following stimulation of right somatosensory cortex during the recognition of fearful, but not happy expressions (Pourtois et al., 2004). In contrast, a more recent repetitive TMS study (Pitcher et al., 2008), using six emotional expressions (anger, disgust, fear, happiness, sadness and surprise), found an expression-general impairment following stimulation of the right somatosensory cortex. Further study is needed to clarify this discrepancy.

Furthermore, in both previous TMS studies a same-different matching task was used to assess participants' expression recognition abilities. The nature of these tasks requires some degree of working memory in which the participant must not only recognize a sample expression but store the information in memory to match it to a sequential expression. Therefore it is difficult to disentangle whether TMS impairment results from a disruption of fronto-parietal working memory networks (cf. Harris, Harris, and Diamond, 2001; Mottaghy, Gangitano, Sparing, Krause, and Pascual-Leone, 2002; Oliveri et al., 2001) or sensorimotor simulation mechanisms per se[4].

To address this, this study sought to establish: i) whether neural activity in the right primary somatosensory cortex (rSI) and right inferior frontal gyrus (rIFG) is central to recognizing the facial expressions of others and ii) whether, at the cortical

---

[4] Note that this is controlled for in Chapter 7 because of the task-specific dissociation observed.

level, sensorimotor simulation is expression-general or expression-selective. To do so, participants performed a four-forced-choice expression categorization task (*disgust, happy, neutral, sadness*) following continuous theta burst TMS (cTBS) targeted at the rSI, rIFG, and right V5 / MT (visual control TMS site). Facial expressions of disgust, happiness, sadness, and neutral (expression control) were used. All expressions were selected from the Karolinska Directed Emotional Faces set (Lundqvist, Flykt, and Őhman, 1998). Based on previous TMS findings (Pitcher et al., 2008) it was predicted that cTBS targeted at rSI would result in an impairment of participants' abilities to correctly categorize expression types, but not neutral (control expression). If rIFG activity plays a causal role in the emotional expression recognition abilities of healthy adults then an impairment for categorizing emotional expression types (but not neutral) following cTBS targeted at the rIFG site was expected. Whether this impairment would be expression specific or expression selective remains to be determined. No cTBS disruption was expected following stimulation at right V5 / MT, which acted as a visual control site.

8.2 Method

Participants

Eleven healthy adult participants, 3 female and 8 male (aged 24 to 45 years), took part in the study. All participants were right handed and had normal or corrected to normal vision. Each participant gave written informed consent in accordance with the ethics committee of University College London and was naïve to the hypothesis of the experiment.

Materials and Procedure

The experiment consisted of three testing sessions conducted over three non-consecutive days. At each testing session one of the three brain regions were stimulated: rSI, rIFG and right V5 / MT (TBS control site; Figure 8.1). The order of site of stimulation was randomized between subjects. Each session consisted of two blocks, one run prior to TBS (baseline performance) and the other following TBS.

During each block, participants completed a four-forced-choice emotion recognition task, comprised of 140 trials (preceded by 20 practice trials) in which participants had to indicate the emotional expression of a target face. Each trial began with the presentation of a fixation cross (1500 ms) followed by the presentation of the target stimuli. Target stimuli were presented in the centre of the screen for 250 ms. Following the offset of the target stimuli participants were asked to indicate the emotion expressed in the target emotion (either happy, sad, neutral or disgust) using a key press (Figure 8.1d). Each block lasted approximately ten minutes. Stimuli were displayed on an SVGA 17 inch monitor with a refresh rate of 100Hz. Thirty-five grey-scale standardised images per emotion were used. Stimuli were selected from the Karolinska Directed Emotional Faces set (Lundqvist, Flykt, and Őhman, 1998).

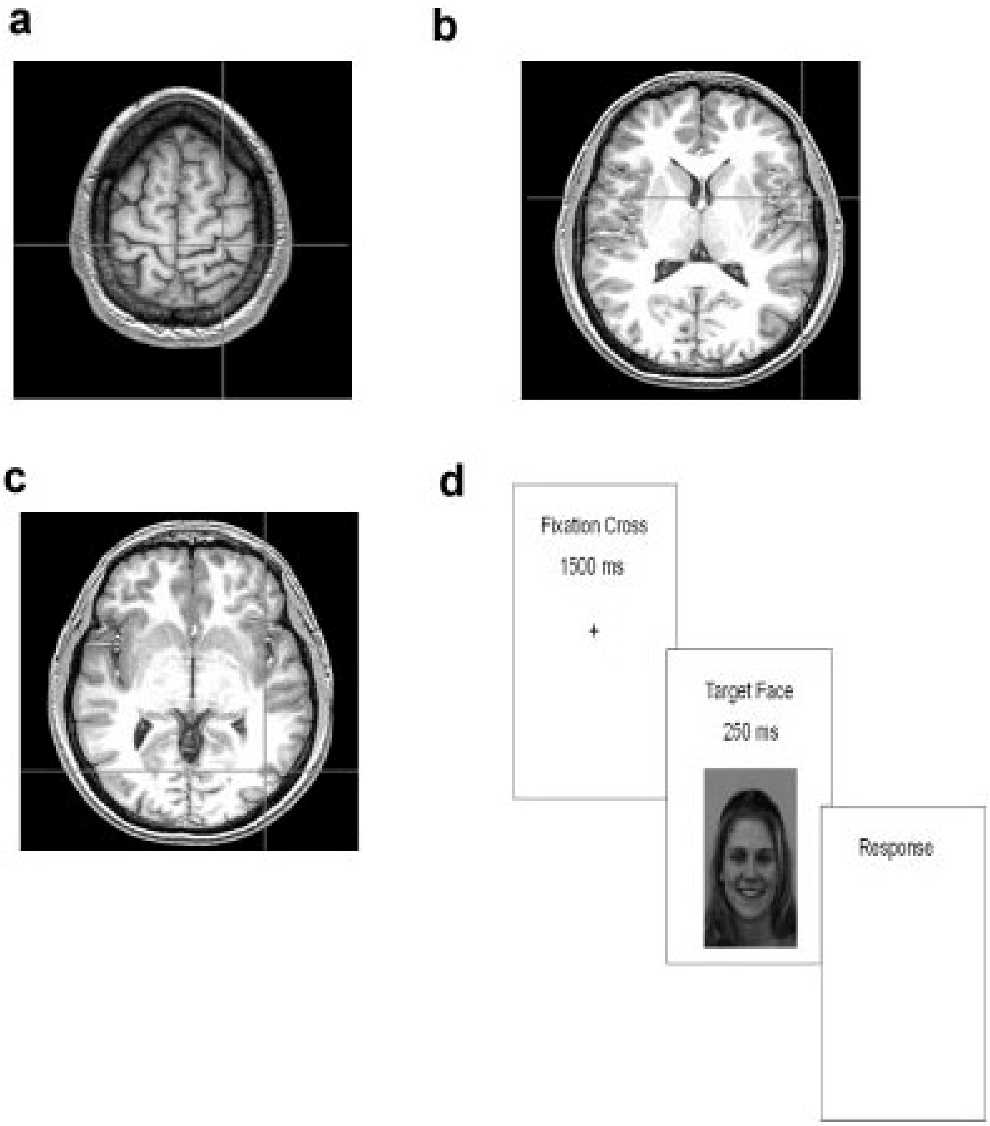


Figure 8.1 Summary of TMS sites simulated, right SI (a), rIFG (b), V5 / MT (c), and single trial protocol (d). (a, b, c) Locations of TMS were determined using the Brainsight Coregistration System. In addition to coregistration, the location of area V5 / MT was confirmed functionally via phosphenes. Continuous TBS parameters were used to stimulate each site. (d) Participants completed pre- and post-TBS blocks. Within each block, trials began with a fixation cross followed by the presentation of a target face displaying emotional expressions of happy, sad, neutral or disgust. Participants were asked to indicate the expression of the target face using a key press.

TMS Protocol and Site Localisation

TMS was delivered via a figure of eight coil with a 70mm diameter using a Magstim Super Rapid Stimulator (Magstim, UK). An offline continuous theta burst TMS paradigm was used to prevent any influence of proprioceptive effects of TMS on reaction time performance (Terao et al., 1997). The parameters were identical to those used in Chapter 7. TMS machine output was set to 80% of each participant's motor threshold with an upper limit of 50% of machine output. Motor threshold was defined using visible motor twitch of the contralateral first dorsal interosseus following single pulse TMS delivered to the best scalp position over motor cortex and was calculated using a modified binary search paradigm (MOBS; Tyrell and Owens, 1988). For each subject, motor threshold was calculated following pre-TMS baseline and prior to coregistration.

Following the pre-TMS block, locations for TMS were identified using BrainSight TMS-magnetic resonance coregistration system (Rogue Research, Montreal, Canada). FSL software (FMRIB, Oxford) was used to transform coordinates for each site to each subject's individual MRI scan (Figure 1a, b, c). Talairach coordinates for rSI (27, -27, 69) were taken from Blakemore and colleagues (2005) and were averages for twelve neurologically normal subjects in an fMRI study following touch to their own face (the same rSI site as that used in Chapter 7). The MNI coordinates for rIFG (60, 8, 6) were the averages of twelve neurologically normal subjects in an fMRI study of facial emotion (Hennenlotter et al., 2005) and the region broadly corresponding to BA 44 of the inferior frontal gyrus. Coordinates for V5 / MT (44, -67, 0) were taken from Dumoulin and colleagues (2000). In addition to BrainSight coregistration, V5 / MT was also confirmed functionally using phosphenes.

8.3 Results

To assess the influence of speed and accuracy, reaction times were corrected for accuracy in each condition. This was achieved by dividing reaction time (± 3 standard deviations and all errors removed) by accuracy in each condition.

The role of rSI and rIFG in recognizing different facial expressions of emotion

Preliminary analysis confirmed that baseline performance for each expression-type did not significantly differ across the sites stimulated [Disgust - F(2,20) = 1.4 , nsig; Happy – F(2,20) = .280, nsig; Neutral – F(2,20) = .913, nsig; Sad – F(2,20) = 1.01, nsig].

To assess the effects across expression-types and across sites, the difference between the post cTBS and pre-cTBS baseline reaction times for each expression (i.e. baseline RT corrected for accuracy minus post cTBS RT corrected for accuracy) was compared for each site stimulated (as per Chapter 7). A 3 (TMS Site) x 4 (Expression-Type) repeated measures ANOVA showed that neither the main effect of TMS Site [F(2,20) = 1.55, $p = .237$] nor the main effect of Expression-Type reached significance [F(3,30) = 1.39, $p = .265$]. There was however a significant TMS Site x Expression-Type interaction [F(6,60) = 2.82, $p = .017$]. This was because cTBS at rSI resulted in a significantly different pattern of effects across expression types [F(3,30) = 4.34, $p = .012$], whereby cTBS impaired performance on trials involving expressions of happiness relative to neutral facial expressions ($p = < .05$), and on trials involving sadness relative to neutral ($p = < .01$) and disgusted facial expressions ($p = < .05$). This was not the case at rIFG [F(3,30) = .977, $p = .417$] or right V5 / MT [F(1.863,18.629) = .489, $p = .608$], where the effects of cTBS did not significantly differ between the expression-types (Figure 7.2).

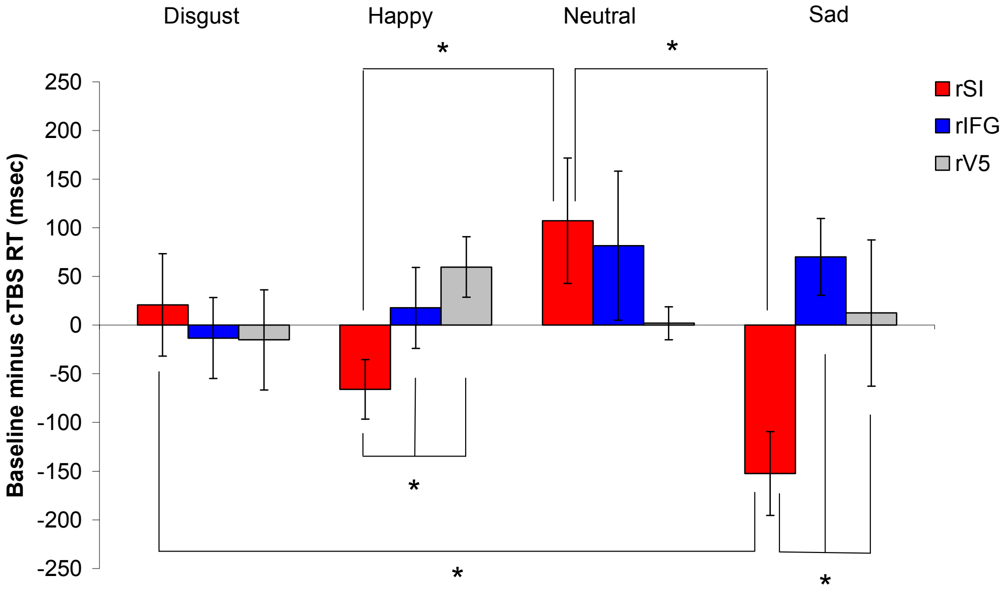


Figure 8.2 Magnitude of disruption or facilitation across expression-types (mean ± s.e.m) following cTBS targeted at rSI, rIFG and right V5 / MT. In order to determine if the magnitude of impairment following cTBS stimulation differed across the sites and expression the difference between the post cTBS and pre-cTBS baseline reaction times (± 3 standard deviations and all errors removed; and corrected for accuracy) were calculated for each expression (i.e. baseline RT/Accuracy minus post cTBS RT/Accuracy for each site stimulated across tasks) and compared across conditions. A disruption in reaction times following stimulation is shown by a negative value and an improvement by a positive value. Stimulation to rSI disrupted performance at recognizing happy and sad facial expressions compared to rIFG and right V5 / MT. The disruption on happy and sad trials at rSI significantly differed from the improvement seen on neutral trials. The pattern of performance on sad trials at rSI also differed significantly from that seen on disgust trials. * = $P < .05$.

Comparisons for each expression-type across TMS sites revealed that the disruption caused by cTBS to rSI on trials involving sadness was significantly different to the effects of cTBS at rIFG and right V5 / MT – a one way repeated measures ANOVA comparing performance on sadness recognition across the three sites revealed dissociable effects of site stimulated [F(2,20) = 4.35, p = .027], and pair-wise comparisons revealed that this was due to participants' showing a significant disruption at recognising sadness following stimulation at rSI compared to rIFG (p = <.01) and right V5 / MT (p = < .05). Similarly, a comparison on happiness recognition across the three sites, revealed a trend towards significance [F(2,20) = 3.04, *p* = .07]. Paired-comparisons conducted on the basis of this strong trend, revealed that this was due to a significantly larger disruption on participants' abilities to recognize happiness following stimulation at rSI compared to rIFG [t(10) = 2.30, *p* = < .05] and right V5 / MT [t(10) = 2.41, *p* = < .05] (Figure 7.2).

8.4 Discussion

This study sought to establish whether i) neural activity in rSI and rIFG is critical for recognizing the facial expressions of others and ii) whether these mechanisms are expression-general or expression selective. The findings first demonstrate that neural activity in rSI, but not rIFG, is critical for the ability to recognize others' facial expressions. They further indicate that neural activity in rSI plays a more crucial role in the recognition of emotional compared with neutral facial expressions.

Previous neuropsychological findings indicate that lesions to right somatosensory-related cortices lead to expression-general face recognition impairments (Adolphs et al., 2000). In healthy adults, focal transcranial magnetic stimulation of rSI has been shown to a) impair fearful, but not happiness, facial expression recognition, implying that rSI is expression selective (Pourtois et al., 2004 - note that only 2 expression types were used and differences only found when participants discriminated between two fearful expressions), and b) to impair general facial expression recognition abilities, including happiness – implying that rSI is expression-general (Pitcher et al., 2008 – note only 12 trials per expression type used). Using neuronavigation procedures, the findings from the current study show that magnetic stimulation of rSI results in selective impairments of happiness and sadness recognition, but not disgust or neutral recognition, and indicate that neural activity in rSI plays a crucial role in the recognition of facial expressions other than fear per se (c.f. Pourtois et al., 2004). The study is also the first to show a facial expression recognition deficit on an emotion categorisation task (as opposed to same-different matching tasks used previously), which further clarifies that previously reported impairments in expression recognition following stimulation to rSI are not linked to a disruption of fronto-parietal working memory networks.

Models of face processing posit a number of expression-selective, expression-general, face-selective and multimodal mechanisms which support our ability to perceive another's emotions (Bruce and Young, 1986; Calder and Young, 2005; Haxby, Hoffman, and Gobbini, 2000). Sensorimotor simulation is likely to be one of these mechanisms, with neural activity in rSI providing a possible candidate to facilitate this process. While the evidence that cTBS stimulation resulted in a disruption of participants' abilities to recognise sadness and happiness, but not disgust, may imply a degree of expression selectivity within this region, it remains possible that rSI is involved in recognizing alternative expression types. Moreover, findings from chapter 7, of a general impairment in auditory expression recognition following cTBS to rSI, and from Pitcher et al. (2008), of general impairments in the facial expression recognition following TMS to rSI would argue against rSI acting as an expression-specific mechanism. Outside of rSI, there is evidence for emotion-specific neuropsychological deficits for expressions of disgust (Calder, Keane, Manes, Antoun, and Young, 2000; Sprengelmeyer et al., 1996, 2003), fear (Calder, Lawrence, and Young, 2001) and anger (Calder, Keane, Lawrence, and Manes, 2004; Lawrence, Calder, McGowan, and Grasby, 2002). This disproportionate role of different brain regions in processing specific expressions indicates that facial expressions are not processed by a single “expression system” and that expression-general and expression-specific representations may interact at varying levels of processing. The lack of impairment on disgust recognition found here may reflect the fact that the neural noise introduced in rSI by TMS is better compensated for by emotions which have more alternative mechanisms / expression-specific representations elsewhere in the brain. For example, there is a good degree of evidence from functional brain imaging (Phillips et al., 1997, 1998; Sprengelmeyer, Rausch, Eysel, and Przuntek, 1998), intracerebral recording (Krolak-Salmon et al., 2003), and neuropsychological studies (Calder et al., 2000; Kipps, Duggins, McCusker, and Calder, 2007) which indicate that the anteroventral insula acts as an expression-specific mechanism for disgust recognition. The anteroventral section of the insula is connected to number of regions which are thought to be involved in emotion processing across modalities (including the primary somatosensory cortex, basal ganglia, amygdala, orbitofrontal cortex and superior temporal cortex; Augustine, 1996; Flynn, Benson, and Ardila, 1999; Mesulam and Mufson, 1982) and has been suggested to act as a point of convergence for sources involved in the processing of disgust recognition to varying degrees (Kipps et al., 2007). It is feasible that suppressing rSI with cTBS reduces one, of the multiple sources, of information which contributes to disgust processing in this section of insula, and therefore does not result in impairment. It is also possible that with alternative paradigms (e.g. same-different expression matching paradigms as opposed to a forced-choice paradigm which could bias responses of disgust and thereby facilitate performance) and stimuli (e.g. dynamic stimuli as opposed to static), stimulation to rSI may lead to a disruption of participants’ abilities to recognise disgusted facial expressions (c.f. Chapter 7; Pitcher et al., 2008).

The findings that cTBS targeted at rIFG did not result in an impairment of participants' abilities to correctly recognise the other's facial emotions are also intriguing, especially in light of evidence that lesions to the IFG have been linked to deficits in self-reported emotional empathy and in the ability to recognise emotions from the eyes (Shamay-Tsoory et al., 2009). These differences are likely to reflect variations in the processes involved in recognising emotional expressions from the whole-face compared with emotional empathy per se, and imply that the IFG may not be critical for all emotion-general tasks. The IFG has been reported as a cytoarchitectonic homologue to monkey F5 (Petrides, Cadoret, and Mackey, 2005) and highlighted as a core component of the classical human mirror system (Rizzolatti and Craighero, 2004). A number of authors have suggested that the human mirror system (including IFG, IPL, and STS) may be pivotal to social cognition (Gallese, Keysers, and Rizzolatti, G, 2004; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007). While caution is urged in interpreting a null result, the evidence that magnetic stimulation targeted at rIFG does not impair the ability to recognise other's facial emotions stands in contrast to this hypothesis. It is of note that this may not imply that motor simulation play no role in emotion processing, because while the human mirror system is one neurophysiological candidate to facilitate this process it need not be the only mechanism and other regions of the motor system may be crucial for facial expression recognition (e.g. the human premotor cortex – c.f. Chapter 7).

In summary, the findings from the current study indicate that rSI is critical for the recognition of emotional (across multiple expression types) compared with neutral facial expressions. They also indicate the rIFG is not critical to facial expression recognition. This adds to the evidence that somatosensory activity may provide a general expression recognition mechanism (Chapter 7; Adolphs et al., 2000; Pitcher et al., 2008). However, the evidence that rSI stimulation disproportionately affected happy and sad expressions but not disgust, indicates that while somatosensory cortex activity may be involved in the processing of a variety of facial expressions, in some cases (e.g. with disgust recognition) alternative facial expression recognition mechanisms (e.g. expression selective) may be sufficient to support facial expression recognition when rSI activity is suppressed.

CHAPTER 9: CONCLUSIONS

In this chapter, the empirical findings from chapters 2-5 and 7-8 of this thesis are discussed in a wider context. Chapters 2-5 addressed the prevalence, neurocognitive mechanisms, and consequences of mirror-touch synaesthesia for perception and social cognition. These findings are discussed in relation to previous research on synaesthesia and future studies on the neurocognitive mechanisms of mirror-touch synaesthesia are also described. Chapters 4 and 5 also used mirror-touch synaesthesia to inform us about the role of sensorimotor resources in social cognition. These findings were complemented by studies in chapters 7 and 8, which investigated the impact of suppressing sensorimotor representations on the expression recognition abilities of healthy adults. The findings from chapters 4, 5, 7 and 8 are discussed in the context of research on social cognition and sensorimotor accounts of social cognition.

9.1 Introduction

As noted in the introduction to this thesis, synaesthesia is a condition in which one attribute of a stimulus (the inducer) triggers a conscious experience of another attribute (the concurrent) not typically associated with the inducer. For example, in grapheme-colour synaesthesia the letter ‘a’ may trigger synaesthetic experiences of colours. A large body of synaesthesia research has focussed on grapheme-colour synaesthesia, which is often reported as being one of the most common forms of the condition (Baron-Cohen, Burt, Smith-Lailtan, Harrison, and Bolton, 1996; Rich, Bradshaw, and Mattingley, 2005; Simner et al., 2006). More recently, a newly documented form of synaesthesia has been described in which individuals experience tactile sensations on their own body simply when observing touch to another’s body (mirror-touch synaesthesia; Banissy and Ward, 2007; Blakemore, Bristow, Bird, Frith, and Ward, 2005). The studies in the first five chapters of this thesis investigated the neurocognitive and perceptual profiles of mirror-touch synaesthesia. In addition, the role of sensorimotor simulation mechanisms in social cognition was examined by using principles of neuropsychology (in the case of mirror-touch synaesthesia) and transcranial magnetic stimulation (TMS). Specifically the following questions were addressed:

1. What is the prevalence of mirror-touch synaesthesia and what characteristics identify the condition (Chapter 2)?
2. What neurocognitive mechanisms give rise to mirror-touch synaesthesia (Chapter 2)?
3. Does the presence of synaesthesia have implications for perceptual processing (Chapter 3)?
4. What are the implications of heightened sensorimotor simulation in mirror-touch synaesthesia for social cognition (Chapters 4 and 5)?
5. What are the implications of suppressing sensorimotor resources on expression recognition abilities in healthy adults (Chapters 7 and 8)?

9.2 What is the prevalence of mirror-touch synaesthesia and what characteristics underpin the condition?

As noted previously, in mirror-touch synaesthesia individuals experience tactile sensations on their own body simply when observing touch to another person (Banissy and Ward, 2007; Banissy, Cohen Kadosh, Maus, Walsh, and Ward, 2009; Blakemore et al., 2005). The mapping between synaesthetic experience (i.e. location on the synaesthete’s body) and observed-touch (i.e. the location where touch is perceived on another person’s body) has been shown to vary between mirror-touch synaesthetes (Banissy and Ward, 2007), with some synaesthetes reporting synaesthetic experiences as if looking in a mirror (e.g. observed-touch to the left face elicits a synaesthetic experience on the left cheek of the mirror-touch synaesthete; specular subtype) and others as if they share the same anatomical body space (e.g. observed-touch to the left face elicits a synaesthetic experience on the left cheek of the mirror-touch synaesthete; anatomical subtype). The first reported case of the condition was provided in a single case fMRI study, which linked the condition to heightened neural activity in a network of brain regions which are also activated in non-synaesthetic control subjects when observing touch to others (the mirror-touch system, comprised of the primary and secondary somatosensory cortex, premotor cortex, intraparietal sulcus and superior temporal sulcus; Blakemore et al., 2005). Chapter 2 examined the prevalence and characteristics of the condition.

In the first experiment reported in chapter 2 the prevalence of mirror-touch synaesthesia was assessed by screening a large population of undergraduate students for the presence of mirror-touch synaesthesia and determining the validity of reported cases with a synaesthetic stroop task (Banissy and Ward, 2007). In the task, participants were asked to indicate the site of touch on their own body while observing touch to another person. Participants were asked to report the site of veridical touch and ignore any synaesthetic tactile experience induced. For synaesthetes, but not for controls, veridical touch could be in the same (congruent) or different (incongruent) location to observed / synaesthetic touch (congruency was determined according to each synaesthete's self reports). Synaesthetes performed slower in the incongruent condition and produced more errors linked to their synaesthesia. Nine mirror-touch synaesthetes (from 567 participants screened) were confirmed, which provides an estimated prevalence rate of 1.6%. This places mirror-touch synaesthesia as one of the most common variants of synaesthesia, alongside grapheme-colour synaesthesia (estimated prevalence rate of 2%; Simner et al., 2006) and day-colour synaesthesia (estimated prevalence rate of 2.8%; Simner et al., 2006).

By combining cases of mirror-touch synaesthesia from the prevalence study with cases of mirror-touch synaesthesia from self-referrals, the findings from chapter

2 also indicate a number of features linked to the characteristics of the condition. The findings from experiment 2 indicate that the inducer for synaesthetic experience is not linked to spatial cueing, but is related to bodily touch (and in some cases touch to objects). The findings also indicate the specular subtype is the more common frame of reference adopted by mirror-touch synaesthetes and the relative frequencies (approximately 81% show a specular frame of reference) are similar to those reported in studies investigating the preferred spatial frame adopted when imitating another's behaviour - both adults and children tend to imitate in a specular mode (Schofield, 1976; Franz, Ford and Werner, 2007). Further characteristics indicate commonalities between mirror-touch synaesthesia and other variants of synaesthesia. For example, a general characteristic of synaesthesia is that different variants of synaesthesia tend to co-occur (Simner et al., 2006). This also appears to be the case in mirror-touch synaesthesia. Synaesthetic experiences also tend to be consistent over time (Baron-Cohen, Wyke, and Binnie, 1987) and the mirror-touch synaesthete's spatial sub-type (i.e. whether they belong to the specular or anatomical category) appears to be consistent across time (Chapter 2) and across different body parts (Banissy and Ward, 2007).

While these findings indicate that mirror-touch synaesthesia shares common ground with other types of synaesthesia, possible similarities in the neural basis of the condition are less apparent. A point of dispute in the synaesthesia literature is whether synaesthetic experience is due to cross-activation between brain regions (either through increased structural connectivity or malfunctions in cortical inhibition) or disinhibition of the same cortical networks found in non-synaesthetes (Bargary and Mitchell, 2008; Cohen Kadosh, Henik, Catena, Walsh, and Fuetnes, 2009; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001; Hubbard and

Ramachandran, 2005; Rouw and Scholte, 2007). Cross-activation accounts have tended to focus on adjacent brain regions (e.g. in the case of grapheme-colour synaesthesia - between visual grapheme and colour processing areas in the fusiform gyrus) and suggest that activation in the region responsible for processing the synaesthetic inducer (e.g. the grapheme in grapheme-colour synaesthesia) leads to activation in the adjacent region for processing the synaesthetic concurrent (e.g. colour in grapheme-colour synaesthesia). It is not entirely clear how the principle of adjacency can be applied to mirror-touch synaesthesia, and an alternative mechanism which may bias individuals to this type of synaesthesia is the normal architecture for multi-sensory interactions (Sagiv and Ward, 2006). For example, there is good evidence for an observed-touch mirror system in non-synaesthetes (Keysers, Wicker, Gazzola, Anton, Fogassi, and Gallese, 2004; Blakemore et al., 2005; Ebisch, Perrucci, Ferretti, Del Gratta, Romani, and Gallese, 2008) and mirror-touch synaesthesia has been suggested to reflect over-activity within this network (Blakemore et al., 2005).

Future studies will aim to address the similarities and differences in the neural basis of different subtypes of synaesthesia by investigating structural and functional correlates of different variants of synaesthesia (e.g. grapheme-colour, tone-colour, mirror-touch, and number-space synaesthesia). For example, previous DTI findings indicate that grapheme-colour synaesthesia is linked with increased structural connectivity in right inferior-temporal, right parietal, and bilateral frontal regions (Rouw and Scholte, 2007), and research in progress indicates that tone-colour synaesthesia is linked to increased cortical thickness (a marker of cortical morphology and neurodevelopment; MacDonald, Kabani, Avis, and Evans, 2000; Shaw et al., 2006) in similar right inferior temporal regions (Banissy, Stewart, Ward, Walsh, and Kanai, in prep). I am also starting a combined fMRI-DTI study of mirror-touch synaesthesia, which will investigate functional and structural correlates of mirror-touch synaesthesia at the group level. This will permit further assessment of similarities and differences in the neural substrates of different variants of synaesthesia and across subtypes of mirror-touch synaesthetes.

9.3 What neurocognitive mechanisms may underpin mirror-touch synaesthesia?

In addition to the studies reported in chapter 2, I proposed a neurocognitive model to account for the processes which may underpin mirror-touch synaesthesia (Figure 9.1). Three key mechanisms were highlighted: identifying the type of visual stimulus touched ('What' mechanism), discriminating between self and other ('Who' mechanism), and locating where on the body and in space observed touch occurs ('Where' mechanism).

The 'What' mechanism is considered to be involved in several discriminations, including: 'is this a human or object?' 'Is this a face or body?' One intriguing characteristic shown by some mirror-touch synaesthetes is that observing touch to objects can elicit synaesthetic interactions in some, but not all, synaesthetes (Chapter 2; Banissy and Ward, 2007). One brain region of the observed-touch network (Blakemore et al., 2005) which may be central to this is the intraparietal sulcus (IPS). Recent findings indicate that visual object information is processed along the dorsal stream to areas along the medial bank of the intraparietal sulcus (IPS; including IPS1 and IPS2, Konen and Kaster, 2008). For mirror-touch synaesthetes, this pathway may be particularly important when considered in relationship to visual-tactile body maps within the intraparietal cortex. Single-cell recording in primates has identified bimodal neurons in the intraparietal cortex which fire in response to not only passive somatosensory stimulation, but also to a visual stimulus presented in close proximity to the touched body part (Duhamel, Colby and Goldberg, 1998). Intriguingly, the visual spatial reference frames of such bimodal neurons are dynamic, such that if the monkey is trained to use a tool the visual receptive field extends to incorporate the tool into the representation of the body - potentially as an extension of the body schema (Iriki, Tanaka and Iwamura., 1996). Similar evidence of dynamic multisensory body representations in the parietal cortex have been reported in human subjects (Bremmer et al., 2001; Macaluso and Driver, 2003; also see Colby, 1998; Maravita and Iriki, 2002; Berlucchi and Aglioti, 1997 for review). One hypothesis generated by the model is that the degree to which observing touch to an object is able to elicit visual-tactile synaesthetic interactions depends upon the extent to which the object is incorporated into visual-tactile representations of the body, potentially within the intraparietal cortex. A potential approach to investigate this would be to investigate if extending the body-schema of a mirror-touch synaesthete through tool use can result in a synaesthete who does not normally experience synaesthetic touch for objects showing synaesthetic interactions for observed object-touch.

The key process instigated by the ‘Who’ mechanism is to distinguish between the self and other. I suggest that mirror-touch synaesthesia reflects a breakdown in the mechanisms which normally distinguish between self and other (i.e. processes involved in linking visual representations with internal representations of bodies). One prediction of this is that mirror-touch synaesthetes will show a tendency to over-incorporate viewed bodies onto their own body schema. In accordance with this, research in progress indicates that mirror-touch synaesthetes show a greater degree of the rubber hand illusion (RHI) compared to matched non-synaesthete controls (Banissy, MacDonald, Ward, Walsh, Haggard and Longo, in prep). The RHI is a body schema illusion in which an observer is touched on their own hand while observing a rubber hand being touched. When observed and veridical touch are synchronous the perceived location of the observer's hand drifts towards the location of the rubber hand (Longo, Schuur, Kammers, Tsakiris, and Haggard, 2008; Tsakiris and Haggard, 2005) and participants begin to attribute the rubber hand to their own body representation (Botvinick and Cohen, 1998). This effect is abolished with asynchronous stroking and when participants view a non-hand object rather than a rubber hand (Tsakiris and Haggard, 2005). A comparison of the size of the perceived drift towards the rubber hand (in centimetres) indicates the mirror-touch synaesthetes show a greater incidence of the illusion compared to matched non-synaesthetes when observed and veridical touch are synchronous (i.e. under normal RHI conditions), but no differences are found in conditions in which the illusion is not expected to take place (e.g. non-hand object control conditions; Banissy et al., in prep). Future studies will investigate whether modulations of the RHI differ between mirror-touch synaesthetes and non-synaesthetes. For example, in non-synaesthetes rotating the RHI 180° (i.e. as if from another's perspective) abolishes the illusion (Tsakiris and Haggard, 2005), however given that mirror-touch synaesthetes experience tactile sensations when viewing touch from another's perspective it will be interesting to determine whether they show a similar or different pattern to non-synaesthetes.

The final class of mechanism described in the model involves linking visual representations of body with tactile representations based on spatial frames of reference. For this I draw a distinction between embodied (the sense of being localised within one's own body) and disembodied representations of the body (e.g. autoscopic phenomena in which individuals experience the location of the self outside of one's own body – Brugger 2002; Blanke, Landis, Spinelli and Seeck, 2004; Blanke, Ortigue, Landis and Seeck, 2002). It is postulated that a similar division can be made for the specular-anatomical division in mirror-touch synaesthetes. The specular subtype appear to process the visual representation of the other body in an embodied manner (i.e. as a mirror-image of oneself), while for the anatomical subtype the spatial mapping between self and other could be considered disembodied in that the synaesthete's own body appears to share the same bodily template as the others person (i.e. the synaesthete's body is placed in the perspective of the other person). This difference may suggest that anatomical mirror-touch synaesthesia can be considered to be similar to types of autoscopic phenomena in which individuals experience the location of the self outside of one's own body (Brugger 2002; Blanke, Landis, Spinelli and Seeck, 2004; Blanke, Ortigue, Landis and Seeck, 2002), however, no mirror-touch synaesthetes report typical phenomena of autoscopy – that of seeing one's own body and the world from a location outside of their own physical body[5] (Bünning and Blanke, 2005). Therefore rather than classifying anatomical mirror-touch synaesthesia within the bracket of autoscopic phenomena I would suggest that some mechanisms which give rise to the spatial frames of adopted by mirror-touch synaesthetes are modulated by similar mechanisms as those observed in autoscopy. For example, disembodied experiences have been suggested to arise from functional disintegration of low-level multisensory processing mechanisms (Bünning and Blanke, 2005; Blanke and Mohr, 2005) and abnormal activity at the temporal parietal junction (TPJ; Arzy, Thut, Mohr, Michel and Blanke, 2006; Blanke, Landis, Spinelli and Seeck, 2004; Blanke, Ortigue, Landis and Seeck, 2002) and one may suggest the anatomical sub-type will be associated with these neurocognitive mechanisms.

---

[5] It is of note that while synaesthetes may not have overtly reported autoscopy they may still experience this if tested systematically (e.g. Terhune, 2009).

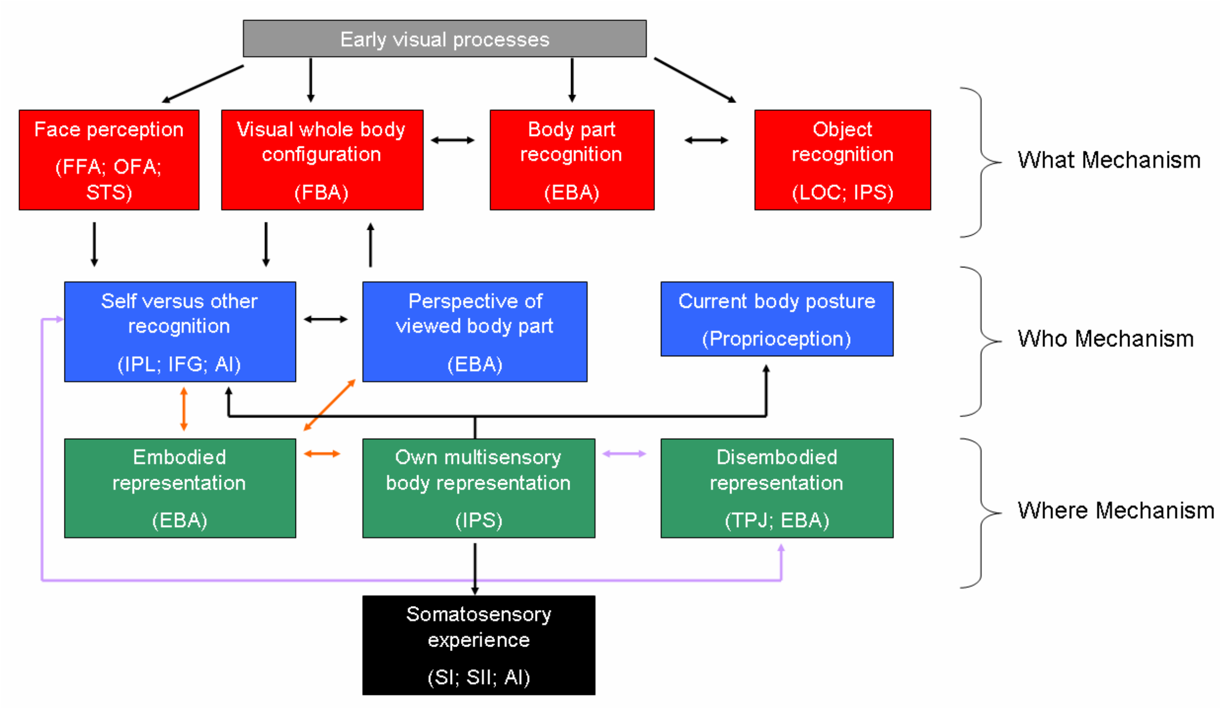


Figure 9.1 The 'What, Who, Where Model of Mirror-Touch Synaesthesia'. 'What' mechanisms are shown in red boxes and are involved in defining the stimulus touched. 'Who' mechanisms implement discriminations between self and other, and are shown in blue boxes. 'Where' mechanisms are shown in green boxes and are involved in locating where on the body and in space observed touch occurs. Processes necessary for all subjects are shown with black arrows, necessary for specular mirror-touch synaesthetes with orange arrows, and for anatomical mirror-touch synaesthetes with purple arrows. Brain regions represented are considered with regard to importance for mirror-touch synaesthesia. AI = Anterior Insula; EBA = Extrastriate Body Area; FBA = Fusiform Body Area; FFA = Fusiform face area; IFG = Inferior Frontal Gyrus; IPL = Inferior Parietal Lobule; IPS = Intraparietal Sulcus; LO = Lateral Occipital Cortex; SI = Primary Somatosensory Cortex; SII = Secondary Somatosensory Cortex; STS = Superior Temporal Sulcus; TPJ = Temporoparietal Junction.

9.4 Does the presence of synaesthesia have implications for perceptual processing?

Chapter 3 investigated whether the presence of synaesthesia has implications for perceptual processing. Previous ERP findings indicated that the presence of synaesthesia may exert a wider influence over sensory processing and impact on the veridical sensory processing of synaesthetes (Barnett et al., 2008; Goller, Otten, and Ward, 2009). For example, Barnett and colleagues (2008) report that, compared to non-synaesthetes, linguistic-colour synaesthetes show differences in early components of the visual evoked potential (VEP) when presented with simple visual stimuli which do not evoke synaesthesia. Further to this, Yaro and Ward (2007) report that synaesthetes who experience colour show superior colour discrimination abilities compared to non-synaesthetic control subjects. To assess whether enhanced perceptual processing was a core property of synaesthesia, colour and tactile sensitivity was contrasted between mirror-touch synaesthetes, synaesthetes who experience colour as evoked sensations (colour synaesthetes), synaesthetes who experience mirror-touch synaesthesia and colour synaesthesia (dual synaesthetes), and a group of non-synaesthetic controls. The findings indicate a relationship between the modality of synaesthetic experience and the modality of sensory enhancement. On a test of tactile discrimination, mirror-touch synaesthetes showed superior tactile discrimination compared to colour synaesthetes and non-synaesthetes. On a test of colour perception, colour synaesthetes outperformed non-synaesthetes. Dual synaesthetes (synaesthetes who experience both touch and colour as evoked sensations) outperformed the non-synaesthetic control group on both tasks, and outperformed colour synaesthetes on the tactile perception task. These findings imply that sensory enhancement in the concurrent perceptual system may be a general property of synaesthesia and show that the presence of synaesthesia exerts a wider influence over sensory processing.

The mechanisms which underpin sensory enhancement in synaesthesia are likely to reflect differences in brain development as a function of synaesthesia (which may be either a cause or consequence of synaesthesia). As noted previously, the neural mechanisms which underpin synaesthesia are a subject of uncertainty, with some authors suggesting that the condition may be due to additional structural connectivity (i.e. structural differences; Bargary and Mitchell, 2008; Rouw and Scholte, 2007), others in favour of malfunctions in cortical inhibition (i.e. functional but not structural differences; Cohen Kadosh and Henik, 2007; Cohen Kadosh and Walsh, 2008; Grossenbacher and Lovelace, 2001), and others for a combination of both (Smilek, Dixon, Cudahy, and Merikle, 2001). In principle, the findings of enhanced sensory perception in synaesthesia could be accounted for by any of these approaches (e.g. mechanisms of inhibition may unmask local anatomical pathways, while altered connectivity may result in alternative local and widespread anatomical pathways which could facilitate performance). Moreover, compatible findings of sensory-enhancement in the deprived brain would suggest that both aberrant connectivity and malfunctions in cortical inhibition could play a role in the sensory-enhancement found in synaesthetes. For example, temporary enhancements in tactile acuity can occur following blindfolding, and are thought to be due to fast-acting unmasking of existing connections to maintain functional behaviour. In comparison, tactile acuity can also be enhanced in blindness, which is though to reflect sustained unmasking of existing connections leading to new local and widespread anatomical pathways (a slow-acting mechanism; Pascual-Leone, Amedi, Fregni, and Merabet, 2005). Future studies should investigate how and whether mechanisms of cortical inhibition and connectivity interact in synaesthesia, and assess the possibility that increased structural connectivity in synaesthesia (Rouw and Scholte, 2007) may reflect sustained unmasking of existing connections (Cohen Kadosh et al., 2009). A further intriguing possibility would be to examine the interaction between fast-acting cortical unmasking mechanisms in sensory-enhancement following deprivation and synaesthesia. For example, if temporary enhancements in tactile acuity following blindfolding are linked to perceptual unmasking, and synaesthesia is linked to reduced cortical inhibition (and therefore increased unmasking; c.f. Cohen Kadosh and Walsh, 2006), then one may suspect that grapheme-colour synaesthetes will show more rapid enhancements in tactile acuity following sensory deprivation compared to non-synaesthetes.

9.5 What are the implications of heightened sensorimotor simulation in mirror-touch synaesthesia for social cognition?

In addition to studies investigating the neurocognitive basis of synaesthesia, there is a growing interest in using the condition to inform us about normal models of cognitive processing (Mattingley and Ward, 2006). This approach rests on the assumption of neuropsychology, where one is able to use a symptom affecting the normal system to inform us about the function of the normal system. In the case of synaesthesia the symptom is a positive one and in the case of mirror-touch synaesthesia one is assessing the impact of facilitated sensorimotor simulation mechanisms on cognition. Moreover, functional brain imaging has linked mirror-touch synaesthesia to heightened neural activity in a network of brain regions which are also activated in non-synaesthetic control subjects when observing touch to others (the mirror-touch system; Blakemore et al., 2005). The mirror-touch system is comprised of brain areas active during both the observation and passive experience of touch (including primary and secondary somatosensory cortices, and premotor cortex; Blakemore et al., 2005; Ebisch et al., 2008; Keyers et al., 2004) and has been suggested to be a candidate neural mechanism to aid social cognition through sensorimotor simulation (Gallese, 2006; Gallese and Goldman, 1998; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007). Accounts of social cognition involving sensorimotor simulation contend that, in order to understand another's emotions and physical states, the perceiver must map the bodily state of the observer onto the same representations involved in experiencing the perceived state (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, G, 2004; Gallese, 2006; Gallese and Goldman, 1998; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007). There is now a good degree of evidence from functional brain imaging, neuropsychological, transcranial magnetic stimulation, and electrophysiological studies to indicate a role for sensorimotor resources in this process (Adolphs, Damasio, Tranel, Cooper, and Damasio, 2000; Carr, Iacoboni, Dubeau, Mazziotta, and Lenzi, 2003; Dapretto et al., 2006; Hennenlotter et al., 2006; Jabbi, Swart, and Keysers, 2007; Kesler-West et al., 2001; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; Nummenmaa, Hirvonen, Parkkola, and Hietanen, 2008; Oberman, Winkielman, and Ramachandran, 2007; Pitcher, Garrido, Walsh, and Duchaine., 2008; Schulte-Ruther, Markowitsch, Fink, and Piefke, 2007; Seitz et al., 2008; van der Gaag, Minderaa, and Keysers, 2007; Warren et al., 2006; Wildgruber et al., 2005; Winston, O'Doherty, and Dolan, 2003). The studies reported in chapters 4 and 5 attempted to use mirror-touch synaesthesia as a model to inform us about the impact of facilitated sensorimotor simulation on empathy and facial expression recognition.

In chapter 4, the empathic abilities of mirror-touch synaesthetes were compared to control participants in two studies. The first study used a self-report empathy questionnaire (the empathy quotient – Baron-Cohen and Wheelwright, 2004) and showed that mirror-touch synaesthetes have higher levels of emotional reactive empathy (i.e. instinctive responses to others emotions), but do not have higher levels of cognitive or social components of empathy compared with control participants. Higher levels of empathy were not observed in other-variants of synaesthesia, indicating that it relates specifically to mirror-touch synaesthesia (and the mechanisms which underpin it). In the second study, these findings were replicated using the same measure of empathy and on another measure of empathy (Davis, 1980). The findings from the second study also confirmed that differences observed in empathy between mirror-touch synaesthetes and non-synaesthetes were linked to ‘other’ rather than ‘self’ orientated reactions, and found a significant relationship between the openness to experience personality trait and emotional empathy. Mirror-touch synaesthetes were also shown to significantly differ from non-synaesthetes on the openness to experience personality trait. These findings appear consistent with accounts of empathy that posit a role for sensorimotor simulation mechanisms (Gallese, 2006; Gallese and Goldman, 1998; Keysers and Gazzola, 2006; Oberman and Ramachandran, 2007) and with functional brain imaging (Nummenmaa et al., 2008) and neuropsychological findings (Shamay-Tsoory, Aharon-Peretz, and Perry, 2009) which indicate that emotional empathy is linked more closely to sensorimotor simulation of another’s state than cognitive empathy.

In addition to the differences in emotional empathy reported in chapter 4, the study presented in chapter 5 sought to establish whether mirror-touch synaesthetes differed in another aspect of social perception, namely facial expression recognition. The findings from this study showed that mirror-touch synaesthetes outperformed non-synaesthete control participants on tasks of facial expression recognition, but not control tasks involving identity recognition and identity perception. These findings are consistent with functional brain imaging (Carr et al., 2001; Hennenlotter et al., 2005; Leslie, Johnsen-Frey, and Grafton, 2004; Montgomery and Haxby, 2008; van der Gaag, Minderaa, and Keysers, 2007; Winston, O’Doherty, and Dolan, 2003), neuropsychological (Adolphs et al., 2000; Adolphs, Baron-Cohen, and Tranel, 2002) and TMS findings (Pitcher et al., 2008; Pourtois et al., 2004) which indicate a central role for sensorimotor resources in facial expression recognition, and suggest that facilitated sensorimotor simulation appears to be linked with heightened facial expression sensitivity and emotional empathy (Chapter 4).

A number of predictions can also be drawn from the evidence of heightened emotion sensitivity in mirror-touch synaesthesia. For example, given the evidence that mirror-touch synaesthesia has been reported to be linked to heightened activity in the mirror-touch system activated by us all when observing touch to others, one may predict that the extent of activity in this system may correlate with levels of emotional reactive empathy (but not cognitive empathy – where mirror-touch synaesthetes did not significantly differ from controls). Further, one may suspect that the level of activity in sensorimotor cortices when perceiving touch to others should also correlate with an individual subject's facial expression recognition abilities. These possibilities are to be addressed with future studies.

Another interesting point for consideration is whether mirror-touch synaesthesia represents a distinct population or the tail-end of a distribution of how much we simulate / empathize with of others[6]. As noted previously, mirror-touch synaesthesia shares a number of similarities with other types of developmental synaesthesia. For example, there is a tendency for mirror-touch synaesthetes to have other family members with synaesthesia and multiple types of synaesthesia, indicating a genetic component to the condition. Yet, the principles which bias what type of synaesthesia will or will not be developed are largely unclear. One could envisage that if individual differences in emotional sensitivity are in someway heritable /

---

[6] I would like to thank Prof. Christian Keysers for raising and corresponding with me on this issue.

separate from a ‘specific allele’ for synaesthesia[7] then heightened emotional sensitivity may bias these individuals to a form of interpersonal synaesthesia.

9.6 What are the implications of suppressing sensorimotor resources on expression recognition abilities in healthy adults?

While the findings from chapter 5 assessed the influence of facilitated sensorimotor simulation on expression recognition, the studies presented in chapters 7 and 8 assessed what impact suppressing sensorimotor resources has on the expression recognition abilities of healthy adults.

In chapter 7, a continuous theta burst (cTBS) TMS paradigm was used to suppress cortical activity in the right primary somatosensory cortex (rSI), right lateral premotor cortex (rPM), and the vertex. Participants completed two tasks. In experiment 1, participants were asked to complete a same-different auditory expression recognition task. In experiment 2, a new group of participants were asked to complete a same-different auditory identity task. Stimuli were non-verbal auditory emotions (amusement, disgust, fear and sadness), adapted from a previous study documenting the role of sensorimotor resources in non-verbal auditory emotion recognition (Warren et al., 2006), and were identical in each task. A comparison across tasks and sites, revealed that cTBS targeted at rSI and rPM impaired participants’ abilities to discriminate between the auditory emotions, but not identities, of others. This was not found to be the case following cTBS to the vertex (cTBS control site). Therefore consistent with simulation accounts of expression recognition (Adolphs, 2002; Adolphs, 2003; Damasio, 1990; Gallese, Keysers, and Rizzolatti, G, 2004; Goldman, and Sripada, 2005; Keysers and Gazzola, 2006),

---

[7] The genetic mechanisms for synaesthesia are of course likely to be more complex than this (e.g. see Asher et al., 2009).

suppressing sensorimotor activity resulted in a task-specific impairment on participants' abilities to discriminate emotions but not identities from vocal signals. These findings add to previous studies documenting a pivotal role for sensorimotor cortices in facial expression recognition (Adolphs et al., 2000; Pitcher et al., 2008; Pourtois et al., 2004) and suggest that they are central to the discrimination of emotion across modalities.

In chapter 8, I again used a cTBS paradigm, but investigated the role of neural activity in rSI and the right inferior frontal gyrus (rIFG) on facial expression recognition. Previous findings had indicated that rSI activity is central to facial expression discrimination (Adolphs et al., 2000; Pitcher et al., 2008; Pourtois et al., 2004; Winston et al. 2003), but whether this was expression-general or expression-specific remained a point of dispute. Further, rIFG activity had been reported in a number of brain imaging experiments investigating the neural correlates of facial expression recognition or evaluation (Carr et al., 2001; Dapretto et al., 2006; Hennenlotter et al., 2006; Kesler-West et al., 2001; Seitz et al., 2008), but whether the region is critical for the facial expression recognition abilities of healthy adults remained to be clarified. Using a four-forced-choice expression recognition task, the findings indicated that cTBS to rSI impaired the recognition of emotional facial expressions (happy and sad) relative to neutral expressions. This is consistent with previous findings documenting a central role for somatosensory cortices in facial expression discrimination (Adolphs et al., 2000; Pitcher et al., 2008; Pourtois et al., 2004) and compliments the findings of chapter 7 by indicating that rSI activity is involved in discriminating emotional expressions across modalities. No cTBS effect was observed following stimulation to rIFG or right V5 / MT (visual control site). This is interesting given that rIFG is considered to be a part of the human mirror system (Rizzolatti and Craighero, 2004) and has been reported in a number of fMRI studies on facial expression evaluation (Carr et al., 2001; Dapretto et al., 2006; Hennenlotter et al., 2006; Kesler-West et al., 2001; Seitz et al., 2008). The lack of impairment following cTBS to rIFG would suggest that although this region may be involved in facial expression recognition (Carr et al., 2001; Dapretto et al., 2006; Hennenlotter et al., 2006; Kesler-West et al., 2001; Seitz et al., 2008), it may not be critical to the process. Other components of motor simulation may play a more critical in facial expression discrimination (e.g. premotor cortex as studied in chapter 7) and future studies should address this.

Further possibilities for future research include combining TMS with other methodologies to consider the role of cortico-cortical interactions play in discriminating another's expressions. Moreover, while the effects of online TMS are spatially discrete, the effects of offline stimulation will spread to other cortical areas along the greatest lines of conductivity from the stimulated area. By combining cTBS with fMRI paradigms one should be able to assess any secondary effects of cTBS on other regions involved in expression recognition.

9.7 General Summary

In summary, this thesis has investigated the neurocognitive and perceptual profiles of mirror-touch synaesthesia (Chapters 2-5). I have provided a neurocognitive model of the condition (which provides testable predictions for future studies) and used mirror-touch synaesthesia as a tool to inform us about the neurocognitive mechanisms of synaesthesia more generally. The studies presented have also used mirror-touch synaesthesia as a model to inform us about the impact that heightened sensorimotor activity has on social cognition (Chapters 4 and 5), and the findings from these studies are compatible with research presented in chapters 7 and 8 which investigated the impact of suppression of sensorimotor activity on expression recognition. This has resulted in a number of interesting possibilities for further studies, some of which are currently in progress and others open to be conducted.

REFERENCES

Adolphs, R. (2002). Neural systems for recognizing emotion. *Current Opinion in Neurobiology, 12*, 169-77.

Adolphs, R. (2003). Cognitive neuroscience of human social behaviour. *Nature Reviews Neuroscience, 4,* 165-178.

Adolphs, R., Baron-Cohen, S., and Tranel, D. (2002). Impaired recognition of social emotions following amygdala damage. *Journal of Cognitive Neuroscience, 14,* 1264-1274.

Adolphs, R., Damasio, H., Tranel, D., Cooper, G., and Damasio, A. R. (2000). A role for somatosensory cortices in the visual recognition of emotion as revealed by three-dimensional lesion mapping. *Journal of Neuroscience, 20*, 2683-2690.

Aghajanian, G. K., and Marek, G. J. (1999). Serotonin and hallucinogens. *Neuropsychopharmacology, 21,* 16S-23S.

Aleman, A., Rutten, G. J., Sitskoorn, M. M., Dautzenberg, G., and Ramsey, N. F. (2001). Activation of striate cortex in the absence of visual stimulation: An fMRI study of synesthesia. *Neuroreport, 12,* 2827-2830.

Aluja, A., Garcia, O., and Garcia, L. F. (2002). A comparative study of Zuckerman's three structural models for personality through the NEO-PI-R, ZKPQ-III-R, EPQ-RS and Goldberg's 50-bipolar adjectives. *Personality and Individual Differences, 33,* 713-725.

Amassian, V.E., Cracco, R.Q., Maccabee, P.J., Cracco, J.B., Rudell, A.P., and Eberle, L. (1993). Unmasking human visual perception with the magnetic coil and its relationship to hemispheric asymmetry. *Brain Res, 605,* 312-316.

Amassian, V.E., Eberle, L., Maccabee, P., and Cracco, R.Q. (1992). Modeling magnetic coil excitation of human cerebral cortex with a peripheral nerve immersed in a brain-shaped volume conductor: The significance of fiber bending in excitation. *Electroencephalography and Clinical Neurophysiology, 85*, 291–301.

Anderson, A. K., Spencer, D. D., Fullbright, R. K., and Phelps, E. A. (2000). Contribution of the anteromedial temporal lobes to the evaluation of facial emotion. *Neuropsychology, 14,* 526-536.

Armel, K. C., and Ramachandran, V. S. (2001). Acquired synethesia in retinitis pigmentosa. *Neurocase, 5,* 293-296.

Arzy, S., Thut, G., Mohr, C., Michel, C. M., and Blanke, O. (2006). Neural basis of embodiment: Distinct contributions of the temporoparietal junction and the extrastriate body area. *Journal of Neuroscience, 26,* 8074-8081.

Ashbridge,E., Walsh,V., and Cowey, A. (1997). Temporal aspects of visual search studied by transcranial magnetic stimulation. *Neuropsychologia, 35,* 1121-1131.

Asher, J. E., Lamb, J. A., Brocklebank, D., Cazier, J. B., Maestrini, E., Addis, L., et al. (2009). A whole-genome scan and fine-mapping linkage study of auditory-visual synesthesia reveals evidence of linkage to chromosomes 2q24, 5p33, 6p12, and 12p12. *Am J Hum Genet, 84,* 279-285.

Ashley, V., Vuilleumier, P., and Swick, D. (2004). Time course and specificity of event-related potentials to emotional expressions. *NeuroReport, 15,* 211-216.

Augstine, J. R. (1996). Circuitry and functional aspects of the insular lobe in primates including humans. *Brain Res Brain Res Rev., 22,* 229-244.

Avenanti, A., Bueti, D., Galati, G., and Aglioti, S. M. (2005). Transcranial magnetic stimulation highlights the sensorimotor side of empathy for pain. *Nature Neuroscience, 8,* 955-960.

Avenanti, A., Minio-Paluello, I., Bufalari, I., and Aglioti, S. M. (2009). The pain of a model in the personality of an onlooker: Influence of state-reactivity and personality traits on embodied empathy for pain. *Neuroimage, 44,* 275-283.

Banissy, M. J., Cohen Kadosh, R., Maus, G. W., Walsh, V., and Ward, J. (2009). Prevalence, characteristics, and a neurocognitive model of mirror-touch synaesthesia. *Experimental Brain Research, 198,* 261-272.

Banissy, M. J., MacDonald, L., Ward, J., Walsh, V., Haggard, P., and Longo, M. R. (in preparation). The rubber hand illusion in mirror-touch synaesthesia.

Banissy, M. J., Stewart, L., Ward, J., Walsh, V., and Kanai, R. (in prepartion). Neuroanatomical correlates of tone-colour synaesthesia.

Banissy, M. J., and Ward, J. (2007). Mirror-touch synaesthesia is linked with empathy. *Nature Neuroscience, 10,* 815-816.

Bargary, G., and Mitchell, K. J. (2008). Synaesthesia and cortical connectivity. *Trends in Neurosciences, 31,* 335-342.

Barker, A.T., Freeston, I.L., Jalinous, R., Merton, P.A., and Morton, H.B. (1985). Magnetic stimulation of the human brain. *J. Physiol. (Lond.), 369*, 3P.

Barnett, K. J., Feeney, J., Gormley, M., and Newell, F. N. (2009). An exploratory study of linguistic-colour assocaitions across languages in multilingual synaesthetes. *Q J Exp Psychol, 62,* 1343-1354.

Barnett, K. J., Finucane, C., Asher, J. E., Bargary, G., Corvin, A. P., Newell, F. N., et al. (2008). Familial patterns and the origins of individual differences in synaesthesia. *Cognition, 106,* 871-893.

Barnett, K. J., Fox, J. J., Molholm, S., Kelly, S. P., Shalgi, S., Mitchell, K. J., and Newell, F. N. (2008). Differences in early sensory-perceptual processing in synaesthesia: A visual evoked potential study. *Neuroimage, 43,* 605-613.

Barnett, K. J., and Newell, F. N. (2008). Synaesthesia is associated with enhanced, self rated imagery. *Consciousness and Cognition, 17,* 1032-1039.

Baron-Cohen, S., Burt, L., Smith-Laittan, F., Harrison, J., and Bolton, P. (1996). Synaesthesia: Prevalence and familiality. *Perception, 25,* 1073-1079.

Baron-Cohen, S., Harrison, J., Goldstein, L. H., and Wyke, M. (1993). Coloured speech perception: Is synaesthesia what happens when modularity breaks down. *Perception, 22,* 419-426.

Baron-Cohen, S., Richler, J., Biarya, D., Gurunathan, N., and Wheelwright, S. (2003). The systemizing quotient: An investigation of adults with Aspergers syndrome or high-functioning autism, and normal sex differences. *Philos Trans R Soc Lond B Biol Sci., 358,* 361-374.

Baron-Cohen, S. and Wheelwright, S. (2004). The empathy quotient: An investigation of adults with asperger syndrome or high functioning autism, and normal sex differences. *J. Aut. and Dev. Disorders, 34,* 163-175.

Baron-Cohen, S., Wyke, M. A., and Binnie, C. (1987). Hearing words and seeing colours: An experimental investigation of synaesthesia. *Perception, 16,* 761-767.

Barrick, M. R., and Mount, R. K. (1991). The Big Five personality dimensions and job performance: A meta-analysis. *Personnel Psychology, 44,* 1-26.

Basser, P. J. (1995). Inferring microstructural features and the physiological state of tissues from diffusion-weighted images. *NMR Biomed., 8,* 333-344.

Batson, C. D. (1991). *The altruism question: Towards a social-psychology answer.* Erlbaum, Hillside, NJ.

Beck, D., Muggleton, N., Walsh, V., and Lavie, N. (2006). The right parietal cortex plays a critical role in change blindness. *Cereb. Cortex, 16,* 712-717.

Beeli, G., Esslen, M., and Jäncke, L. (2005). Synaesthesia: When coloured sounds taste sweet. *Nature, 434,* 38.

Beeli, G., Esslen, M., and Jäncke, L. (2008). Time course of neural activity correlated with colored-hearing synesthesia. *Cereb Cortex, 18,* 379-385.

Berlucchi, G., and Aglioti, S. (1997). The body in the brain: Neural basis of corporeal awareness. *Trends Neurosci., 20,* 560-564.

Bestmann, S., Baudewig, J., Siebner, H.R., Rothwell, J.C., and Frahm, J. (2004). Functional MRI of the immediate impact of transcranial magnetic stimulation on cortical and subcortical motor circuits. *European Journal of Neuroscience, 19,* 1950-1962.

Bjoertomt, O., Cowey, A., and Walsh, V. (2002). Spatial neglect in near and far space investigated by repetitive transcranial magnetic stimulation. *Brain, 125*, 2012-2022.

Blake, R, Palmeri, T.J., Marois, R., and Kim, C. Y. (2004). On the perceptual reality of synesthetic color. In: L. Robertson and N. Sagiv, Editors, Synesthesia: Perspectives from Cognitive Neuroscience, Oxford University Press, Oxford (2004), pp. 47–73.

Blakemore, S. J., Bristow, D., Bird, G., Frith, C., and Ward, J. (2005). Somatosensory activations during the observation of touch and a case of vision-touch synaesthesia. *Brain, 128,* 1571-1583.

Blanke, O., Landis, T., Spinelli, L., and Seeck, M. (2004). Out-of-body experiences and autoscopy of neurological origin. *Brain, 127,* 243-258.

Blanke, O., and Mohr, C. (2005). Out-of-body experience, heautoscopy, and autoscopic hallucinations of neurological origin: Implications for neurocognitive mechanisms of corporeal awareness and self-consciousness. *Brain Res Brain Res Rev., 50,* 184-199.

Blanke, O., Ortigue, S., Landis, T., and Seeck, M. (2002). Stimulating illusory own body perceptions. *Nature, 419,* 269-270.

Bohning, D.E., Shastri, A., McConnell, K.A., Nahas, Z., Lorberbaum, J., and Roberts, D. (1999). A combined TMS/fMRIstudy of intensity-dependent TMS over motor cortex. *Biol Psychiatry, 45*, 385–394.

Botvinick, M., and Cohen, J. (1998). Rubber hands feel touch that I see. *Nature, 391,* 756.

Bradshaw, J. L., and Mattingley, J. B. (2001). Allodynia: A sensory analogue of motor mirror neurons in a hyperaesthetic patient reporting instantaneous discomfort to another's perceived sudden minor injury? *J Neurol Neurosurg Psychiatry, 70,* 135-136.

Bremmer, F., Schlak, A., Shah, N. J., Zafiris, O., Kubishik, M., Hoffmann, K., et al. (2001). Polymodal motion processing in posterior parietal and premotor cortex: A human fMRI study strongly implies equivalences between humans and monkeys. *Neuron, 29,* 287-296.

Bruce, V., and Young, A. W. (1986). Understanding face recognition. *Br. J. Psychol., 77*, 305-327.

Brugger, P. (2002). Reflective mirrors: Persepective-taking in autoscopic phenomena. *Cognitive Neuropsychiatry, 7,* 179-194.

Bryant, G., and Barrett, H. C. (2007). Recognizing intentions in infant-directed speech: Evidence for universals. *Psychological Science, 18,* 746-751.

Buccino, G., Binkofski, F., Fink, G. R., Fadiga, L., Fogassi, L., Gallese, V., et al. (2001). Action observation activates premotor and parietal areas in a somatotopic manner. *European Journal of Neuroscience, 13,* 400-404.

Bufalari, I., Aprile, T., Avenanti, A., Di Russo, F., and Aglioti, S. M. (2007). Empathy for pain and touch in the human somatosensory cortex. *Cereb Cortex, 17,* 2553-2661.

Bünning, S., and Blanke, O. (2005). The out-of body experience: Precipitating factors and neural correlates. *Prog Brain Res., 150,* 331-350.

Burrack, A., Knoch, D., and Brugger, P. (2006). Mitempfindung in synaesthetes: Co-incidence or meaningful association? *Cortex, 42,* 151-154.

Bushara, K. O., Grafman, J., and Hallett, M. (2001). Neural correlates of auditory-visual stimulus onset asynchrony detection. *J Neurosci, 21,* 300-304.

Calder, A. J., Keane, J., Lawrence, A. D., and Manes, F. (2004). Impaired recognition of anger following damage to the ventral striatum. *Brain, 127,* 1958-1969.

Calder, A. J., Keane, J., Manes, F., Antoun, N., and Young, A. W. (2000). Impaired recognition and experience of disgust following brain injury. *Nature Neuroscience, 3,* 1077-1078.

Calder, A. J., Lawrence, A. D., and Young, A. W. (2001). The neuropsychology of fear and loathing. *Nature Reviews Neuroscience, 2,* 352-363.

Calder, A. J., and Young, A. W. (2005). Understanding the recognition of facial identity and facial expression. *Nature Reviews Neuroscience, 6,* 641-651.

Campana, G., Cowey, A., and Walsh, V. (2002). Priming of motion direction and area V5/MT: A test of perceptual memory. *Cereb Cortex, 12,* 663-669.

Carr, L., Iacoboni, M., Dubeau, M. C., Mazziotta, J. C., and Lenzi, G. L. (2003). Neural mechanisms of empathy in humans: A relay from neural systems for imitation to limbic areas. *Proc. Natl. Acad. Sci.*, *100*, 5497-5502.

Cohen, L., and Dehaene, S. (2004). Specialization within the ventral stream: The case for the visual word form area. *Neuroimage, 22,* 466-476.

Cohen Kadosh, R., Cohen Kadosh, K., and Henik, A. (2007). The neural correlate of bidirectional synaesthesia: A combined ERP and fMRI study. *Journal of Cognitive Neuroscience, 19,* 2050-2059.

Cohen Kadosh, R., and Henik, A. (2006). When a line is a number: Colour yields magnitude information in a digit-colour synaesthete. *Neuroscience, 137,* 3-5.

Cohen Kadosh, R., and Henik, A. (2007). Can synaesthesia research inform cognitive science? *Trends in Cognitive Sciences, 11,* 177-184.

Cohen Kadosh, R., Henik, A., and Walsh, V. (2007). Small is bright and big is dark in synaesthesia. *Current Biology, 17,* R834-R835.

Cohen Kadosh, R., Henik, A., Catena, A., and Walsh, V. (2009). Induced Cross-Modal Synesthetic Experience without Abnormal Neuronal Connections. *Psychological Science*, *20,* 258-265.

Cohen Kadosh, R., Tzelgov, J., and Henik, A. (2008). A synethetic walk on the mental number line: The size effect. *Cognition, 106,* 548-557.

Cohen Kadosh, R., and Walsh, V. (2006). Cognitive neuroscience: Rewired or crosswired brains. *Current Biology, 16,* 962-963.

Cohen Kadosh, R., and Walsh, V. (2008). Synaesthesia and Cortical Connections: Cause or Correlation? *Trends in Neurosciences*, *31,* 549-550.

Colby, C. L. (1998). Action-orientated spatial reference frames in cortex. *Neuron, 20,* 15-24.

Coslett, B. (1998). Evidence for a disturbance of the body schema in neglect. *Brain and Cognition, 37,* 527-544.

Costa, P. T., and McCrae, R. R. (1985). *The NEO Personality Inventory manual.* Odessa, FL: Psychological Assessment Resources.

Cowey, A., and Gross, C. G. (1970). Effects of foveal prestriate and inferotemporal lesions on visual discrimination by rhesus monkey. *Experimental Brain Research, 11,* 128-144.

Craig, A. D. (2002). How do you feel? Interoception: The sense of the physiological condition of the body. *Nature Reviews Neuroscience, 3,* 655-666.

Crawford, J. R., and Garthwaite, P. H. (2002). Investigation of the single case in neuropsychology: Confidence limits on the abnormality of test scores and test scores differences. *Neuropsyhcologia, 40,* 1196-1208.

Cytowic, R. E., and Wood, F. B. (1982). Synaesthesia II: Psychophysical relations in the synaesthesia of geometrically shaped taste and colored hearing. *Brain and Cognition, 1,* 36-49.

Damasio, A. R. (1990). Time-locked multiregional retroactivation: A systems-level proposal for the neural substrates of recall and recognition. In *Neurobiology of Cognition,* Edited by Eimas, P. D., and Galaburda, A. M. MIT Press, Cambridge, 25-62.

Dapretto, M., Davies, M. S., Pfeifer, J. H., Scott, A. A., Sigman, M., Bookheimer, S. Y., et al. (2006). Understanding emotions in others: Mirror neuron dysfunction in children with autism spectrum disorders. *Nature Neuroscience, 9*, 28-30.

Davidoff, J. (2001). Language and perceptual categorisation. *Trends in Cognitive Sciences, 5,* 382-387.

Davis, M. H. (1980). A multidimensional approach to individual differences in empathy. *Catal. Sel. Doc. Psychol., 10,* 85.

Davis, M. H. (1994). *Empathy: A social psychology approach.* Colorado: Westview Press.

Day, S. (2005). In: L. Robertson and N. Sagiv, Editors, Synesthesia: Perspectives from Cognitive Neuroscience, Oxford University Press, Oxford (2004),

Decety, J., and Jackson, P. L. (2004). The functional architecture of human empathy. *Behav Cogn Neurosci Rev., 3,* 71-100.

del Barrio, V., Aluja, A., and Garcia, L. F. (2004). Relationship between empathy and the Big Five personality traits in a sample of Spanish adolescents. *Social Behavior and Personality*, *32*, 677-681.

De Waal, F. B. (2007). Putting the altruism back into altruism: The evolution of empathy. *Ann Rev Psychol, 59,* 1-22.

Di Lazzaro, V., Pilato, F., Saturno, A., Oliviero, M., Dileone, M., Mazzone, P., et al. (2005). Theta-burst repetitive transcranial magnetic stimulation suppresses specific excitatory circuits in the human motor cortex. *J. Physiology, 565* 945-950.

Dietrich, S., Szameitat, D., Ackermann, H., and Alter, K. (2006). How to disentangle lexical and prosodic information? Psychoacoustic studies on the processing of vocal interjections. Prog Brain Res. *156*, 295-302.

Dimberg, U., Thunberg, M., Elmehed, K. (2000). Unconcious facial reactions to emotional facial expressions. *Psychological Science, 11,* 86-89.

Dixon, M. J., Smilek, D., and Merikle, P. M. (2004). Not all synaesthetes are created equal: Projector versus associator synaesthetes. *Cogn Affect Behav Neurosci, 4,* 335-343.

Donner, T. H., Kettermann, A., Diesch, E., Ostendorf, F., Villringer, A., and Brandt, S. A. (2002). Visual feature and conjunction searches of equal difficulty engage only partially overlapping frontoparietal networks. *Neuroimage, 15,* 16-25.

Downing, P.E., Jiang, Y., Shuman, M., and Kanwisher, N. A. (2001). Cortical area selective for visual processing of the human body. *Science, 293,* 2470-2473.

Duchaine, B., and Nakayama, K. (2006). The Cambridge Face Memory Test: Results from neurologically intact individuals and an investigation of its validity using inverted performance and prosopagnosic subjects. *Neuropsychologia, 16,* 166-173.

Duchaine, B., Germine, L., and Nakayama, K. (2007). Family resemblance: Ten family members with prosopagnosia and within-class object agnosia. *Cognitive Neuropsychology, 24,* 419-430.

Duhamel, J. R., Colby, C. L., and Goldberg, M. E. (1998). Ventral intraparietal area of the macaque: Congruent visual and somatic response properties. *Journal of Neurophysiology, 79.* 126-136.

Dumoulin, S.O., Bittar, R. G., Kabani, N. J., Baker, C. L. Jr, Le Goualher, G., Bruce Pike, G., et al. (2000). A new anatomical landmark for reliable identification of human area V5 / MT: A quantative analysis of sulcal patterning. *Cereb Cortex, 10,* 454-463.

Eagleman, D. M., Kagan, A. D., Nelson, S. S., Sagaram, D., and Sarma, A. K. (2007). A standardized test battery for the study of synaesthesia. *Journal of Neurosciences Methods, 159,* 139-145.

Ebisch, S. J. H., Perucci, M. G., Ferretti, A., Del Gratta, C., Luca Romani, G., and Gallese, V. (2008). The sense of touch: Embodied simulation in a visuo-tactile mirroring mechanism for observed animate or inanimate touch. *Journal of Cognitive Neuroscience, 20,* 1611-1623.

Eimer, M., and Holmes, A. (2002). An ERP study on the time course of emotional face processing. *NeuroReport, 13,* 427-431.

Eimer, M., and Holmes, A. (2007). Event-related brain potential correlates of emotional face processing. *Neuropsychologia, 45,* 15-31.

Eimer, M., Holmes, A., and McGlone, F. (2003). The role of spatial attention in the processing of facial expression: An ERP study of rapid brain responses to six basic emotions. *Cognitive, Affective and Behavioural Neuroscience, 3,* 97-110.

Eisenberg, N. (2000). Emotion, regulation, and moral development. *Annu Rev Psychol., 51,* 665-697.

Ekman, P., and Friesen, W. V. (1976). *Pictures of facial affect.* Palo Alto, CA: Consulting Psychologists.

Elias, L. J., Saucier, D. M., Hardie, C., and Sart, C. E. (2003). Dissocaiting semantic and perceptual components of synaesthesia: Behavioural and functional neuroanatomical investigations. *Cognitive Brain Research, 16,* 232-237.

Esterman, M., Verstynen, T., Ivry, R. B., and Robertson, L. C. (2006). Coming unbound: Disrupting automatic integration of synesthetic color and graphemes by transcranial magnetic stimulation of the right parietal lobe. *J Cogn Neuroci, 18,* 1570-1576.

Fadiga, L., Fogassi, L., Pavesi, G., and Rizzolatti, G. (1995). Motor facilitation during action observation: A magnetic stimulation study. *J. Neurophsyiology, 73,* 2608-2611.

Fink, G. R., Markowitsch, H. J., Reinkemeier, M., Bruckbauer, T., Kessler, J., and Heiss, W. D. (1996). Cerebral representations of one's own past: Neural networks involved in autobiographical memory. *Journal of Neuroscience, 16,* 4275-4282.

Flynn, F. G., Benson, D. F., and Ardila, A. (1999). Anatomy of the insula – Functional and clinical correlates. *Aphasiology, 13,* 55-78.

Franz, E. A., Ford, S., and Werner, S. (2007). Brain and cognitive processes of imitation in bimanual situations: Making inference about mirror neuron systems. *Brain research, 1145,* 138-149.

Friedman-Hill, S. R., Robertson, L. C., and Treisman, A. (1995). Parietal contributions to visual feature binding: Evidence from a patient with bilateral lesions. *Science, 269,* 853-855.

Gallagher, S. (1995). Body schema and intentionality. In J. L. Bermudez, A. Marcel, and N. Eilan (Eds.), *The body and the self*, Cambridge, MA: MIT Press.

Gallese, V. (2006). Intentional atonement: A neurophysiological perspective on social cognition and its disruption in autism. *Brain Res Cog Brain Res., 1079,* 15-24.

Gallese, V., Fadiga, L., Fogassi, L., and Rizzolatti, G. (1996). Action recognition in the premotor cortex. *Brain, 119,* 593-609.

Gallese, V., and Goldman, A. (1998). Mirror neurons and simulation theory of mind reading. *Trends in Cognitive Sciences, 12,* 493-501.

Gallese, V., Keysers, C., and Rizzolatti, G. (2004). A unifying view of the basis of social cognition. *Trends in Cognitive Sciences, 8,* 396-403.

Galton, F. (1880). Visualised numerals. *Nature (1880)*, 252-256.

Garrido, L., Furl, N., Draganski, B., Weiskopf, N., Stevens, J., Tan, G. C-Y., et al. (in press) VBM reveals reduced grey matter volume in the temporal cortex of developmental prosopagnosics. *Brain.*

Gazzola, V., Aziz-Zadeh, L., and Keysers, C. (2006). Empathy and the somatotopic auditory mirror system in humans. *Current Biology, 16,* 1824-1829.

Giummarra, M. J., Gibson, S. J., Georgiou-Karistianis, N., and Bradshaw, J. L. (2008). Mechanisms underlying embodiment, disembodiment and loss of embodiment. *Neuroscience and Biobehavioural Reviews, 32,* 143-160.

Goldberg, L. R. (1992). The development of markers for the Big-Five factor structure. *Psychological Assessment, 4,* 26-42.

Goldman, A., and Sripada, C. S. (2005). Simulationist models of face-based emotion recognition. *Cognition, 94,* 193-213.

Goldreich, D., and Kanics, I. M. (2003). Tactile acuity is enhanced in blindness. *Journal of Neuroscience, 23,* 3439-3445.

Goller, A., Otten, L., and Ward, J. (2009). Seeing sounds and hearing colours: An event-related potential study of audio-visual synaesthesia. *Journal of Cognitive Neuroscience, 21,* 1869-1881.

Gray, J. A., Chopping, S., Nunn, J., Parslow, D., Gregory, L., Williams, S., et al. (2002). Implications of synaesthesia for functionalism. *Journal of Consciousness Studies, 9,* 5-31.

Gray, J. A., Parslow, D. M., Brammer, M. J., Chopping, S., Vythelingum, G. N., and ffytche, D. H. (2006). Evidence against functionalism from neuroimaging of the alien colour effect in synaesthesia. *Cortex, 42,* 309-318.

Grossenbacher, P.G., and Lovelace, C.T. (2001). Mechanisms of synaesthesia: Cognitive and physiological constraints. *Trends in Cognitive Sciences, 5,* 36-41.

Hadjikhani, N., and Roland, P. E. (1998). Cross-modal transfer of information between the tactile and the visual representations in the human brain: A positron emission tomographic study. *Journal of Neuroscience, 18,* 1072-1084.

Haggard, P. (2006). Just seeing you makes me feel better: Interpersonal enhancements of touch. *Social Neuroscience, 1,* 104-110.

Halligan, P. W., Hunt, M., Marshall, J. C., and Wade, D. T. (1996). When seeing is feeling: Acquired synaesthesia or phantom touch? *Neurocase, 2,* 21-29.

Harris, J. A., Harris, I. M., Diamond, M. E., (2001). The topography of tactile working memory. *J Neurosci, 21,* 8262-8269.

Haxby, J. V., Hoffman, E. A., and Gobbini, M. I. (2000). The distributed human neural system for face processing. *Trends in Cognitive Sciences, 4,* 223-233.

Head, H., and Holmes, G. (1911-1912). Sensory disturbances from cerebral lesions. *Brain, 34,* 102-254.

Hennenlotter, A., Schroeder, U, Erhard, P., Castrop, F., Haslinger, B., Stoecker, D., et al. (2005). A common neural basis for receptive and expressive communication of pleasant facial affect. *Neuroimage, 26***,** 581-591.

Hoekert, M., Bais, L., Kahn, R. S., and Aleman, A. (2008). Time course of the involvement of the right anterior superior temporal gyrus and the right fronto-parietal operculum in emotional prosody perception. PlOS One *3*, doi: 10.1371/journal.pone.0002244.

Holmes, A., Vuilleumier, P., and Eimer, M. (2003). The processing of emotional facial expressions is gated by spatial attention: Evidence from event-related brain potentials. *Cognitive Brain Research, 16,* 174-184.

Hong, S. W. and Blake, R. (2008). Early visual mechanisms do not contribute to synaesthetic colour experience. *Vision Research, 48,* 1018-1026.

Howell, D. C. (2002). *Statistical Methods for Psychology*. Thomson Learning: USA.

Huang, Y. Z., Edwards, M. J., Rounis, E., Bhatia, K. P., and Rothwell, J. C. (2005). Theta burst stimulation of the human motor cortex. *Neuron, 45***,** 201-206.

Huang, Y. Z., Rothwell, J. C., Lu, C. S., Wang, J., Weng, Y. H., Lai, S. C., et al. (2009). The effect of continuous theta burst stimulation over premotor cortex on circuits in primary motor cortex and spinal cord. *Clin Neurophysiol., 120,* 796-801.

Hubbard, E. M. (2007). A real red-letter day. *Nat Neurosci, 10,* 671-672.

Hubbard, E. M., Arman, A. C., Ramachandran V. S., and Boynton, G. M. (2005). Individual differences among grapheme-color synesthetes: brain-behavior correlations. *Neuron, 45***,** 975–985.

Hubbard, E. M., Manohar, S., and Ramachandran, V. S. (2006). Contrast affects the strength of synesthetic colors. *Cortex, 42,* 184-194.

Hubbard, E.M., and Ramachandran, V. S. (2003). Refining the experimental lever: A reply to Shannnon and Pribram. *J Consciousness Stud, 9,* 77-84.

Hubbard, E.M., and Ramachandran, V. S. (2005). Neurocognitive mechanisms of synaesthesia. *Neuron, 48,* 509-520.

Iacoboni, M., and Dapretto, M. (2006). The mirror neuron system and the consequences of its dysfunction. *Nat Rev Neurosci, 7,* 942-951.

Iriki, A., Tanaka, M., and Iwamura, Y. (1996). Coding of modified body schema during tool use by macaque postcentral neurones. *Neuroreport, 7,* 2325-2330.

Jabbi, M., Swart, M., and Keysers, C. (2007). Empathy for positive and negative emotions in the gustatory cortex. *Neuroimage, 34*, 1744-1753.

Jäncke, L., Beeli, G., Eulig, C., and Hänggi, J. (2009). The neuroanatomy of grapheme-color synethesia. *Eur J Neurosci, 29,* 1287-1293.

Jewanski, J., Day, S. A., and Ward, J. (2009). A colourful albino: The first documented case of synaesthesia, by George Tobias Ludwig Sachs in 1812. *Journal of the History of Neurosciences, 18,* 1-11.

John, O. P., Donahue, E. M., and Kentle, R. L. (1991). *The Big Five Inventory – Versions 4a and 54*. Berkeley: University of California, Berkeley, Institute of Personality and Social Research.

John, O. P. and Srivastava, S. (1999). The Big Five trait taxonomy: History, measurement and theoretical perspectives. In *Handbook of personality: Theory and research (2nd ed.),* Edited by Pervin, L., and John, O. P. New York: Guilford.

Johnson, R., Burton, P., and Ro, T. (2006). Visually induced feelings of touch. *Brain Research, 1073-1074,* 398-406.

Johnsen, K. O., and Philips, J. R. (1981). Tactile spatial resolution. I. Two-point discrimination, gap detection, grating resolution, and letter recognition. *Journal of Neurophysiology, 46,* 1177-1191.

Juan, C. H., and Walsh, V. (2003). Feedback to V1: A reverse hierarchy in vision. *Exp Brain Res., 150,* 259-263.

Kalla, R., Muggleton, N., Cowey, G., and Walsh, V. (2009). Human dorsolateral prefrontal cortex is involved in visual search for conjunctions but not features: A theta TMS study. Cortex *45*, 1085-1090.

Kammer. T. (1999). Phosphenes and transient scotomas induced by magnetic stimulation of the occipital pole: their topographic relationship. *Neuropsychologia, 37,* 191–198.

Kaplan, E. (1991). The receptive field of retinal ganglion cells in cat and monkey. In: Leventhal, A. G. (Ed.), Vision and Visual Dysfunction. CRC Press: Boston. pp 10-40.

Kauffman, T., Théoret, H., Pascual-Leone, A. (2002). Braille character discrimination in blindfolded human subjects. *Neuroreport, 13,* 571-574.

Keane, J., Calder, A. J., Hodges, J. R., and Young, A. W. (2002). Face and emotion processing in frontal variant frontotemporal dementia. *Neuropsychologia, 40,* 655-665.

Kesler-West, M. L., Andersen, A. H., Smith, C. D., Avison, M. J., Davis, C. E., Kryscio, R. J., et al. (2001). Neural substrates of facial emotion processing using fMRI. *Brain Res. Cogn. Brain Res., 11,* 213-226.

Keysers, C., and Gazzola, V. (2006). Towards a unifying theory of social cognition. *Progress in Brain Research, 156,* 379-401.

Keyers, C., Wicker, B., Gazzola, V., Anton, J. L., Fogassi, L., and Gallese, V. (2004). A touching sight: SII/PV activation during the observation and experience of touch. *Neuron, 42,* 335-346.

Kim, C. Y., Blake, R., and Palmeri, T. J. (2006). Perceptual interaction between real and synesthetic colors. *Cortex, 42,* 195–203.

Kipps, C. M., Duggins, A. J., McCusker, E. A., and Calder, A. J. (2007). Disgust and happiness recognition correlate with anteroventral insula and amygdala volume respectively in preclinical Huntigton's disease. *Journal of Cognitive Neuroscience, 19,* 1206-1217.

Kircher, T. T., Senior, C., Phillips, M. L., Rabe-Hesketh, S., Benson, P. J., Bullmore, E. T., et al. (2001). Recognizing one's own face. *Cognition, 78,* B1-B15.

Konen, C. S., and Kaster, S. (2008). Two hierarchically organized neural systems for object information in human visual cortex. *Nature Neuroscience, 11,* 224-231.

Krolak-Salmon, P., Henaff, M. A., Isnard, J., Tallon-Baudry, C., Guenot, M., Vighetto, A., et al. (2003). A specific response to disgust moudlated by attention in human ventral anterior insula. *Annals of Neurology, 53,* 446-453.

Lamm, C., Batson, C. D., and Decety, J. (2007). The neural substrate for human empathy: Effects of perspective-taking and cognitive appraisal. *Journal of Cognitive Neuroscience, 19,* 42-58.

Lavidor, M., and Walsh, V. (2003). A magnetic stimulation examination of orthographic neighborhood effects in visual word recognition. *Journal of Cognitive Neuroscience, 15,* 354-363.

Lawrence, A. D., Calder, A. J., McGowan, S. W., and Grasby, P. M. (2002). Selective disruption of the recognition of facial expressions of anger. *Neuroreport, 13,* 881-884.

Lawrence, E. J., Shaw, P., Baker, D., Baron-Cohen, S., and David, A. S. (2004). Measuring empathy: Reliability and validity of the Empathy Quotient. *Psychological Medicine, 34,* 911-924.

Leslie, K. R., Johnson-Frey, S. H., and Grafton, S. T. (2004). Functional imaging of face and hand imitation: Towards a motor theory of empathy. *Neuroimage, 21***,** 601-607.

Lewis, S., Thoma, R. J., Lanoue, M. D., Miller, G. A., Heller, W., Edgar, C., et al. (2003). Visual processing of facial affect. *Neuroreport, 14,* 1841-1845.

Lomber, S. (1999). The advantages and limitations of permanent or reversible deactivation techniques in the assessment of neural function. *Journal of Neuroscience Methods, 86,* 109-118.

Longo, M. R., Schüür, F., Kammers, M. P., Tsakiris, M., and Haggard, P. (in press). Self awareness and the body image. *Acta Psychologica*.

Lundqvist, D., Flykt, A., and Őhman, A. (1998). *The Karolinska Directed Emotional Faces (KDEF).* Stockholm: Department of Neurosciences Karolinska Hospital.

Macaluso, E., and Driver, J. (2003). Multimodal spatial representations in the human parietal cortex: Evidence from functional neuroimaging. *Adv Neurology, 93,* 219-233.

MacDonald, D., Kabani, N., Avis, D., and Evans, A. C. (2000). Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI. *Neuroimage, 12,* 340-356.

MacLeod, C. M., and Dunbar, K. (1988). Training and stroop-like interference: Evidence for a continuum of automaticity. *J Exp Pscyhol Learn Mem Cogn, 14,* 126-135.

Maravita, A., and Iriki, A. (2002). Tools for the body (schema). *Trends in Cognitive Sciences, 8,* 79-86.

Marks, L. E. (1975). On coloured hearing synaesthesia: Cross-modal translations of # sensory dimensions. *Psychological Bulletin, 82,* 303-331.

Marzi, C. A., Miniussi, C., Maravita, A., Bertolasi, L., Zanette, G., Rothwell, J. C., and Sanes, J. N. (1998). Transcranial magnetic stimulation selectively impairs interhemispheric transfer of visuo-motor information in humans. *Exp. Brain. Res., 118,* 435-438.

McCabe, C., Rolls, E. T., Bilderbeck, A., and McGlone, F. (2008). Cognitive influences on the affective representations of touch and the sight of touch in the human brain. *Social Cognitive and Affective Neuroscience, 3,* 97-108.

Mesulam, M. M., and Mufson, E. (1982). Insula of the old world monkey, III: Efferent cortical output and comments on function. *Journal of Comparative Neurology, 212,* 38-52.

Meyer, M., Zysset, S., von Cramon, D. Y., and Alter, K. (2005). Distinct fMRI responses to laughter, speech, and sounds along the human perisylvian cortex. Cog Brain Res. *24,* 291-306.

Milner, B. (1966). Amnesia following operation on the temporal lobes. In *Amnesia,* C.W.M. Whitty and O.L. Zangwill (eds.). London: Botterworths, pp 109-133.

Mills, C. B., Boteler, E. H., and Oliver, G. K. (1999). Digit synaesthesia: A case study using a stroop-type test. *Cognitive Neuropsychology, 16,* 181-191.

Mitchell, R. L., and Crow, T. J. (2005). Right hemisphere language functions and schizophrenia: The forgotten hemisphere? *Brain, 128,* 963-978.

Montgomery, K. J., and Haxby, J. (2008). Mirror neuron system differentially activated by facial expressions and social hand gestures: A functional magnetic resonance imaging study. *Journal of Cognitive Neuroscience, 20,* 1866-1877.

Morrison, I., Lloyd, D., di Pellegrino, G., and Roberts, N. (2004). Vicarious responses to pain anterior cingulated cortex: Is empathy a multisensory issue? *Cogn Affect Behav Neurosci, 4,* 270-278.

Mottaghey, F. M., Gangitano, M., Sparing, R., Krause, B. J., Pascual-Leone, A. (2002). Segregation of areas related to visual working memory in the prefrontal cortex revealed by rTMS. *Cereb Cortex, 12,* 369-375.

Mufson, E., and Mesulam, M. M. (1982). Insula of the old world monkey, II: Afferent cortical input and comments on the claustrum. *Journal of Comparative Neurology, 212,* 23-37.

Muggleton, N., Tsakanikos, E., Walsh, V., and Ward, J. (2007). Disruption of synaesthesia following TMS of the right posterior parietal cortex. *Neuropsychologia, 45,* 1582-1585.

Muncer, S., and Ling, J. (2006). Psychometric analysis of the empathy quotient (EQ) scale. *Personality and Individual Differences, 40,* 1111-1119.

Nagarajan, S.S., Durand, D., and Warman, E.N. (1993). Effects of induced electric fields on finite neuronal structures: a simulation study. *IEEE Trans. in Biomedical Engineering, 40*, 1175-1188.

Nikolić, D., Lichti, P., and Singer, W. (2007). Color opponency in synaesthetic experiences. *Psychological Science, 18,* 481-486.

Nummenmaa, L., Hirvonen, J., Parkkola, R., and Hietanen, J. K. (2008). Is emotional contagion special? An fMRI study on neural systems for affective and cognitive empathy. *Neuroimage, 43,* 571-580.

Nunn. J. A., Gregory, L. J., Brammer, M., Williams, S. C., Parslow, D. M., Morgan, M .J., et al. (2002). Functional magnetic resonance imaging of synesthesia: Activation of V4 / V8 by spoken words. *Nature Neuroscience, 5,* 371-375.

Oberman, L. M., Hubbard, E. M., McCleery, J. P., Altschuler, E. L., Ramachandran, V. S., and Pineda, J.A. (2005). EEG evidence of mirror neuron dysfunction in autism spectrum disorders. *Brain Res Cogn Brain Res., 24,* 190-198.

Oberman, L. M., and Ramachandran, V. S. (2007). The simulating social mind: The role of the mirror neuron system and simulation in the social and communicative deficits of autism spectrum disorders. *Psychol Bull., 133,* 310-327.

Oberman, L.M. , Winkielman, P., and Ramachandran, V. S. (2007). Face to face: Blocking facial mimicry can selectively impair recognition of emotional expressions. *Social Neuroscience, 2*, 167-178.

Olausson, H., Lamarre, Y., Backlund, H., Morin, C., Wallin, B. G., Starck, G., Ekholm, S., Strigo, I., Worsley, K., Valbo, Ǻ. B., and Bushnell, M. C. (2002). Unmyelinated tactile afferents signal touch and project to insular cortex. *Nature Neuroscience, 5,* 900-904.

Oliveri, M., Turriziani, P., Carlesimo, G. A., Koch, G., Tomaiuolo, F., Panella, M., et al. (2001). Parieto-frontal interactions in visual-object and visual-spatial working memory. *Cereb Cortex, 11,* 606-618.

Olson, I. R., Gatenby, J. C., and Gore, J. C. (2002). A comparison of bound and unbound audio-visual information processing in the human cerebral cortex. *Cognitive Brain Research, 14,* 129-138.

O'Shea, J., Muggleton, N. G., Cowey, A., and Walsh, V. (2004). Timing of target discrimination in human frontal eye fields. *Journal of Cognitive Neuroscience, 16*, 1060-1067.

Parise, C. V., and Spence, C. (2009). 'When birds of a feather flock together': Synesthetic correspondances modulate audiovisual integration in non-synesthetes. *PloS One, 4,* e5664.

Pascual-Leone, A., Amedi, A., Fregni, F., and Merabet, L. B. (2005). The plastic human brain cortex. *Ann. Rev. Neuroscience, 28,* 377-401.

Paulesu, E., Harrison, J., Baron-Cohen, S., Watson, J. D., Goldstein, L., Heather, J., et al. (1995). The physiology of coloured hearing. A PET activation study of colour-word synaesthesia. *Brain, 118,* 661-676.

Peelen, M. V., and Downing, P. E. (2005). Selectivity for the human body in fusiform gyrus. *Journal of Neurophysiology, 93,* 603-608.

Petrides, M., Cadoret, G., and Mackey, S. (2005). Orofacial somatomotor responses in the macaque monkey homolouge of Broca's area. *Nature, 435,* 1235-1238.

Philips, M. L., Young, A. W., Scott, S. K., Calder, A. J., Andrew, C., Giampietro, V., et al. (1998). Neural responses to facial and vocal expressions of fear and disgust. *Proc. Biol. Sci., 265,* 1809-1817.

Philips, M. L., Young, A. W., Senior, C., Brammer, M., Andrew, C., Calder, A. J., et al. (1997). A specific substrate for perceiving facial expressions of disgust. *Nature, 389,* 495-498.

Pitcher, D., Charles, L., Devlin, J. T., Walsh, V., and Duchaine, B. C. (2009). Triple dissociation of faces, bodies, and objects in extrastraite cortex. *Current Biology, 19,* 319-324.

Pitcher, D., Garrido, L., Walsh, V., and Duchaine, B. C. (2008). Transcranial magnetic stimulation disrupts the perception and embodiment of facial expressions. *Journal of Neuroscience, 28,* 8929-8933.

Pitcher, D., Walsh, V., Yovel, G., and Duchaine, B. C. (2008). TMS evidence for the involvement of the right occipital face area in early face processing. *Current Biology, 17,* 1568-1573.

Pourtois, G., Sander, D., Andres, M., Grandjean, D., Reveret, L., Olivier, E., et al. (2004). Dissociable roles of the human somatosensory and superior temporal cortices for processing social face signals. *Eur. J. Neurosci., 20,* 3507-3515.

Preston, S. D., and de Waal, F. B. (2002). Empathy: It's ultimate and proximal basis. *Behav Brain Sci., 25,* 1-20.

Ramachandran, V. S., and Hubbard, E. (2001). Synaesthesia – A window into perception, thought and language. *Journal of Consciousness Studies, 8,* 3-34.

Rao, A., Nobre, A. C., Alexander, I., and Cowey, A. (2007). Auditory evoked visual awareness following sudden ocular blindness: An EEG and TMS investigation. *Exp Brain Res, 176,* 288-298.

Rich, A. N., and Mattingley, J. B. (2002). Anomalous perception in synaesthesia: A cognitive neuroscience. *Nature Reviews Neuroscience, 3,* 43-52.

Rich, A. N., Bradshaw, J. L., and Mattingley, J. B. (2005). A systematic large-scale study of synaesthesia: Implications for the role of early experience in lexical-colour assocaitions. *Cognition, 98,* 53-84.

Rich, A. N., Williams, M. A., Pruce, A., Syngeniotis, A., Howard, M. A., McGlone, F., et al. (2006). Neural correlates of imagined and synaesthetic colours. *Neuropsychologia, 44,* 2918-2925.

Rizzo, M., and Eslinger, P. J. (1989). Colored hearing synesthesia: An investigation of neural factors. *Neurology, 39,* 781-784.

Rizzolatti, G., and Craighero, L. (2004). The mirror-neuron system. *Annual Review of Neuroscience, 27,* 169-192.

Ro, T., Farnè, A., Johnson, R. M., Wedeen, V., Chu, Z., Wang, Z. J., et al. (2007). Feeling sounds after a thalamic lesion. *Ann Neurol., 62,* 433-441.

Robertson, L. C. (2003). Binding, spatial attention, and perceptual awarness. *Nat Rev Neurosci., 4,* 93-102.

Robertson, D., Davies, I., and Davidoff, J. (2000). Colour categories are not universal: Replications and new evidence from a stone-age culture. *Journal of Experimental Psychology, 129,* 369-398.

Robertson, I. H., and Murre, J. M. J. (1999). Rehabilitation of brain damage: Brain plasticity and principles of guided recovery. *Psychological Bulletin, 125,* 544-575.

Rorden, C., Heutink, J., Greenfield, E., and Robertson, I. H. (1999). When a rubber hand 'feels' what the real hand cannot. *NeuroReport, 10,* 135-138.

Rouw, R., and Scholte, H. S. (2007). Increased structural connectivity in grapheme-colour synesthesia. *Nat Neurosci., 10,* 792-797.

Ruby, P., and Decety, J. (2001). Effect of subjective perspective taking during simulation of action: A PET investigation of agency. *Nature Neuroscience, 4,* 546-550.

Ruff, C.C., Blankenburg, F., Bjoertomt, O., Bestmann, S., Freeman, E., Haynes, J-D., Rees, G., Josephs, O., Deichmann, R., and Driver, J. (2006). Concurrent TMS-fMRI and psychophysics reveal frontal influences on human retinotopic visual cortex. *Current Biology, 16,* 1479-1488

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

Russell, R., Duchaine, B., and Nakayama, K. (2009). Super-recognizers: People with extraordinary face recognition ability. *Psychonomic Bulletin and Review, 16*, 252-257.

Saarela, M. V., Hlushchuk, Y., Williams, A. C., Schürmann, M., Kalso, E., and Hari, R. (2007). The compassionate brain: Humans detect intensity of pain from another's face. *Cereb Cortex, 17,* 230-237.

Sachs, G. T. L. (1812). *Historiae naturalis duorum leucaetiopum: Auctoris ipsius et sororis eius.* Erlangen.

Saenz, M., and Koch, C. (2008). The sound of change: Visually-induced auditory synesthesia. *Current Biology, 18,* 650-651.

Sagiv, N. (2004). In: L. Robertson and N. Sagiv, Editors, Synesthesia: Perspectives from Cognitive Neuroscience, Oxford University Press, Oxford (2004),

Sagiv, N., Simner, J., Collins, J., Butterworth, B., and Ward, J. (2006). What is the relationship between synaesthesia and visuo-spatial number forms? *Cognition, 101,* 114-128.

Sagiv, N., and Ward, J. (2006). Cross-modal interactions: Lessons from Synaesthesia. *Progress in Brain Research, 155,* 263-275.

Sauter, D. A., and Eimer, M. (in press). Rapid detection of emotion from human vocalizations. *Journal of Cognitive Neuroscience.*

Sauter, D. A., and Scott, S. K. (2007). More than one kind of happiness: Can we recognise vocal expressions of different positive states? *Motivation and Emotion, 31,* 192-199.

Saxe, R., Jamal, N., and Powell, L. (2006). My body or yours? The effect of visual perspective on cortical body representations. *Cerebral Cortex, 16,* 178-182.

Schiltz, K., Trocha, K., Wieringa, B. M., Emirch, H. M., Johannes, S., and Münte, T. F. (1999). Neurophysiological aspecrs of synesthetic experience. *J Neuropsychiatry Clin Neurosci., 11,* 58-65.

Schofield, W. N. (1976). Do children find movements which cross the body midline difficult? *Q. J. Exp. Psychol. 28,* 571-582.

Schröder, M. (2003). Experimental study of affect bursts. *Speech communication, 40,* 99-116.

Schulte-Rüther, M., Markowitsch, H. J., Fink, G. R., and Piefke, M. (2008). Miror neuron and theory of mind mechanisms involed in face-to-face interactions: A functional magnetic resonance imaging approach to empathy. *Journal of Cognitive Neuroscience, 19,* 1354-1372.

Scott, S. K., Sauter, D. A., and McGettigan, C. (In press). Brain mechanisms for processing perceived emotional vocalizations in humans. To appear in Handbook of Mammalian Vocalizations: A Neuroscience Approach, S Brudzynski ed. (Elsevier).

Scott, S. K., Young, A. W., Calder, A. J., Hellawell, D. J., Aggleton, J. P., and Johnsen, M. (1997). Impaired auditory recognition of fear and anger following bilateral amygdala lesions. *Nature, 385,* 254-257.

Seitz, R. J., Schäfer, R., Scherfield, D., Friederichs, S., Popp, K., Wittsack, H. J., et al. (2008). Valuating other people's emotional face expression: A combined functional magnetic resonance imaging and electroencephalography study. *Neuroscience, 152,* 713-722.

Serino, A., Pizzoferrato, F., and Làdavas, E. (2008). Viewing a face (especially one's own face) being touched enhances tactile perception on the face. *Psychological Science, 19,* 434-438.

Seron, X., Pesenti, M., Nöel, M. P., Deloche, G., and Cornet, J. A. (1992). Images of numbers, or 'When 98 is upper left and 6 is sky blue". *Cognition, 44,* 159-196.

Shallice, T. (1988). *The neuropsychology of mental structure.* Cambridge: Cambridge University Press.

Shamay-Tsoory, S. G., Aharon-Peretz, J., and Perry, D. (2009). Two systems for empathy: A double dissociation between emotional and cognitive empathy in inferior frontal gyrus versus ventromedial prefrontal lesions. *Brain, 132,* 617-627.

Shaw, P., Greenstein, D., Lerch, J., Clasen, L., Lenroot, R., Gogtay, N., et al. (2006). Intellectual ability and cortical development in children and adolescents. *Nature, 440,* 676-679.

Siebner HR, Willoch F, Peller M, Auer C, Boecker H, Conrad B, and Bartenstein P. 1998). Imaging brain activation induced by long trains of repetitive transcranial magnetic stimulation. *NeuroReport, 9,* 943-948.

Simner, J. (2007). Beyond perception: Synaesthesia as a psycholingustic phenomenon. *Trends in Cognitive Sciences, 11,* 23-29.

Simner, J., and Holenstein, E. (2007). Ordinal linguistic personification as a variant of synaesthesia. *Journal of Cognitive Neuroscience, 19,* 694-703.

Simner, J., Mulvenna, C., Sagiv, N., Tsakanikos, E., Witherby, S., Fraser, C., Scott, K., and Ward, J. (2006). Synaesthesia: The prevalence of atypical cross-modal experiences. *Perception, 35,* 1024-1033.

Simner, J., Ward, J., Lanz, M., Jansari, A., Noonan, K., Glover, L., and Oakley, D. (2005). Non-random associations of graphemes and colour in the synaesthetic and normal populations. *Cognitive Neuropsychology, 22,* 1069-1085.

Singer, T., Seymour, B., O'Doherty, J., Kaube, H., Dolan, R. J., and Frith, C. D. (2004). Empathy for pain involves the affective but not sensory components of pain. *Science, 303,* 1157-1162.

Singh, K.D., Hamdy, S., Aziz, Q., and Thompson, D.G. (1997). Topographic mapping of trans-cranial magnetic stimulation data on surface rendered MR images of the brain. *EEG Clin Neurophysiol, 105*, 345-351.

Sirigu, A., Grafman, J., Bressler, K., and Sunderland, T. (1991). Multiple representations contribute to body knowledge processing. *Brain, 114,* 629-642.

Smilek, D., Dixon, M. J., Cudahy, C., and Merikle, P. M. (2001). Synaesthetic photisms influence visual perception. *Journal of Cognitive Neuroscience, 13,* 930-936.

Smilek, D., Malcolmson, K. A., Carriere, J., Eller, M., Kwan, D., and Reynolds, M. (2007). When "3" is a jerk and "E" is king: Personifying inanimate objects in synaesthesia. *Journal of Cognitive Neuroscience, 19,* 981-992.

Smilek, D., Moffatt, B. A., Pasternak, J., White, B. N., Dixon, M. J., and Merikle, P. M. (2002). Synaesthesia: A case study of discordant monozygotic twins. *Neurocase, 8,* 338-342.

Smith, H. L. (1905). Synesthesia. *John Hopkins Hospital Bulletin, 16,* 258-263.

Southgate, V., and Hamilton, A. F. (2008). Unbroken mirrors: Challenging a theory of autism. *Trends in Cognitive Sciences, 12,* 225-229.

Sperling. J. M., Prvulovic, D., Linden, D. E., Singer, W., and Stirn, A. (2006). Neuronal correlates of colour-graphemic synaesthesia: A fMRI study. *Cortex, 42,* 295-303.

Spiller, M. J., and Jansari, A. S. (2008). Mental imagery and synaesthesia: Is synaesthesia from internally-generated stimuli possible. *Cognition, 109,* 143-151.

Sprengelmeyer, R., Raush, M., Eysel, U. T., and Przuntek, H. (1998). Neural substrates associated with recognition of facial expressions of basic emotions. *Proc. Biol. Sci., 265,* 1927-1931.

Sprengelmeyer, R., Young, A. W., Calder, A. J., Karnat, A., Lange, H., Hömberg, V., et al. (1996). Loss of disgust: Perception of faces and emotions in Huntington's disease. *Brain, 119,* 1647-1665.

Sprengelmeyer, R., Young, A. W., Mahn, K., Schroeder, U., Woitalla, D., Buttner, T., et al. (2003). Facial expression recognition in people with medicated and unmedicated Parkinson's disease. *Neuropsychologia, 41,* 1047-1057.

Stefan, K., Gentner, R., Zeller, D., Dang, S., and Classen, J. (2008). Theta-burst stimulation: Remote physiological and local behavioural after-effects. *Neuroimage, 40,* 265-274.

Steven, M. S., and Blakemore, C. (2004). Visual synaesthesia in the blind. *Perception, 33,* 855-868.

Steven, M. S., Hansen, P. C., and Blakemore, C. (2006). Activation of color-selective areas of the visual cortex in a blind synesthete. *Cortex, 42,* 304-308.

Stewart, L., Ellison, A., Walsh, V., and Cowey, A. (2001). The role of transcranial magnetic stimulation in studies of vision, attention and language. *Acta Psychologica, 107*, 275-291.

Stewart, L., Mulvenna, C., Griffiths, T., and Ward, J. (in prep). Neural correlates of audio-visual synaesthesia induced from tone sequences.

Stewart, L., Walsh, V., Frith, U., and Rothwell, J. C. (2001). TMS produces two dissociable types of speech arrest. *Neuroimage, 13,* 472-478.

Sugiura, M., Watanabe, J., Maeda, Y., Matsue, Y., Fukuda, H., and Kawashima, R. (2005). Cortical mechanisms of visual self-recognition. *Neuroimage, 24,* 143-149.

Tang, J., Ward, J., and Butterworth, B. (2008). Number forms in the brain. *Journal of Cognitive Neuroscience, 20,* 1547-1556.

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

Taylor-Clarke, M., Kennett, S., and Haggard, P. (2004). Persistence of visual-tactile enhancement in humans. *Neuroscience Letters, 354,* 22-25.

Terao, Y., Fukuda, H., Ugawa, Y., Hikosaka, O., Furubayashi, T., Hanajima, R., Sakai, K., and Kanazawa, I. (1998). Visualization of the information through human oculomotor cortical regions by transcranial magnetic stimulation. *J Neurophysiol, 80*, 936-946.

Terao, Y., Ugawa, Y., Suzuki, M., Sakai, K., Hanajima, R., Gemba-Shimizu, K., and Kanazawa, I. (1997). Shortening of simple reaction time by peripheral electrical and submotor-threshold magnetic cortical stimulation. *Experimental Brain Research, 115,* 541-545.

Terhune, D. B. (2009). The incidence and determinants of visual phenomenology during out-of-body experiences. *Cortex, 45,* 236-242.

Thilo, K. V., Santoro, L., Walsh, V., and Blakemore, C. (2004). The site of saccadic suppression. *Nature Neuroscience, 7,* 13-14.

Treisman, A. (2004). In: L. Robertson and N. Sagiv, Editors, Synesthesia: Perspectives from Cognitive Neuroscience, Oxford University Press, Oxford (2004).

Tsakiris, M., and Haggard, P. (2005). The rubber hand illusion revisited: Visuotactile integration and self-attribution. *J Exp Psychol Hum Percept Perform., 31,* 80-91.

Tyrell, R. A., and Owens, D. A. (1988). A rapid technique to assess the resting states of eyes and other threshold phenomena: The modified binary search (MOBS). *Behav. Res. Methods Instrum. Comput., 20,* 137-141.

Uddin, L. Q., Iacoboni, M., Lange, C., and Keenan, J. P. (2007). The self and social cognition: The role of cortical midline structures and mirror neurons. *Trends in Cognitive Sciences, 11,* 153-157.

Uddin, L. Q., Kaplan, J. T., Molnar-Szakacs, I., Zaidel, E., and Iacoboni, M. (2005). Self-face recognition activates a frontoparietal "mirror" network in the right hemisphere: An event –related fMRI study. *Neuroimage, 25,* 926-935.

Uddin, L. Q., Molnar-Szakacs, I., Zaidel, E., and Iacoboni, M. (2006). rTMS to the right inferior parietal lobule disrupts self-other recognition. *Soc. Cogn. Affect. Neurosci., 1,* 65-71.

Ueno, T., Tashiro, T., and Harada, K. (1988). Localized stimulation of neural tissues in the brain by means of a paired configuration of time-varying magnetic fields. *J. Appl. Phys, 64,* 5862–5864.

Vallesi, A., Shallice, T., and Walsh, V. (2007). Role of the prefrontal cortex in the foreperiod effect: TMS evidence for dual mechanisms in temporal preparation. *Cerebral Cortex, 17,* 466-474.

Van Boven, R. W., and Johnson, K. (1994). A psychophysical study of the mechanisms of sensory recovery following nerve injury in humans. *Brain, 117,* 149-167.

Van Boven, R. W., Hamilton, R. H., Kauffman, T., Keenan, P., and Pascual-Leone, A. (2000). Tactile spatial resolution in blind Braille readers. *Neurology, 54,* 2230-2236.

van der Gaag, C., Minderaa, R. B., and Keysers, C. (2007). Facial expressions: What the mirror neuron system can and cannot tell us. *Social Neuroscience, 2*, 179-222.

Van Lacker, D., and Fromkin, V. A. (1973). Hemispheric specialization for pitch and tone: Evidence from Thai. *Journal of Phonetics, 1,* 101-109.

van Rijn, S., Aleman, A., van Diessen, E., Berckmoes, C., Vingerhoets, G., Kahn, R. S. (2005). What is said or how it is said makes a difference: Role of the right fronto-parietal operculum in emotional prosody as revealed by repetitive TMS. Eur J. Neurosci. *21*, 3195-3200.

Vega-Bermudez, F., and Johnsen, K. O. (1999). SA1 and RA receptive fields, response variability, and population response mapped with a probe array. *Journal of Neurophysiology, 81,* 2701-2710.

Wade, A. R., Brewer, A. A., Rieger, A. W., and Wandell, B. A. (2002). Functional measurements of human ventral occipital cortex: Retinotopy and colour. *Philos. Trans. R. Soc. Lond. B. Biol. Sci., 357,* 963-973.

Walsh, V., and Butler, S. R. (1996). Different ways of looking at seeing. *Behavioural Brain Research, 76,* 1-3.

Walsh, V., and Cowey, A. (2000). Transcranial magnetic stimulation and cognitive neuroscience. *Nature Reviews Neuroscience, 1*, 73-79.

Walsh, V., and Pascual-Leone, A. (2003). Transcranial Magnetic Stimulation: A neurochromometrics of mind, (MIT Press).

Walsh, V., and Rushworth, M. (1999). A primer of magnetic stimulation as a tool for neuropsychology. *Neuropsychologia, 37,* 125-135.

Ward, J. (2004). Emotionally mediated synaesthesia. *Cognitive Neuropsychology, 71,* 761-772.

Ward, J., Banissy, M. J., and Jonas, C. (2008). Haptic perception in synaesthesia. In *Human Haptic Perception: Basics and Applications*, Edited by M.Grunwald. Birkhäuser, Basel.

Ward, J., Huckstep, B., Tsakanikos, E. (2006). Sound-colour synaesthesia: To what extent does it use cross-modal mechanisms common to us all. *Cortex, 42,* 264-280.

Ward, J., Li, R., Salih, S., and Sagiv, N. (2007). Varieties of grapheme-colour synaesthesia: A new theory of phenomenological and behavioural differences. *Conscious Cogn., 16,* 913-931.

Ward, J., and Mattingley, J. B. (2006). Synaesthesia: An overview of contemporary findings and controversies. *Cortex, 42*, 129-136.

Ward, J., and Simner, J. (2003). Lexical-gustatory synaesthesia: Linguistic and conceptual factors. *Cognition, 89,* 237-261.

Ward, J., and Simner, J. (2005). Is synaesthesia an X-linked trait lethality in males? *Perception, 34,* 611-623.

Ward, J., Simner, J., and Auyeung, V. (2005). A comparison of lexical-gustatory and grapheme-colour synaesthesia. *Cognitive Neuropsychology, 22,* 28-41.

Warren, J. E., Sauter, D. A., Eisner, F., Wiland, J., Dresner, M. A., Wise, R. J. S., et al. (2006). Positive emotions preferentially engage an auditory-motor “mirror” system. *Journal of Neuroscience, 26,* 13067-13075.

Wassermann, E. M. (1998). Risk and safety of repetitive transcranial magnetic stimulation: Report and suggested guidelines from the International Workshop on the Safety of Repetitive Transcranial Magnetic Stimulation. *Electroencephalogr Clin Neurophysiol., 108,* 1-16.

Wassermann, E.M., McShane, L.M., Hallett, M., and Cohen, L.G. (1992). Noninvasive mapping of muscle representations in human motor cortex. *Electroencephalogr Clin Neurophysiol, 85*, 1-8.

Weiss, P. H., Shah, N. J., Toni, I., Zilles, K., and Fink, G. R. (2001). Associating colours with people: A case of chromatic-lexical synaesthesia. *Cortex, 37,* 750-753.

Weiss, P. H., Zilles, K., and Fink, G. R. (2005). When visual perception causes feelings: Enhanced cross-modal processing in grapheme-color synesthesia. *Neuroimage, 28,* 859-868.

Wheeler, R. H., and Cutsforth, T. D. (1921). The role of synaesthesia in learning. *J Exp Psychology, 4,* 448-468.

Wicker, B., Keysers, C., Plailly, J., Royet, J. P., Gallese, V., and Rizzolatti, G. (2003). Both of us disgusted in my insula: The common neural basis of seeing and feeling disgust. *Neuron, 40,* 655-664.

Wig, G., Grafton, S., Demos, K., and Kelley, W. (2005). Specificity of priming: a cognitive neuroscience perspective. *Nat. Neurosci. 8,* 1228 – 1234.

Wildgruber, D., Riecker, A., Hertrich, I., Erb, M., Grodd, W., Ethofer, T., et al. (2005). Identification of emotional intonation evaluated by fMRI. *Neuroimage, 24,* 1233-1241.

Winston, J., O'Doherty, J., and Dolan, R. (2003). Common and distinct neural during direct and incidental processing of multiple facial emotions. *Neuroimage, 20***,** 84-97.

Wittenberg, G. F., Werhahn, K. J., Wassermann, E. M., Herscovitch, P., and Cohen, L. G. (2004). Functional connectivity between somatosensory and visual cortex in early blind humans. *European Journal of Neuroscience, 20,* 1923-1927.

Witthoft, N., and Winawer, J. (2006). Synesthetic colors determined by having refrigerator magents in childhood. *Cortex, 42,* 175-183.

Yaro, C., and Ward, J. (2007). Searching for Shereshevski: What is superior about the memory of synaesthetes? *Quarterly Journal of Experimental Psychology, 60,* 681-695.

Appendix 1: Questionnaire used to recruit potential synaesthetes in Experiment 2.1 (Chapter 2).

PLEASE READ THIS FIRST

People with synaesthesia experience certain things (e.g. colours, tastes) when engaged in activities (e.g. reading) that would not elicit such a response in non-synaesthetic people. For instance, colours may be experienced in response to music or words, or shapes may be experienced in response to tastes. Synaesthesia is quite rare, but the questionnaire below asks whether you regularly have these types of experiences.

Everything you write will be treated in confidence, in accordance with the data protection act. You do not have to answer any questions if you feel uncomfortable about them. We may wish to contact a small number of people (by phone/e-mail/letter) to invite them to take part in a further study of memory and perception. None of the tasks are harmful or stressful. It would be helpful then, if you included contact details below, in case you are one of the people we would like to contact. You are in no way obliged to part in any further experiments. Your personal details (name, email, etc.) will not be passed on to anybody else.

Name: ____ Age: ____________

Profession/Degree Course: ______________________________ Year: ______________

Telephone number: _________________________ E-mail: __________________________

(1) Do you think about the letters of the alphabet (and/or words and numbers) as having specific colours (i.e. the letter A is experienced as red)?

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

If SO, Which ones? Letters Words Numbers

Other? _____________

(2) Do you think about the letters of the alphabet (and/or days of the week/months of the year/numbers) as being arranged in a specific pattern in space?

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

If SO, Which ones? Letters Days Months Numbers

Other? _____________

(3) Do you experience taste sensations when you observe another person eating or drinking something (i.e. observing someone eating strawberries and experiencing a sweet taste in your own mouth)?

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

(4) Do you experience touch sensations on your own body when you see them on another person's body?

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

(5) When experiencing touch to your own body do you experience visual sensations (i.e. colour)?

Strongly disagree Disagree Neither agree nor disagree Agree Strongly agree

(6) Do these experiences have specific locations (e.g. on your body, on words or objects in the environment, in front of your eyes) or not (e.g. they feel as if they are in 'your minds eye')? Please describe.

(7) To the best of your knowledge have you always had these sensations?

YES NO DON'T KNOW

If YES – at what age did you realise that other people did not have the same sensations as you?

If NO – at what age did they arise and was there a triggering incident?

(8) Do the sensations that you have to particular things change over time or are they fixed (e.g. if the word 'book' is green then is it always green and always has been)?

FIXED VARIABLE DON'T KNOW

(9) On the next page please match the triggers on the left with synaesthetic experiences on the right. For instance, if you experience colours in response to numbers then draw a line in between 'numbers' (left) and 'colours' (right).

IMPORTANT: Please do not connect the same things (e.g. colours–colours) as this is assumed true of everyone. We also assume (without you having to indicate) that letters/ words etc. as experienced as shapes on a written page, and musical instruments/ voices/ spoken words as noise. Moreover, if you have no synaesthetic experiences then there is no need to connect any triggers with experiences.

TRIGGERS
Letters of alphabet
English words
Foreign words
People’s names
Addresses/places
Numbers
Days of week
Months of year
Pains/touches
Music (instrumental)
Noises
Smells
Tastes
Colours
Shapes/Patterns

EXPERIENCES
Colours
Shapes/Patterns
Tastes
Smells
Pains/touches
Noises
Flashes
Music
Movements

Thanks for your time.