Face processing in typical and congenitally prosopagnosic adults: Behavioural and neuroimaging investigations

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This thesis is submitted in fulfillment of the requirements for the degree of

Doctor of Philosophy (PhD)

December 2010

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Thesis summary

Faces are crucial for human social interaction. For most people, recognizing familiar faces is seemingly effortless. However, people who suffer from *congenital prosopagnosia* (CP) never develop this skill. The current thesis consists of a series of five studies investigating the cognitive as well as neural aspects of both atypical (CP) and typical face processing.

In the first study, I adopted "covert" (implicit) face recognition tasks to characterize the exact nature of the cognitive impairment of a participant with CP, showing that "covert tasks" can represent a more sensitive assessment tool for this purpose than traditional "overt tasks".

In the second study, I demonstrated that covert recognition is a general feature of CP by assessing a group of eleven CPs with three behavioural tasks. Importantly, I showed that different behavioural tasks vary in the sensitivity of detecting covert recognition.

In a third study, by coupling Magnetoencephalography (MEG) with structural brain images (MRIs), I demonstrated that CPs show typical face-selective neuromagnetic activity within the right lateral occipital cortex (rLO) and fusiform gyrus (rFG). Crucially, I characterized the link between brain activity and behaviour, by examining the correlation between MEG activity and the performance on a series of face processing tasks.

In a fourth study, using functional Magnetic Resonance Imaging (fMRI), I demonstrated that the pattern of fMRI activity within the right anterior temporal lobe (rAT) differs between CPs and people with normal face processing skills.

Finally, in a fifth study, I investigated the spatio-temporal dynamics of typical face perception by coupling MEG recording with MRIs. I demonstrated that the human visual

system can categorize places just as rapidly as it categorizes faces, suggesting that early categorization of visual stimuli may be a more general phenomenon than so far assumed. Altogether, these five studies make a significant contribution to our current understanding of the cognitive as well as neural mechanisms underlying face processing difficulties in CP. In addition, they provide crucial insights into the temporal dynamics of typical visual processing.

Declaration

I certify that the work in this thesis entitled "**Face processing in typical and congenitally prosopagnosic adults: Behavioural and neuroimaging investigations**" has not previously been submitted for a degree nor has it been submitted as part of requirements for a degree to any other university or institution other than Macquarie University.

I also certify that the thesis is an original piece of research and it has been written by me. Any help and assistance that I have received in my research work and the preparation of the thesis itself have been appropriately acknowledged.

In addition, I certify that all information sources and literature used are indicated in the thesis. The research presented in this thesis was approved by Macquarie University Ethics Review Committee, reference number: **HE27JUL2007-D05347** on **2nd August 2007**.

Signed:

Davide Rivolta (Student Number:)

3rd December 2010

Acknowledgements

This thesis would not have been possible without my supervisors' constant help. Hence, I owe my deepest gratitude to: Prof. Max Coltheart, for the opportunity he gave me to initiate a PhD project very far from my home country and for the support he gave me during the entire duration of my candidature; Dr Romina Palermo, for the constant academic and psychological support, patience (being almost an "Italian mum") and constructive criticism; A/Prof. Mark Williams for successfully introducing me to the intriguing world of human neuroimaging and for the crucial support given during my candidature; Dr Laura Schmalzl for the precious and broad support provided during the last three years.

A special thanks goes to Isabella Premoli who, by sharing with me this Oz experience, gave me the strength to enterprise and complete this journey. Thanks to my parents who accepted their only son to be 16,000 km away from home for such a long time. I would not have been here today without the teaching and strong support that Dr Alessio Toraldo and Prof. Gabriella Bottini gave me during my undergraduate studies in Pavia. Further acknowledgment goes to Loes Koelewijn who provided essential assistance during the MEG data processing, Dr Graciela Tesan, Melanie Reid and Christopher Sewell for the help provided during MEG data acquisition, people from S. Vincent's Hospital for the technical support given during fMRI acquisition, Dr Anina Rich for providing constructive criticism on all my neuroimaging work, and to all people from MACCS who gave me insightful advice on my research.

I would like to thank everyone who has participated in my research, in particular all the participants with congenital prosopagnosia. I sincerely hope that the research

contained within this thesis will lead to an improved understanding, awareness and assessment of the condition.

Finally, I wish to thank Sydney. This lovely city with its beautiful nature provides an exceptional source of inspiration – no better place for a PhD!

Note

The published, under revision or submitted for publication manuscripts forming the thesis chapters are reported respecting the original submission format specific for each journal. The “Introduction” and “General discussion” sections follow the APA style (5th ed.).

[The Reverend Hugh Stretton, Anglican Minister of Hennacombe, Devon. England] "could meet you four times and still not recognize your face. It was this, a serious disability in a person, which accounted for the uncertain smile he would bestow on total strangers, ready to broaden if responded to, snatch back if not."

Carey, Peter (1988). *Oscar and Lucinda*. University of Queensland Press, St. Lucia, Queensland, Australia, 511 pp, p.47.

Chapter 1

General introduction and literature review

Chapter 1

Chapter 1

One of the most difficult scientific enterprises of all times is the understanding of the human mind and its relation with its hardware: The brain. Over the past decades, scientists from different disciplines such as psychology, cognitive science and neuroscience have joined efforts trying to understand the mind-brain relationship. One of the domains that has received a great deal of research attention over the past fifty years involves the investigation of the cognitive and neural aspects of face processing in humans. This is not surprising, given that faces are ubiquitous in our environment, and we rely on them during social interactions. The human face processing system is so well developed that just a brief glance of a face allows us to extract information about the identity, gender, age, mood, race, attractiveness and approachability of a person. This is remarkable, especially if we consider that all faces share the same general 3D structure and the same disposition of internal features (i.e. two eyes above a nose and a mouth).

In this introductory chapter I will briefly review some of the most important investigations of face processing, with particular emphasis on the topics that are relevant for the five research papers presented in this thesis. I will start by introducing a condition termed "prosopagnosia", which refers to a specific deficit in face recognition, with particular emphasis on the congenital form of the disorder, that is congenital prosopagnosia (CP). I will then provide more specific background information in relation to my research, by characterizing the features of behavioural covert (implicit) face recognition in CP, and by analyzing the neural aspects of visual cognition in typical subjects and in people with CP.

Acquired and congenital prosopagnosia

While many people can recognize thousands of faces without effort, individuals with "prosopagnosia" (from the Greek words "prosopon" which means *face,* and "a-

gnosis" with means *without knowledge*) have a specific impairment in recognizing other people by their faces (Bodamer, 1947). There are two known forms of prosopagnosia. *Acquired prosopagnosia* (AP) refers to the loss of previously intact face recognition abilities following brain damage due to stroke (Barton, 2008; Rossion, 2009), traumatic brain injury (Farah, Wilson, Drain, & Tanaka, 1995), degenerative conditions (Williams, Savage, & Halmagyi, 2006) or carbon monoxide poisoning (Sparr, Jay, Drislane, & Venna, 1991). In contrast, *developmental* (DP) or *congenital prosopagnosia* (CP) refers to a failure to develop normal face recognition abilities in the absence of any obvious sign of brain damage, and despite normal low level vision as well as intact sensory, intellectual and social functioning (i.e. absence of autistic traits) (Behrmann & Avidan, 2005; Behrmann, Avidan, Marotta, & Kimchi, 2005; Duchaine, 2000; Duchaine & Nakayama, 2006; Wilson, Palermo, Schmalzl, & Brock, In press). It is important to note here that the terms DP and CP have not always been used consistently in the literature. In particular, DP has been used to describe cases suffering from developmental brain diseases (i.e. cases who sustained brain damage before, during or immediately after birth) (Barton, Cherkasova, & O'Connor, 2001), as well as more generally, and interchangeably with CP, to describe face recognition difficulties occurring in the absence of any brain injury and in the context of intact sensory and intellectual functioning (Duchaine, Yovel, Butterworth, & Nakayama, 2006; Kress & Daum, 2003). Given that none of the prosopagnosic individuals described in the research studies of this thesis suffered from any kind of developmental brain disease or neurological condition (that I was aware of), the term CP will be used throughout to avoid any misunderstandings.

CP was believed to be a very rare condition (Kress & Daum, 2003), but recent studies suggest that the prevalence of the condition is as high as 2-3 % of the general

population (Bowles, et al., 2009; Kennerknecht, et al., 2006). This means that, in Australia alone, over half a million people may suffer from CP! Recent research has also demonstrated that CP runs in families (Lee, Duchaine, Wilson, & Nakayama, 2010; Schmalzl, Palermo, & Coltheart, 2008) thus suggesting a genetic contribution to the condition, possibly reflecting a simple autosomal dominant inheritance pattern of transmission (Grueter, et al., 2007).

In CP, the impairment can be restricted to the recognition of facial identity, with no impairment recognising other facial cues such as expression and eye gaze (Duchaine, Parker, & Nakayama, 2003; Duchaine, et al., 2006; Duchaine & Nakayama, 2006; Duchaine, Nieminen-von Wendt, New, & Kulomaki, 2003) or discriminating between other similar objects (Duchaine & Nakayama, 2005). However, in some cases face recognition impairments co-exist with more general difficulties discriminating between similar objects (Duchaine, Germine, & Nakayama, 2007; Wilson, et al., In press).

Even though the prevalence of CP is high, the condition may often be undetected for a variety of reasons. For example, manly people with CP might not be aware of their face recognition difficulties as they were born with the condition and thus have no means of comparison with normal face processing abilities. They may have also developed compensatory strategies for recognizing people in everyday life (e.g. by using non-facial cues such as voice, clothes, gait or hairstyle). In addition, since face processing difficulties might impact on social functioning, people with CP might sometimes be misdiagnosed as having behavioural problems or even autistic tendencies (Yardley, McDermott, Pisarski, Duchaine, & Nakayama, 2008). Given its developmental nature and its often-reported selectivity, CP represents a unique window into the understanding of the neuro-cognitive aspects of both atypical and typical face processing. The main aim of my PhD research was therefore to increase our current

knowledge of both the cognitive and neural mechanisms of typical face processing, by assessing face processing skills in both atypical (CPs) and typical (healthy control) participants. This was accomplished by means of both behavioural and neuroimaging techniques.

Covert face recognition in congenital prosopagnosia

There is evidence from both cognitive science and neuroscience research that brain damaged patients can show indices of covert or implicit processing of stimuli they can not overtly or explicitly recognize (Schacter, 1992). For example, some people with severe memory problems (i.e. amnesia) can show indices of implicit recollection of facts they can not consciously remember. Demonstrating this fact, the French neurologist Claparede (1873-1940) described a scenario in which he repeatedly put a pin in his hand before shaking hands with an amnesic patient. Despite the fact that the patient could not remember the doctor, this led to the patient becoming very reluctant to shake hands with the doctor every time he saw him (Faulkner & Foster, 2002).

Similarly, some people with brain lesions encompassing the primary visual area (V1) (i.e. blindsight) can detect, localize and even discriminate visual stimuli they do not consciously report (Cowey, 2010). These findings indicate that the human brain can process some information without conscious awareness. Recognition "without awareness" (De Haan, Young, & Newcombe, 1987) has received much attention in the context of face processing research, mostly being referred to as covert (or implicit) face recognition. The first reports of covert face recognition in prosopagnosia were studies of AP adopting both physiological and behavioural measures (see Schweinberger & Burton, 2003 for a review).

The most commonly adopted physiological technique used to assess covert face

recognition in AP is the measurement of autonomic activity through Skin Conductance Responses (SCRs). It has been demonstrated that some people with AP display larger SCRs for familiar than unfamiliar faces (Bauer, 1984; Tranel & Damasio, 1985). This presence of differential autonomic arousal in the absence of overt recognition of the familiar faces has been interpreted as an index of covert recognition. In terms of behavioural tasks used for the assessment of covert face recognition, one of the most frequently used tasks involves making a *forced choice*. In these tasks, participants have to guess which one of two simultaneously presented faces is famous, or which face corresponds to a given name cue. Using this task it has been shown that some prosopagnosic individuals, despite their inability to overtly discriminate familiar and unfamiliar faces apart, perform above chance if forced to guess which one of two simultaneously shown faces is famous, or which face corresponds to a given name cue (De Haan, et al., 1987; Sergent & Signoret, 1992; Young & Hellawell, 1988).

More recently researchers have begun to characterize covert face recognition in CP. Given that people with CP never develop a normal face recognition system, it is of considerable theoretical importance to determine whether covert recognition can be demonstrated in this population, and if so, the conditions under which it is present. Early case studies addressing this issue typically failed to demonstrate covert face recognition in CP (Bentin, Deouell, & Soroker, 1999; De Haan & Campbell, 1991), supporting the proposal that covert face recognition is only present when previously intact face representations have been damaged (as in AP), but not when face representations have never been formed (as is presumably the case in CP) (Barton, Cherkasova, & Hefter, 2004). More recent behavioural studies (Avidan & Behrmann, 2008; Bate, Haslam, Jansari, & Hodgson, 2009; Bate, Haslam, Tree, & Hodgson, 2008)

and physiological investigations (Jones & Tranel, 2001) have, however, demonstrated covert face recognition in CP.

Even though recent work has demonstrated the presence of covert face recognition in CP, many aspects remain to be explored. Hence, the first two studies of this thesis focus on behavioural covert face recognition in CP. The first of these is a case study of a CP, in which I investigated whether the assessment of covert face processing can actually provide a more sensitive tool compared to traditional overt assessment tasks, for pinpointing the locus of impairment within the face processing system in individuals with CP. This fact has potentially important clinical implications, since it may affect the way clinicians and researchers interested in the cognitive aspects of face processing assess patients with face recognition difficulties. In the second study, I assessed covert face recognition in a group of eleven individuals with CP. The aim of this study was to understand whether covert recognition represents a common feature of CP, and shed light on the conditions under which it is shown. The findings of this study have important theoretical implications for developmental models of face recognition and theories of covert face recognition in CP.

The neural aspects of face processing

Over the past twenty years, the development of non-invasive neuroimaging techniques has enabled researchers to investigate the neural correlates of cognitive processes both in terms of their time course (*when* they take place) and localization (*where* in the brain they occur). Magnetoencephalography (MEG) and Event Related Potentials (ERP) represent the two most commonly adopted techniques to investigate the time course of cognitive processing. MEG enables the measurement of minute neuro-magnetic fields generated by the brain while participants perform a given task.

Given its excellent temporal resolution (in the order of milliseconds), MEG represents a powerful tool to adopt when trying to answer *when* a cognitive process is performed in the brain. In addition, if MEG data analysis is coupled with structural brain images (MRIs), MEG also has good spatial resolution. Similarly to MEG, ERP has excellent temporal resolution, but because of the nature of the signal, the spatial resolution is not as good (Singh, 2006).

Both ERP and MEG have been extensively adopted in face processing investigations. It has been demonstrated that face perception generates specific physiological components that peak at around 100 ms and 170 ms post stimulus onset. The first component, known as P100 when measured using ERP (Debruille, Guillem & Renauls, 1998) or M100 when measured using MEG (Liu, Harris & Kanwisher, 2002) stems from the medial occipital cortex (Tanskanen, Nasanen, Montez, Pallysaho & Hari, 2004), and has bigger amplitude for faces than other categories of visual stimuli. The second component, known as the N170 when measured using ERP (Bentin et al., 1996) or M170 when measured using MEG (Liu, Higuchi, Marants & Kanwisher, 2000) stems from the occipito-temporal cortex, and has bigger amplitude for face than non-face (i.e. object) stimuli. Recent findings suggest that the N/M170, and not the N/M100, is involved in the recognition of familiar faces (Harris & Aguirre, 2008; Liu et al., 2002). Since some patients with AP fail to show a face selective N170 (Eimer & McCarthy, 1999), this component has been proposed to represent the physiological correlate of typical face processing.

A number of research studies conducted over the past ten years have focused on characterizing the neuro-physiological aspects of face processing in CP. Results are inconsistent, with some CPs showing a typical, face-selective, N170 and/or M170, and others failing to do so. The reasons for these inconsistent findings are not clear, since

none of the studies described any specific correlation between neurophysiological activity and behavioural performance on face processing tasks (Harris, Duchaine, & Nakayama, 2005; Minnebusch, Suchan, Ramon, & Daum, 2007). In the third study of this thesis I used MEG in a group study of CP to address this issue. In particular, I aimed to investigate (i) whether people with CP show a typical, face-selective, M170, and (ii) whether there is a correlation between MEG activity and performance on different behavioural face processing tasks (thus potentially accounting for the heterogeneity found in previous investigations). This investigation has the potential to provide crucial insights into the neuro-physiological features of CP and on the relation between neural activity (as measured by MEG) and behavioural face processing skills.

Despite MEG represents a very useful technique for the investigation of "when" something is happening in the brain, only functional Magnetic Resonance Imaging (fMRI) has the spatial resolution (in the order of millimeters) to enable the accurate localization of brain activity (Amaro & Barker, 2006). The use of fMRI has demonstrated that face processing is mediated by a network of cortical and subcortical brain regions. Haxby and colleagues (Haxby, Hoffman, & Gobbini, 2000) proposed an influential neural model of face processing that still represents a frame of reference for the research in the field. At the heart of their model is the proposal that most face processing functions are accomplished by the coordinated participation of multiple brain areas, such as the inferior occipital gyri, the lateral fusiform gyrus, the superior temporal sulcus, the amygdala and the anterior temporal cortex. According to the model, different structures have (at least partially) distinct functions. For example the most investigated region involved in face processing, the Fusiform Face Area (FFA) on the lateral fusiform gyrus, shows stronger activity for faces than other categories of visual stimuli (Kanwisher, McDermott, & Chun, 1997), and is involved in face

identification (Haxby et al., 2000; Rotshtein, Geng, Driver, & Dolan, 2007; Rotshtein, Henson, Treves, Driver, & Dolan, 2005). The critical role played by the fusiform gyrus (FG) (and FFA in particular) in face recognition is demonstrated by reports of AP following brain damage encompassing the FG (Barton et al., 2008).

Given the apparently crucial role played by the FG in face identification, much research has focused on the functional examination of this brain area in individuals with CP. While some early single case investigations of CP reported atypical activity within the FG (Bentin, DeGutis, D'Esposito, & Robertson, 2007; Hadjikhani & De Gelder, 2002), a number of group studies of CP found typical FG activation (Avidan & Behrmann, 2009; Avidan, Hasson, Malach, & Behrmann, 2005; Furl, Garrido, Dolan, Driver, & Duchaine, in press), suggesting that FG may be necessary, but not sufficient, for normal face processing.

In fact, the FG is not the only region involved in face processing. On the contrary, converging evidence from neuroimaging and lesion studies posits for the existence of a whole face processing network (Haxby, et al., 2000) involving also more anterior temporal regions (AT). The importance of these AT regions has been demonstrated both with fMRI studies in typical subjects (Kriegeskorte, Formisano, Sorger, & Goebel, 2007; Rajimehr, Young, & Tootell, 2009) as well as lesion studies with individuals with AP (Evans, Heggs, Antoun, & Hodges, 1995; Gainotti, 2007; Glosser, Salvucci, & Chiaravalloti, 2003; Williams, et al., 2006).

Despite the absence of any obvious signs of brain damage in CP, a few recent studies were able to detect some structural abnormalities in this population. For example, Thomas and colleagues (Thomas, et al., 2009) found that behavioural face recognition difficulties in CP were related to a reduction in the connectivity (as measured by white matter volume) between posterior and anterior temporal regions.

Importantly, the behavioural face recognition performance of CPs was also related to a volume reduction of the anterior temporal regions: The bigger the volume reduction, the worse the performance on face identification tasks (Behrmann, Avidan, Gao, & Black, 2007; Garrido, et al., 2009).

While these findings suggest the involvement of the AT in face processing, so far no study has directly attempted to investigate the functional characteristics of the AT in CP. Such an investigation would have the potential to uncover the biological substrate of CP. Thus, the fourth study of my thesis was aimed at the functional characterization of the AT in individuals with CP. This was achieved by adopting a novel fMRI analysis approach, that is Multi-Voxel Pattern Analysis (MVPA) (Cox & Savoy, 2003; Haynes & Rees, 2006; Norman, Polyn, Detre, & Haxby, 2006; Pereira, Mitchell, & Botvinick, 2009). So far, most fMRI studies of CP have employed more traditional "activation-based" analyses, focusing on comparing the Blood Oxygen Level Detection (BOLD) signal of various experimental conditions within selected regions of interest (ROIs) (Avidan et al., 2005; 2009; Furl et al., in press). These methods, despite having been widely adopted for face processing as well as other domains, have several known limitations. For example, the activation-based approach erroneously assumes the independence of all voxels, ignoring the functional link between them (O'Toole, et al., 2007). MVPA in contrasts takes this factor into account, making it a more sensitive tool for the analysis of fMRI data (Mur, Bandettini, & Kriegeskorte, 2009; Sapountzis, Schluppeck, Bowtell, & Peirce, 2010; Yoon, et al., 2008).

The temporal dynamics of place and face categorization

The fifth and last study of this thesis addresses the question of whether faces represent the only category of visual stimuli that evoke very rapid selective brain

responses, or whether other visual stimuli such as places (which, as explained below, share many similarities with faces) are processed according to similar temporal dynamics. Both places and faces are ubiquitous in our environment. Their fast and accurate recognition is crucial for everyday functioning. Places represent crucial reference points that we use to localize ourselves in space and navigate through our environment. Faces, on the other hand, represent the most important cue for the identification of other people, and allow us to infer their gender, attractiveness, mood, and approachability.

Research in cognitive neuroscience has shown that both places and faces represent *specific* categories of stimuli for the visual system. For example, studies using functional magnetic imaging resonance (fMRI) have shown that there are areas within the human brain that respond preferentially to places (parahippocampal place area [PPA] or faces (fusiform face area [FFA]) (Epstein & Kanwisher, 1998; Kanwisher, et al., 1997) compared to other categories of visual stimuli. Corroborating this fact, lesion studies have documented topographical agnosia (a specific impairment in navigating around familiar environments) (McCarthy, Evans, & Hodges, 1996) and AP (De Renzi, Faglioni, Grossi, & Nichelli, 1991) following brain injuries encompassing the PPA and FFA respectively.

Given the special "status" the human brain seems to attribute to both places and faces, much behavioural research has been devoted to the investigation of the temporal dynamics of brain activity related to the processing of both categories of stimuli. In her pioneering work, Mary Potter (Potter & Levy, 1969) described the rapidity with which our visual system processes places or scenes. By using a Rapid Visual Serial Presentation (RVSP) paradigm, characterized by the rapid and sequential presentation of visual stimuli, Potter (1976) showed that participants perform above chance when

asked to detect specific targets within scenes presented for 125 ms. More recently, and even more impressively, Thorpe and colleagues (Thorpe, Fize & Marlot, 1996) found that humans can accurately detect the presence of a target animal in a natural scene even when pictures are shown for as little as 20 ms in an RVSP paradigm.

Similar to places, faces are also processed very rapidly by our visual system. For example, using a two-alternative forced choice visual masking paradigm it has been shown that a faces can be detected in a visual scene when shown for only 20 ms (Purcell & Stewart, 1986, 1988). In addition, by using an RVSP paradigm, Grill-Spector and Kanwisher (2005) showed that object categorization (i.e. deciding whether a visual stimulus is a face, an animal or an object), occurs just as rapidly as the mere detection of an object within a visual field (even when stimuli were shown for only 17 ms). This suggests that object detection and categorization occur, at least to some extent, in parallel. In sum, much behavioural evidence suggests that places and faces are processed very rapidly by our visual system.

Recent investigations using MEG have documented the physiological correlates of rapid face processing. Specifically, it has been shown that faces elicit a category-specific MEG component around 100 ms post stimulus onset. This component, generating from the medial occipital lobes (Halgren, Raij, Marinkovic, Jousmaki, & Hari, 2000), reflects the categorization of a stimulus as a face rather than its identification. It has also been shown that place perception generates a category specific MEG component. This component, stemming from the parahippocampal cortex, occurs at around 200-300 ms post stimulus onset (Sato, et al., 1999). Such latency is surprising given the rapidity of place processing documented with behavioural studies.

The fifth study of this thesis aims to examine the existence of a place-selective MEG component occurring earlier than the one described in previous studies. In a

nutshell, it aims to pinpoint the neural correlates of the rapid place processing and categorization described in previous behavioural studies, an endeavour which has not been completely accomplished so far.

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Chapter 2

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Manuscript published in the

Journal of Clinical and Experimental Neuropsychology

The reference for this publication is:

Rivolta, D., Schmalzl, L., Coltheart, M., & Palermo, R. (2010). Semantic information can facilitate covert face recognition in congenital prosopagnosia. *Journal of Clinical and Experimental Neuropsychology, 32*(9), 1002-1016.

Chapter 2

Semantic information can facilitate covert face recognition in congenital prosopagnosia

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Abstract

People with congenital prosopagnosia have never developed the ability to accurately recognize faces. This single case investigation systematically investigates covert and overt face recognition in "C", a 69 year-old woman with congenital prosopagnosia. Specifically, we: 1) describe the first assessment of covert face recognition in CP using multiple tasks; 2) show that semantic information can contribute to covert recognition; 3) provide a theoretical explanation for the mechanisms underlying covert face recognition.

Keywords: congenital prosopagnosia, covert face recognition, name recognition, developmental prosopagnosia, models of face recognition, face recognition

Faces convey a wealth of information, such as identity, age, sex, mood, attractiveness, and race. It is therefore not surprising that faces are relied upon so much in social interactions. Particularly important is the ability to determine the identity of others from their face. A familiar face can often be recognised from a single glance, despite poor lighting conditions or different viewpoints. The ease with which we can discriminate between faces is remarkable, particularly given that all faces share the same three-dimensional structure and configuration of features (i.e., two eyes above a nose and a mouth).

Although most people are able to accurately and rapidly recognise many familiar faces, individuals with prosopagnosia find it difficult to recognise other people by their face. Individuals with acquired prosopagnosia (AP) have lost previously intact face processing skills following a brain injury or other neurological condition. In contrast, individuals with developmental or congenital prosopagnosia (CP) have not developed adequate face processing skills, despite intact sensory and intellectual functions (Behrmann & Avidan, 2005). Some individuals with CP show quite selective face recognition deficits, displaying a normal ability to encode other aspects of faces, such as expression and eye (Duchaine, Parker & Nakayama, 2003; Duchaine, Jenkins, Germine & Calder, 2009; Duchaine, Nieminen-von Wendt, New & Kulomaki, 2003) and recognise objects (Duchaine & Nakayama, 2005).

In order to compensate for their poor face recognition, people with CP often report that they rely on cues such as clothing, hairstyle, voice and gait for person identification. The prevalence of CP has been estimated to be as high as 2.5% of the general population (Bowles et al., 2009; Kennerknecht et al., 2006).

In addition, there is evidence for a genetic contribution to CP

(Schmalzl, Palermo & Coltheart, 2008), possibly reflecting a simple autosomal dominant inheritance pattern (Grueter et al., 2007).

By definition, people with AP have impaired face recognition as measured by overt or explicit tasks (e.g., when presented with famous and personally familiar faces they are unable to provide their names or any identifying information). Despite this, studies have shown that some people with AP can "recognise" faces when tested with tasks that do not require overt recognition. This partly spared face recognition ability is known as covert face recognition. Covert recognition in AP has most often been investigated with behavioural tasks, in which covert recognition is indexed by a change in performance as a function of the individual's familiarity with the presented faces, on tasks that do not require direct recognition as such (Sergent & Poncet, 1990).

Many behavioural tasks have been used to assess covert face recognition in AP (see Schweinberger & Burton, 2003 for a review). Barton, Cherkasova and Hefter (2004) proposed that these behavioural tasks could be classified into direct and indirect tasks. In direct tasks, participants are asked to make identity related decisions that directly involve the presented faces. For instance, in forced-choice cued tasks patients are shown a pair of faces and asked to match a name cue to the correct face. Similarly, in forced-choice familiarity tasks patients are shown a pair of faces (one famous and one unfamiliar) and are asked to select the famous face. In contrast, in indirect tasks, identity related decisions are measured by performance on another task. One of the most common indirect tasks is the semantic priming task, in which participants are asked to categorize target names as familiar or unfamiliar after viewing faces. It has been shown that participants are able to categorise the name more quickly when the target name (e.g., "Prince Charles") is preceded by a closely related prime face (e.g., Lady Diana) than when the face is unrelated (e.g., Elvis Presley) (Young & Hellawell, 1988b).

Covert recognition in AP has been assessed with both direct and indirect tasks, and while some individuals with AP fail to show covert recognition (Riddoch, Johnston, Bracewell, Boutsen & Humphreys, 2008; Sergent & Signoret, 1992), others show covert recognition on some, but not all, tasks (Barton, Cherkasova & O'Connor, 2001; Barton et al., 2004; De Haan, Young & Newcombe, 1992; Sergent et al., 1992; Young & DeHaan, 1988a).

For example, patient PH demonstrated covert recognition when tested with a semantic priming (indirect) task but not on a forced-choice familiarity (direct) task (Young et al., 1988b). In contrast, patient 008 displayed covert recognition on a forced-choice cued (direct) task but did not show covert recognition with either semantic priming (indirect) or forced-choice familiarity (direct) tasks (Barton et al., 2001; 2004). These studies, where participants have been assessed with more than one type of task, are of particular interest because they suggest that different tasks can tap into different aspects of covert recognition.

Studies using multiple tasks to assess covert recognition also suggest that names play an important role in the genesis of covert face recognition in AP. For example, Barton and colleagues (2001) assessed covert recognition in five participants and found that they all displayed covert recognition in a direct task in which a name was included as a cue (forced-choice cued task) but not in a direct task that did not involve names (forced-choice familiarity task). In sum, the literature on AP suggests that a full assessment of covert recognition in prosopagnosia should include multiple tasks, with one of these tasks involving names as a cue.

However, the few studies assessing covert recognition in CP have either focussed on one task, or not included tasks with name cues. For instance, Case AB assessed by DeHaan and Campbell (1991) did not show covert recognition when tested with a

forced-choice familiarity (direct) task, a matching (both direct and indirect) task or a semantic priming (indirect) task (also seeBentin, Deouell & Soroker, 1999 for a case of CP with absent covert recognition).

However, AB was not tested with the task that most consistently reveals covert recognition in AP - the forced-choice cued task (Barton et al., 2001; 2004). Thus, it's possible that AB may have shown covert face recognition when cued with names. More recently, Avidan and Behrmann (2008) examined covert recognition in six adults with CP with a sequential face-matching task. In their task, faces were either familiar or unfamiliar, and subjects were asked to decide whether two consecutive images were the same person or not. The authors referred to this task as being both direct (i.e., participants made their judgments directly on the faces, rather than on other dimensions such as names or occupations) and indirect (i.e., it was expected that participants would be quicker matching familiar than unfamiliar faces, even though the familiarity was orthogonal to the task). Like controls, the group of CPs was quicker at matching familiar than unfamiliar faces, even when they failed to overtly recognise them. This is the only study to reveal covert recognition in congenital prosopagnosia using a purely behavioural technique. However, participants' familiarity with the famous faces was assessed before the matching task, and even if in one of the task conditions (i.e. Different picture-Same identity) two different pictures of the same famous faces were shown, only one of these two pictures was used to test the level of overt recognition (in the famous faces questionnaire), making it difficult to know whether the famous faces were not able to be overtly recognized.

In addition to Avidan and Behrmann's (2008) study, two further studies have documented covert recognition in individual cases of CP using physiological and visual scan path techniques rather than traditional behavioural methods. In the first of these

studies, Jones and Tranel (2001) showed that skin conductance responses (SCRs) were greater in a 5 year-old child with CP when he viewed familiar, as compared to unfamiliar faces. In the second study, Bate, Haslam, Tree, and Hodgson (2008) showed that AA, an adult with CP, showed different visual scan paths for familiar compared to unfamiliar faces (e.g., a higher number of fixations, a higher number of sampled face regions, a higher number of fixations made before returning to a previously-sampled region). This was the case even though AA failed to overtly recognise these faces as familiar. We would like to note here that while there appears to be a correlation between the extent of residual overt recognition abilities and the presence of covert recognition as measured with behavioural tasks (suggesting that both mechanisms may be mediated by common cognitive systems), the relationship between overt recognition and covert recognition indexed by physiological measures is less clear (for a discussion see Schweinberger & Burton, 2003).

In sum, three studies using different techniques have shown evidence for covert face recognition in CP. These studies certainly deserve special attention, as the mere fact that covert recognition has been documented in CP is intriguing and somewhat puzzling. In contrast to AP, covert recognition in CP cannot simply be explained by postulating the presence of underlying "residual" overt face recognition mechanisms, because people with CP presumably have never developed normal overt face recognition skills in the first place. However, a weak point of previous behavioural investigations of covert recognition in CP is that they have either employed only one task (Avidan & Behrmann, 2008; Bate et al., 2008) or those using more than one task have failed to use tasks involving name cues (De Haan & Campbell, 1991). Given the dissociations between tasks documented in the AP literature, we believe that it is crucial to include at least three types of tasks when assessing behavioural covert recognition in

CP: one direct task involving names (e.g., a forced-choice cued task), one direct task that does not involve names (e.g., a forced-choice familiarity task), and an indirect task (e.g., a priming task). Thus, in the present study we describe the first assessment of behavioural covert face recognition in CP using multiple direct and indirect tasks, including one that involves name cues.

THE PRESENT STUDY

We report a single case investigation aimed at contributing to our current understanding of covert recognition in CP. Our study differs from previous research in three main ways. First, we conducted a thorough behavioural assessment of covert recognition in CP using both direct and indirect tasks and crucially, included a direct task involving names. Second, we interpret the assessment results within Bruce and Young's (1986) model of face recognition, providing a theoretical explanation for the mechanisms underlying covert recognition in CP as assessed with each of the administered tasks. Third, this study demonstrates how covert recognition tasks can not only be used to uncover partially preserved face recognition abilities, but can also be used as an assessment tool to assist in the localization of the impairment within the face recognition system.

We used Bruce and Young's (1986) model of face recognition as a frame of reference for the assessment of overt, as well as covert, face processing. In a nutshell, this model proposes that face recognition occurs in four main sequential stages (Figure 1).

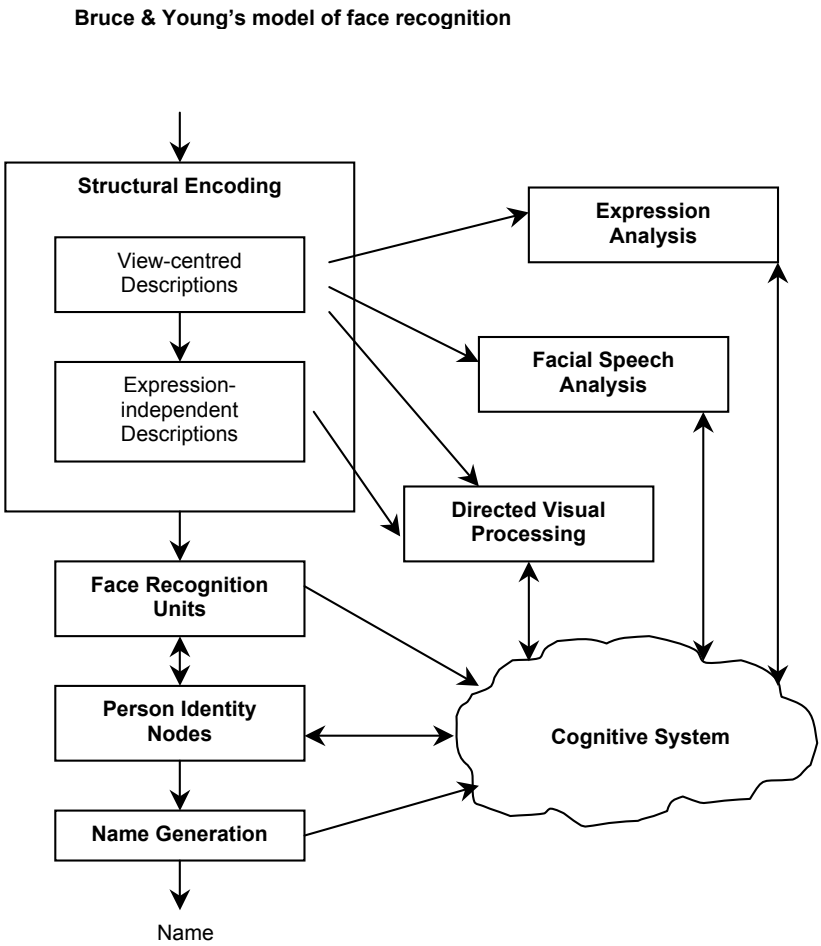

Figure 1. Bruce & Young (1986) model of face recognition.

For instance, when we see the face of Barack Obama, an initial representation of the face is formed through the Structural Encoding stage. In a second stage of processing, representations of familiar faces are accessed within the Face Recognition Units (FRUs), allowing a sense of familiarity for Barack Obama's face to be reached. Subsequently, semantic (biographical) information is accessed through the Person Identity Nodes (PINs) (e.g., the current president of the USA). Finally, the Name Retrieval stage allows the name "Barack Obama" to be retrieved. The model also proposes that additional types of information that can be extracted from faces, such as facial expressions or lip-speech, are processed in (at least partly) independent systems.

However, for the purpose of the current investigation we will limit our focus on the aspects of the model underlying the recognition of facial identity.

We began by conducting a neuropsychological assessment to confirm intact intellectual and sensory function in case "C". Subsequent tests confirmed C's poor overt face recognition and confirmed that she is a CP. We also demonstrated that C was able to provide semantic information about faces from names (indicating intact PINs) and retrieve the names of faces she could recognise (indicating intact name generation). Given that C showed no impairment retrieving semantic information or names, we then examined her face perception skills in more detail. Impaired face perception would suggest a deficit of structural encoding. Finally, we examined covert face recognition on three sensitive behavioural tasks.

CASE HISTORY

C is a 69 year-old woman with a life long history of face recognition difficulties. Her face recognition impairments were formally diagnosed in a study by Schmalzl et al. (2008), which also revealed significant face recognition impairments in several members of C's extended family. Thus, given the family history and the absence of any brain injury or other neurological condition, C's prosopagnosia is likely to be genetic in origin. C reported that it had always been difficult for her to recognise faces but that she was not aware of prosopagnosia being a "condition" until taking part in research. In fact, she said that finding out about it was a relief, as it provided her with an explanation for many of the difficulties she had been experiencing for years. C noted that she first became aware of her difficulties in school, where she found herself having trouble recognising most of her classmates except from a few very close friends that she would spend a lot of time with on a daily basis. Now she especially notices her difficulties in

church, where she organizes events in collaboration with people that she is unable to recognise from one week to the next. C's face recognition difficulties have had an impact on her life, as since her teenage years she has avoided social situations involving a large number of people because they are a source of embarrassment and frustration. We note with interest that C also described being unable to "get" the whole face, and a necessity to focus on "single bits at the time". For example, she said that she could recognise one of her daughters easier than the other because of her almond shaped eyes.

NEUROPSYCHOLOGICAL AND VISUAL PROCESSING ASSESSMENTS

C was initially assessed with an extensive battery of tasks assessing her general neuropsychological profile, lower level visual processing, early visual analysis and basic level object processing.

General neuropsychological profile

A neuropsychological assessment revealed intact general intellectual functioning. On the Wechsler Adult Intelligence Scale - Third Edition (WAIS-III) (Wechsler, 1998), C obtained a Full Scale IQ of 105 with no significant difference between her verbal (VIQ: 108) and nonverbal (PIQ: 101) skills. No difficulties were observed in terms of working memory, verbal fluency, problem solving and processing speed. On the Wechsler Memory Scale – Third Edition (WMS-III) (Wechsler, 1997), C showed a selective impairment for immediate recall of faces (Scaled Score: 5), placing her performance below the 5th percentile. In contrast, her memory for other types of visual (e.g., geometric figures, scenes) and verbal (e.g., single words, short stories) information was well within normal limits.

Lower level vision, early visual analysis and basic level object processing.

C showed normal contrast sensitivity as measured by the FACT (Vision Sciences Research Corporation, 2002). C also performed well within normal limits on all subtests of the Birmingham Object Recognition Battery (BORB) (Riddoch & Humphreys, 1993) (Table 1). Thus, there was no indication of any difficulties with early visual analysis or with basic level structural encoding, semantic knowledge and naming of objects.

Basic configural processing

Basic configural processing, i.e., processing of the relations between the global shape and local elements of visual stimuli, was assessed with a "global-local task". Stimuli were compound geometric figures in which the shape of the local elements was either congruent or incongruent with that of the global shape (i.e., large circles and squares composed of either small circles or squares). In two separate blocks of 40 trials, C was asked to identify the geometric shapes either at a global or local level. In each block, half the stimuli were congruent and half incongruent. C's performance was compared to that of five age-matched controls (60-67 years, M = 63.01 years) using SINGLIMS, statistics designed to compare individual test data with a small control group (Crawford & Garthwaite, 2002). C was 100% accurate and like controls, she was quicker for global as compared to local judgments (Table 2). Our results are in line with those of (Duchaine, Yovel & Nakayama, 2007) who have argued that CPs do not show global-local deficits (but see Behrmann, Avidan, Marotta & Kimchi, 2005).

Table 1. C's performance on selected subtests of the Birmingham Object Recognition Battery (BORB) (Riddoch & Humphreys, 1993). Displayed are C's raw scores for each subtest, as well as her performance expressed in standard deviations (SD) with reference to normative data.

BORB subtets	C	SD
Length match	30/30	+1.93
Size match	27/30	-0.12
Orientation match	27/30	+0.84
Position of gap	36/40	+0.22
Minimal feature view	25/25	+1.00
Foreshortened view	25/25	+1.30
Object decision	28/32	-0.90
Item match	32/32	+0.90
Associative match	30/30	+1.04
Picture naming	76/76	+1.78
Copying	OK	
Drawing from memory	OK	

Table 2. C.'s performance on face perception test. SINGLIMS *p* values for comparison with controls, and Wilcoxon test *p* values for within-subject and within-control group comparisons. *One-tailed sig *p* values **Two-tailed sig *p* values. Note: No SINGLIMS *p* values could be calculated for tasks in which there was no variability in the control group.

General face processing assessment tasks	C % accuracy	Control mean % accuracy	SINGLIMS p=	C RT	Control mean RT	SINGLIMS p=
Global local task						
Global congruent	100.00	100.00	no p value	646.56	555.02	0.19
Global incongruent	100.00	99.00	0.42	642.10	580.45	0.27
Local congruent	100.00	100.00	no p value	810.16	695.64	0.10
Local incongruent	100.00	100.00	no p value	910.00	746.56	0.12
Wilcoxon t test p=						
Global vs. local	1.00	0.32		0.00**	0.04**	
Face detection	100.00	100.00	no p value	1125.69	873.54	0.21
Composite faces						
Intact	89.58	90.42	0.48	2285.02	3655.78	0.06
Misaligned	89.58	96.25	0.25	2485.31	2516.27	0.49
Wilcoxon test p=						
Intact vs. misaligned	1.00	0.11		0.60	0.04**	
Jane task						
Upright						
Spacing	60.00	85.33	0.05*	2820.59	3082.26	0.47
Feature	90.00	98.00	0.09	2730.50	2624.93	0.34
Contour	73.33	86.00	0.27	4426.95	3858.24	0.23
Inverted						
Spacing	46.67	64.67	0.07	3169.93	5109.02	0.06
Feature	93.33	95.33	0.38	2200.93	3528.28	0.17
Contour	71.33	85.33	0.05	3936.13	3823.66	0.21
Wilcoxon test p=						
Spacing upright vs. inverted	0.41	0.04**		0.28	0.04**	
Feature upright vs. inverted	0.56	0.10		0.08	0.14	
Contour upright vs. inverted	0.16	0.78		0.47	0.89	
Different viewpoint match	95.00	95.33	0.35	4701.39	3844.19	0.20

Chapter 2

OVERT FACE RECOGNITION AND LEARNING

C initially completed three tasks to confirm that her overt face recognition was impaired. Control participants also completed the latter two tasks. None of the control subjects had a history of head injury or any other neurological condition, and all had normal low-level vision as measured by the FACT. We also examined whether C was able to provide semantic information from names (indicating intact PINs) and whether she was able to retrieve the names of faces that she could overtly recognise (indicating intact name retrieval).

Recognition of personally familiar faces

C was shown a set of 40 greyscale photographs that were presented in a random order on a computer screen. Half of the photographs were of personally familiar faces (i.e., members of her extended family and close friends) and half of unfamiliar faces (matched to the familiar faces for sex, approximate age and similarity in terms of visual characteristics of the face - e.g., bushy eyebrows, a pointy nose, narrow lips etc.). The photographs were edited using Adobe Photoshop editing software to remove the hair so that this could not be used as a cue. The task was programmed with PsyScript (Bates & D'Oliviero, 2003) and presented on a 15-inch Macintosh Power Book G4. Upon seeing each photograph, C initially indicated whether each face was familiar to her or not, and then for each face she had classified as familiar she was asked to provide the name.

C correctly identified only 60% (12/20) of the familiar faces and also mistakenly stated that 15% (3/20) of the unfamiliar faces were familiar. In contrast, some other members of C's family performed at ceiling on this task (see Schmalzl et al., 2008). This low level of performance reflects the face recognition difficulties C reportedly experiences in everyday life.

To ensure that C was familiar with all people whose faces were presented, she was subsequently shown each name and asked to indicate her relation to them (e.g., mother, grandmother, friend, neighbour), their approximate age and their profession (or school activities for children). She had no difficulty retrieving personal information about any of the familiar people, suggesting intact PINs. C was also asked to retrieve the name of familiar people, provided with a description of their relation to her (e.g., "your grandson", "your neighbour" etc.). She had no difficulties on this task, suggesting her ability to retrieve names was intact.

Recognition of famous faces

In order to assess C's ability to recognise the faces of famous people, 40 coloured photographs of famous faces were sourced from the Internet. The famous individuals (23 male and 17 female) were selected from a range of professions (e.g., politicians, actors, athletes and musicians) and were selected to be familiar to an Australian participant pool. All images were chosen to be front views, and to display (as far as possible) neutral expressions. The images were edited using Photoshop to remove all hair, jewellery and clothing.

C was shown one face at the time and was asked to type either the person's name or some other identifying information, such as "Julia Roberts" or "American actress starring in Pretty Woman" (responses that were not specific enough to ensure identification, e.g., "actress" were not considered correct). There was no time limit. Immediately after typing each response, C was provided with feedback about the correct identity of the face and asked to indicate whether she: a) Had correctly identified the face; b) Had not correctly identified the face but did know the person; c) Had not correctly identified the face and did not know the person. Four practice trials were

initially completed to ensure that she understood the format of the task and were not considered in the analysis. The task was programmed with SuperLab (Cedrus Corporation, 2007).

C's performance was compared to that of five age-matched controls using SINGLIMS. Of the 36 faces included in the experiment, 3 (8.3%) were categorised as response "c" (not identified because the famous person was unknown to C) and were excluded from further analysis. Thus, all subsequent analyses were based on the 33 remaining faces. C correctly identified only 17 (51.5%) of the 33 known faces (response "a", e.g., a "hit"), which was significantly lower than controls ($M = 90.2\%$, $t = -8.37$, $p < .001$). Of the 16 (48.5%) faces that she failed to overtly recognise (response "b", e.g., a "miss"), a small proportion (3 or 6.2%) were misidentified as another famous person (e.g., a "false-alarm") whereas for the others she noted a sense of familiarity for the face (e.g., "I know I have seen this person before but I can't place her"), suggesting at least partial FRU activation.

C was presented with the names of these famous faces and was able to retrieve semantic information about the individuals (e.g., occupations, movie roles), again suggesting intact PINs. C also always retrieved the correct name of the famous faces that she was able to identify, indicating intact name generation.

New learning and memory for unfamiliar faces - Cambridge Face Memory Test (CFMT) (Duchaine & Nakayama, 2006)

The CFMT is a test of new learning and immediate memory for unfamiliar faces. It consists of three phases with increasing difficulty: a) Introduction phase: Recognition of six previously memorized target face images amongst distractors, b) Recognition of novel images: Recognition of images of the six target faces presented from a different

viewpoint or with different lighting, c) Recognition of novel images with noise: Recognition of images of the six target faces presented with different levels of Gaussian noise. C and controls were administered the CFMT twice, initially with all the faces being presented upright and then with all the faces inverted. C's performance was compared to that of the same controls who completed the Famous Face Task, using SINGLIMS. A Wilcoxon test was also used to compare upright to inverted performance.

In the upright version, C performed significantly worse than controls in all three phases and overall (see Table 2). However, when the faces were shown inverted C's performance was within the range of controls for all phases. Moreover, while controls showed a typical inversion effect (a significant drop in accuracy for inverted compared to upright faces), C did not (see Table 3).

Table 3. Performance on the Cambridge Face Memory Test (CFMT – Duchaine & Nakayama, 2006). SINGLIMS *p* values for comparison with controls, and Wilcoxon test *p* values for within-subject and within-control group comparisons. **Two-tailed sig *p* values.

CFMT	C	Control mean	t-values	SINGLIMS
Upright				
Introduction	77.78	98.89	-7.74	0.00**
Novel images	53.33	85.33	-4.49	0.01**
Novel images with noise	33.33	79.17	-4.28	0.01**
Total	52.78	86.66	-6.10	0.00**
Inverted				
Introduction	72.22	81.11	-0.58	0.30
Novel images	46.67	53.33	-0.58	0.30
Novel images with noise	50.00	44.17	0.43	0.34
Total	54.17	57.78	-0.37	0.37
Inversion effect (upright VS inverted)	**C**	**Control mean**	**Wilcoxon p values**	
Introduction	0.74	17.78	0.04**	
Novel images	0.56	32.00	0.04**	
Novel images with noise	0.21	35.00	0.04**	
Total	0.86	28.89	0.04**	

Summary

C performed poorly on all three overt face recognition tasks, demonstrating that she is poor at recognising both personally familiar and famous faces and at learning and remembering newly seen faces. The formal cognitive neuropsychological assessment confirmed the face recognition difficulties that C reportedly experiences in everyday life. Given her neuropsychological profile, C's deficit for faces appears to be relatively selective, manifesting in the context of general intellectual functioning as well as normal low level vision, basic configural processing and basic level object recognition. C was also able retrieve semantic information from names and was able to generate names from semantic information, suggesting intact PINs and name generation.

FACE PERCEPTION ASSESSMENT

Having confirmed C's poor overt face recognition, we investigated her face perception skills in more detail. We started by confirming that she was able to discriminate a face from a scrambled face. We then assessed her ability to encode featural and configural/holistic information from faces to form face representations in the structural encoding stage. We also investigated how well C matched faces from different viewpoints. For all these tasks, C's performance was compared to five age matched controls, (59-66 years, M = 62.65 years, 3 females). Stimuli were edited using Adobe Photoshop editing software, and tasks were administered using a 15-inch Macintosh Power Book G4. All tasks were programmed with PsyScript software (Bates & D'Oliviero, 2003). Participants were placed at a distance of approximately 50 cm from the computer screen and gave their responses by pressing the relevant keys on the keyboard. Both accuracy and reaction times (RT) were recorded.

C's performance was compared to the performance of controls using SINGLIMS and within subject (and within control group) comparisons were performed using Wilcoxon tests, McNemar's tests or Cochran's Q tests. For RT data, only correct responses were included in the analyses. In addition, for each participant, RT greater or less than two standard deviations from the mean were excluded as outliers. RT were also log transformed, a normalizing transformation suggested for the use of RT data in SINGLIMS statistics.

Face detection

Face detection based on sensitivity to first order relations (i.e., two eyes, above a nose and a mouth) was assessed with a "Mooney Faces Task" [1] (Mondloch, Le Grand & Maurer, 2003). C was presented with 40 pictures of faces in which the perception of local features had been degraded by transforming all luminance values to black or white, as well as 40 scrambled versions of the same pictures (Figure 2a). The stimuli were presented in pairs (i.e., each Mooney face with its scrambled version), and C had to indicate which of the two stimuli looked more like a face than the other. C's performance was within the range of controls for both accuracy and RT (Table 2), indicating intact sensitivity to first order relations.

Holistic processing

A characteristic of face processing is that upright faces are processed more holistically (i.e., as a whole gestalt) whereas other types of objects are processed in a

[1] Stimuli for the Mooney Faces Task, the Composite faces task and the Jane Task were provided by the McMaster Vision Lab. For a detailed description of the stimuli see Mondloch, Le Grand & Maurer (2003), Le Grand et al. (2004) and Mondloch, Le Grand & Maurer (2002) respectively.

more part-based manner (Farah, Tanaka & Drain, 1995). Deficits in holistic face processing have also been found to be associated with face recognition impairments (Le Grand, Mondloch, Maurer & Brent, 2004). In order to assess C's ability to process faces holistically we used the "Composite Faces Task" (Le Grand et al., 2004). C was shown 96 pairs of composite faces composed of the top and bottom halves of different faces. For 48 of the pairs the composites were properly aligned, whereas for the other half they were misaligned with the bottom half shifted horizontally to the right (Figure 2b).

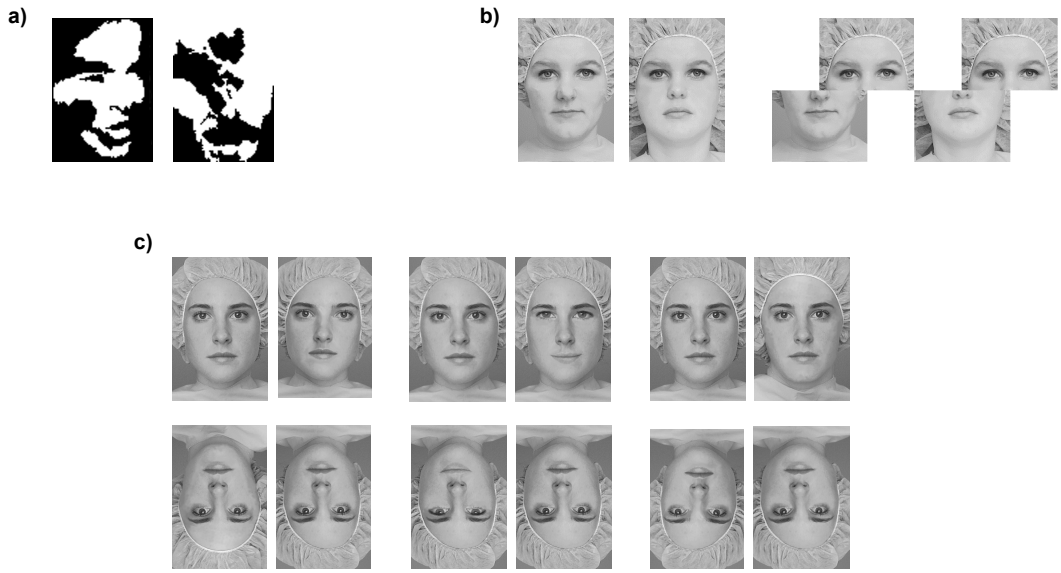

Figure 2. a) Mooney faces; b) Composite faces; c) Jane task stimuli (spacing, feature and contour condition). Stimuli were provided by the McMaster Vision Lab.

The intact and misaligned conditions were blocked, with the intact condition presented first. In both conditions, C had to make same/different judgments about the top halves of two simultaneously presented composites. The "composite effect" refers to reduced performance when the composites are intact (and holistic processing interferes with the processing of individual features) compared to when they are misaligned (a manipulation that disrupts holistic processing). Consistent with previous reports on normal adults (Le Grand et al., 2004), all controls showed a composite effect

(Table 3) [2]. In contrast, C failed to show this effect, suggesting impaired holistic processing.

Detection of spacing, feature and contour changes

Since all faces share the same basic configuration of features (i.e., two eyes above a nose and a mouth), the recognition of individual faces may rely on the ability to process subtle differences in the spacing and shape of these features. In order to assess C's sensitivity to spacing, feature and contour changes in visually presented faces we used the "Jane Task"(Mondloch et al., 2003). C was presented with three sets of face stimuli created from a picture of a female face. In the spacing condition, faces differed in the spacing of their internal features, i.e., features were either moved in/out (eyes) or up/down (eyes and mouth) relative to the original picture. In the feature condition, the eyes, nose and mouth of the original face were replaced with features from a different face. In the contour condition, the internal portion of the original face was combined with the outer contour of a different face (Figure 2c). C was asked to make same/different judgments for a total of 90 pairs of simultaneously presented faces (30 pairs for each condition) [3]. The three conditions were blocked, with C being presented

[2] Whereas in previous studies the Composite Faces Task has mostly been presented as a sequential matching task (i.e., for each pair of composite faces subjects were presented with one stimulus after the other in a rapid sequence), in our study the task was presented as a paired matching task (i.e., the composites of each pair were presented simultaneously). Due to the reduced difficulty of a paired matching vs. sequential matching task, we observed a composite effect only in reaction time (whereas previous studies have reported composite effects for both accuracy and reaction time).

[3] As for the Composite Faces Task, the Jane task has mostly been presented as a sequential matching task in previous studies (i.e., for each pair of faces subjects were presented with one stimulus after the other in a rapid sequence), whereas in our study it was presented as a paired matching task (i.e., the stimuli of each pair were presented simultaneously).

first with the "spacing", then the "feature", and lastly the "contour" set. C's accuracy was significantly lower compared to controls for the detection of spacing changes, but not for the detection of feature or contour changes. C's RT were within the range of controls for all conditions (Table 3).

Sensitivity to second-order relations – face inversion effect

Sensitivity to second-order relations was assessed with the inverted version of the Jane Task. Materials and methods were the same as for the upright Jane Task, the only difference being that the face stimuli were presented upside down (Figure 2c). Previous studies with these stimuli have shown that normal adults typically show a "face inversion effect", with reduced performance, predominantly in the spacing condition, when faces are inverted, a manipulation that disrupts the sensitivity to second-order relations. Consistent with these previous findings, in the spacing condition all controls performed significantly worse with inverted compared to upright faces for both accuracy and RT (Table 3). In contrast, C failed to show a significant face inversion effect, indicating a reduced sensitivity to second-order relations (Table 3).

Different viewpoint match

C's ability to identify faces from different orientations was assessed with a simultaneous matching task in which C was presented with front-on views of a face and asked to match them to one of of three simultaneously presented faces, which were either front-on views, faces rotated in depth by 45 degrees, or profiles. There were 20 items in each condition, for a total of 60 trials. C's performance on this task was within the range of controls for both accuracy and RT (Table 3).

Summary

C was able to judge whether a stimulus was a face or not, as assessed by the Mooney Faces Task. Given her intact low-level visual skills, this was expected (however, it is possible that C might have difficulty detecting faces when more sensitive tasks are used, see Garrido, Duchaine & Nakayama, 2008). In contrast, C displayed impairments on encoding configural/holistic information that is important for face recognition (e.g., Maurer, Le Grand & Mondloch, 2002; Rotshtein, Geng, Driver & Dolan, 2007).

C showed deficits in holistic processing (as assessed by the Composite Faces Task), in differentiating between faces that differed in the spacing of their internal features (as assessed by the Jane Task), and did not show the typical inversion effect for faces with spacing changes, indicating a reduced sensitivity to second-order relations (as assessed by the Jane Task). C did not appear to be impaired at encoding feature and contour differences from faces (as assessed by the Jane Task). Although we cannot exclude that C might have impairments in encoding feature shape on other tests (e.g., Yovel & Duchaine, 2006), her intact feature performance on the Jane Task indicates that C is able to encode "some" information from faces.

We suggest that C's ability to match unfamiliar faces that were simultaneously presented from different viewpoints for unlimited periods of time reflects her ability to match local features of faces. We expect that she would be impaired on versions of this task that used sequential presentation, which would rely more upon forming configural/holistic representations

With reference to Bruce and Young's (1986) model of face recognition, C's performance can be interpreted as a deficit in some (configural/holistic) but not other (feature) aspects of structural encoding. This incomplete impairment at the structural

encoding stage might explain why C was able to overtly recognise some famous and personally familiar faces.

COVERT FACE RECOGNITION ASSESSMENT

C's performance on the tasks described above confirmed her poor overt face recognition. We were also able to show that C's structural encoding impairment involved configural/holistic rather than feature coding deficits. It was also apparent that C has intact PINs and name generation abilities. The Bruce and Young (1986) model suggests that C's structural encoding deficits should impact on the formation of FRUs. However, given that C could recognise some personally familiar and famous faces it is possible that she has functional FRUs. We suggest that if C has FRUs (of some sort) then she should display covert face recognition on at least one of the three covert recognition tasks in our test battery: a priming task, a forced-choice familiarity task and a forced-choice cued task. As well as determining whether C shows covert face recognition, we were interested in comparing her performance on the three tasks, to better understand the mechanisms of covert recognition in a developmental form of prosopagnosia.

In addition to the covert recognition tasks, C completed two additional control tasks, in which she was asked to overtly name a set of faces and judge the familiarity of a set of printed names, to enable us to ascertain which faces she could and could not overtly recognise. We would like to emphasise that C was administered these "control" tasks very soon after completing the covert recognition tasks, thus ensuring that only those faces that could not be recognised after all the covert recognition tasks could be confidently considered as "covert trials". Although these control tasks were administered after the covert recognition tasks, we begin by discussing C's ability to

recognise the famous faces used in the covert recognition tasks and provide semantic information from their names.

Control tasks for the assessment of familiarity and overt recognition.

Stimuli

Colour photographs of 148 famous faces were downloaded from the Internet, along with a set of unfamiliar faces that were matched to the famous faces as closely as possible for age, sex, attractiveness and profession (for example a famous Australian politician was matched with an Italian politician unknown to most Australians). This set of faces were used in each of the three covert recognition tasks described below, although note that each face was used in only one task. Face stimuli were edited using Adobe Photoshop in order to remove hair and background, and had a height of approximately 8 cm. All tasks were programmed using SuperLab (Cedrus Corporation, 2007), and administered on a 15-inch Macintosh Power Book G4. Participants were approximately 50 cm from the computer screen and gave their responses by pressing the relevant keys on the keyboard. Both accuracy and RT were recorded.

Name recognition task

In this task C was presented with a list of 148 printed names, consisting of the names of all famous people used in the covert recognition tasks. C was first asked to indicate whether each name was familiar or unfamiliar, and for those she was familiar with she was asked to provide some information to confirm her familiarity. C was familiar with 91.2% (135/148) of the people. The 13 people whom C was not familiar with were excluded from any subsequent analyses.

Face naming task

The aim of this task was to provide an index of C's overt recognition of the famous faces used in the covert recognition tasks. She was shown each face and was asked to provide either the name or specific identifying information. C could only overtly recognise 34% (46/135) of the faces of people that she was familiar with.

Throughout the following description of the covert recognition tasks, "overt trials" will refer to trials containing faces that C correctly recognised whereas "covert trials" will refer to trials containing faces that C was familiar with but did not recognise in this task.

We took two precautions to ensure that the faces on the "covert trials" were indeed unknown to C during the test session. First, because C was shown faces and names during the covert recognition tasks, priming and/or cueing may have improved her overt recognition during the course of the session. As such, the face naming task was administered to C at the end of the session, shortly after she had completed the covert recognition tasks, when her overt recognition should be most accurate. Second, we tested overt and covert recognition for the exact same face images (i.e., the face images shown in the face naming task were exactly the same faces images as those shown in the covert recognition tasks). As such, we are confident that the faces that C could not overtly recognise in the face naming test were indeed unknown to her during the assessment of covert face recognition. We will now describe the three covert recognition tasks, in the order in which they were given to C.

Priming task

The priming task was a name categorization task, in which participants had to classify names as belonging to either an actor or a politician. Names (e.g., Bill Clinton)

were preceded by one of four types of photographs: 1) a same-face condition, in which the name was preceded by that person's face (e.g., Bill Clinton's face followed by the name "Bill Clinton"); 2) a related-face condition, in which the name was preceded by the face of a person belonging to the same category (e.g., George Bush's face followed by the name "Bill Clinton"); 3) a unrelated-face condition, in which the name was preceded by the face of a person belonging to a different category (e.g., Tom Cruise's face followed by the name "Bill Clinton"), and 4) a baseline condition, in which the name was preceded by a scrambled face.

Stimuli and procedure

Twenty-eight famous faces (14 actors and 14 politicians) were selected from the larger set of 148 described above. The name of each face was presented four times (once per condition), for a total of 112 trials. Each trial began with a fixation cross presented for 500 ms, followed by the prime face for 500 ms, and subsequently the target name which remained on the screen until the participants made their response via a button press. The inter-trial interval was 2000 ms. Both Accuracy and RT were recorded, and RT for correct responses were transformed before the analysis using a Blom transformation to enable a mixed linear model analysis. All priming effects were calculated with respect to the baseline condition.

Analysis

C's performance was compared to that of 10 age- and sex- matched controls (mean age = 67 years.). None of the control subjects had a history of head injury or any other neurological condition, and all had normal low-level vision as measured by the

FACT. Each of the control participants was familiar with all the famous people used in the priming task, so no trials were excluded.

A mixed linear model procedure was used to fit multi-level models to the data to allow for correlations between responses to the same stimulus names. The use of the mixed model procedure for fitting multilevel models is described in Singer (1998). When C's data was analysed, a two-level model was used. The first level consisted of RT, whereas the second level consists of the individual stimulus names (each one is repeated 4 times). When the data for the control subjects was analysed, a three-level model was used. The first two levels of the model were the same as the ones described above, while the third level was made up of the individual participants. This model allowed for correlations among all the responses of individual subjects, as well as for the correlation of participant's responses of individual stimulus names.

Results

For controls, a mixed ANOVA showed a significant effect of condition $F(3, 1060) = 26.16$, $p < .001$. A pair-wise comparison (with alpha adjusted for multiple comparisons) showed that the baseline condition only differed significantly from the same-face condition ($p < .001$) (see Figure 3a). Similar studies have also only found significant priming effects when comparing the same-face and baseline conditions (e.g., Barton et al., 2004).

C was familiar with all the famous people whose faces were used in the priming task (as confirmed by the name recognition task we described earlier). C could overtly recognise 59% of these faces (as confirmed by the face naming task we described earlier). When the model was split into overt and covert trials, the mixed model ANOVA showed a main effect of Condition, $F(6,100) = 4.4$, $p < .001$, with priming

between the baseline and same-face condition evident only for overt (p = .008) but not covert (p = .79) trials. Thus, there was no evidence for priming when C could not overtly recognise the faces (see Figure 3b).

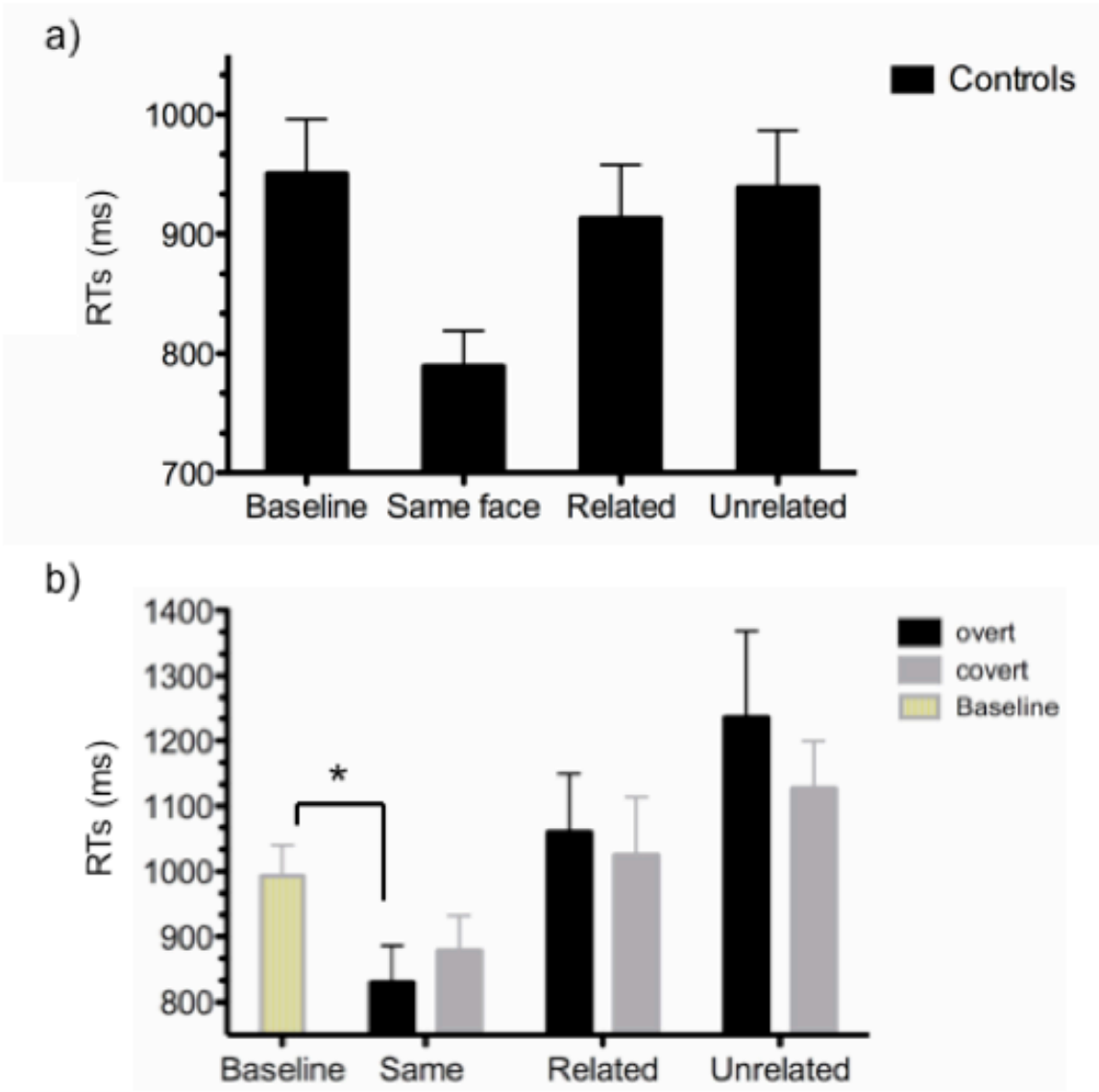

Figure 3. Priming task. a) Controls show priming on a comparison of the baseline and same-face conditions b) C demonstrates priming on the overt, but not covert, trials. * Two tailed p value (p = .008).

Forced-choice familiarity task

In this task C was asked to indicate which one of two simultaneously presented faces was famous. Forty familiar famous faces and forty matched unfamiliar faces were

selected for this task from the larger set of 148 faces. Familiar faces were chosen from a range of professions including actors, politicians, singers, athletes, and models. The faces remained on the screen until C gave her response via a button press. After responding, C was asked to rate her confidence in her response on an 8-point likert scale (0 = pure guess; 8 = very confident). Control participants did not complete this task because pilot testing revealed that they would be at ceiling. Thus, C's performance was compared to chance using the binomial distribution.

Of the 40 trials on this task, five trials contained faces of people that were not familiar to C and were excluded from the analysis. Of the 35 remaining trials, 13 were classified as overt trials (faces that C recognised in the face naming task) and 22 were classified as covert trials (faces that C did not recognise in the face naming task). For the 13 overt trials, C correctly chose the famous face on all trials. In contrast, on the 22 covert trials, C correctly chose the famous face on only 14 trials, which was not significantly different from chance (Binomial one-tailed $p = .143$). Hence, as for the priming task, there was no indication of any covert recognition.

A Mann-Whitney test was conducted to compare RT and confidence ratings on the overt vs. covert trials. With correction for ties and z-score conversion, there was a significant difference between overt and covert trials for both RT, z (N = 35) = -2.9, $p = .003$, two tailed (Overt M = 8.29 sec, Covert M = 11.57 sec) and confidence ratings z (N = 35) = -4.33, $p < .001$ two-tailed (Overt M = 7.23, Covert M = 2.18). Thus, as expected, C was significantly faster and more confident in selecting the familiar face when she could recognise it.

Forced-choice cued task

In this task C was asked to indicate which one out of two simultaneously presented faces corresponded to the written name shown below them on the screen. Forty pairs of famous faces were presented. Each pair of faces consisted of faces from the same category (e.g., actors), and remained on the screen until C gave her response via a button press. Again, after responding, C was asked to rate how confident she was about the response she had just given on an 8-point likert scale (0 = pure guess; 8 = very confident). C's performance was compared to chance using the binomial distribution.

Of the 40 trials of this task, three trials were excluded from the analysis because C was not familiar with the person. Of the 37 remaining trials, 18 were classified as overt trials and 19 were classified as covert trials. C correctly chose the correct face on all the overt trials. On the covert trials, C correctly chose the correct face on 15 of the 19 trials, which was significantly different from chance (Binomial one-tailed, $p < .001$), indicating covert face recognition.

As for the forced-choice face familiarity task, a Mann-Whitney test was conducted to compare RT and confidence ratings between overt and covert trials. With correction for ties and z-score conversion, there was a significant difference between overt and covert trials for both RT, z (N=37)= -2.7, p= .006, two tailed (Overt M = 5.93 sec, Covert M = 8.97 sec) and confidence ratings, z (N=37) = -3.62, p= .001, two-tailed (Overt M = 7.8, Covert M = 5.3). Thus, as expected, C was significantly faster and more confident in selecting the familiar face when she could recognise it.

Summary

Two important findings emerged from testing C with three behavioural covert recognition tasks. First, C displayed covert face recognition on the forced-choice cued

task, which is the first time behavioural covert face recognition has been demonstrated in a single case of CP. Second, although covert face recognition was evident on the forced-choice cued task, her performance on the priming task and the forced-choice familiarity task did not reveal covert face recognition, suggesting that behavioural covert recognition in CP, just like AP, may depend on type of task used in the assessment.

To explain the dissociations between the covert face recognition tasks we will interpret C's pattern of performance within the cognitive model of face recognition proposed by Bruce and Young (1986). The previous assessments revealed that C has deficient configural/holistic perception but relatively intact local feature processing. This partial deficit in structural encoding contrasts with intact PINs and name generation. We assume that impairments to structural encoding will have had a flow on effect to the FRU stage but were unable to test this directly.

C's performance on the forced-choice familiarity task does not enable us to clarify this issue either. This is because the forced-choice familiarity task targets the FRUs directly, requiring familiarity decisions that access representations within the FRUs. While C's absence of covert recognition on this task confirms her inability to access these representations, her performance could be explained by postulating either an impairment to the FRUs as such, or impaired access to them due to a structural encoding deficit.

The priming task involved the processing of both faces and names, so to interpret C's performance we need to add a new component to the face recognition model proposed by Bruce and Young (1986). This "Name recognition Unit" (NRU) can be conceived as an input lexicon for proper names in which all familiar / famous names are stored (Young et al., 1988a) (Figure 4). In individuals with normal face recognition

skills, the priming effect observed when a face precedes the target name belonging to the same person (same-face faster than baseline) can be explained by the familiar prime face activating its representation within the FRU and then the corresponding PIN. From the PIN, the activation spreads to the NRU, lowering the NRU's activation threshold, and hence facilitating the recognition of the written name belonging to the prime face when it is subsequently presented.

We assume that a similar process occurs in C for the subset of faces that she can overtly recognise, as she also displays a priming effect with these faces (see Figure 3). However, C does not show a priming effect for faces that she cannot overtly recognise (i.e., covert trials), suggesting that when the face is not overtly recognised only minimal activation is present in the PINs or NRUs. As for the familiarity task, the fact that C did not show covert recognition in the priming task does not allow us to disambiguate between the two possible hypothesized impairments within her face recognition system: A deficit in structural encoding and subsequent impaired access to the FRUs, or an impairment at the level of the FRUs themselves. In fact, both impairments are consistent with a reduced (or lack of) spreading of activation to the PINs and the NRUs, and a consequent lack of priming.

In contrast to the previous two tasks, C did show covert recognition on the forced-choice cued task. A crucial aspect that differentiated the face-name matching task from the other two tasks was that the faces and names were presented *simultaneously*. It is therefore reasonable to assume that this fact played a central role in contributing to C's covert recognition. With reference to the cognitive model, covert recognition on the face-name matching task in C could be explained as follows: Presentation of the written name leads to activation of the NRU. From there, we can postulate a top-down spread of activation to the PINs and subsequently to the FRUs, which would lower the FRU

activation threshold. At the same time, the FRUs receive visual information about the face via the Structural Encoding unit (Figure 4). Even if this information is partially degraded (due to a partial structural encoding deficit), the convergence of bottom-up and top-down activation (caused by the simultaneous presentation of the name) appears to be sufficient to give rise to covert face recognition.

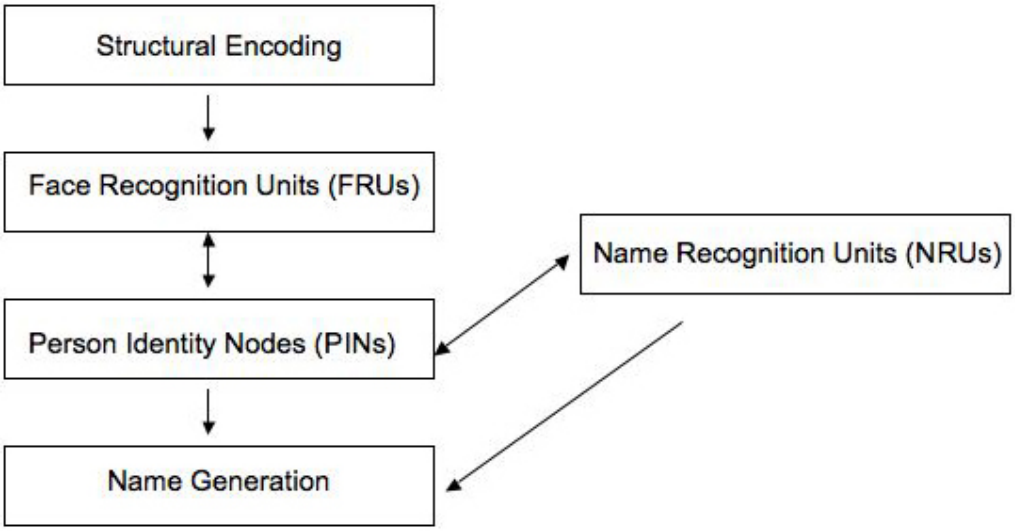

Figure 4. Interpretation of C's performance on the covert processing tasks within the cognitive model of face processing (simplified figure adapted from Bruce & Young, 1986). The use of covert assessment allows us to pinpoint C's deficit within the cognitive model of face processing.

We suggest that covert recognition was evident on the forced-choice cued task because this task presented name cues simultaneously with faces, rather than simply reflecting task difficulty. We were careful to make this task as difficult as possible, by presenting pairs of famous faces (rather than one famous and one unfamiliar face, c.f., Barton et al., 2001) and selecting the famous faces from the same category (e.g., George Bush was paired with Bill Clinton). In addition, if this task was simply easier than other covert recognition tasks then we would expect that other CPs, who display covert recognition on other behavioural tasks, would also show covert recognition on this task;

but this is not the case (Rivolta, Palermo, Schmalzl & Coltheart, 2010). Further evidence against the task difficulty issue comes from patient P.C. (Sergent and Signoret, 1992) who did not show covert face recognition in the forced choice cued task, but showed covert recognition in other tasks such as the matching task.

In sum, the covert face recognition assessment suggests that there are some FRUs that cannot be accessed by degraded perceptual input alone but are sufficient for covert recognition when augmented with semantic information.

GENERAL DISCUSSION

In the current report we have described an investigation with C, a 69 year-old woman with CP. C reported long standing face recognition difficulties in everyday life, and a detailed cognitive neuropsychological assessment confirmed a selective face recognition impairment in the context of intact general intellectual functioning, as well as normal low level vision, basic configural processing and basic level object recognition. C's performance on a series of overt face processing tasks suggested impairments at the level of Structural Encoding and perhaps the FRUs. However, on the basis of these tasks alone we were not able to specify whether her FRUs as such were affected, or whether her poor ability to access the FRUs was simply a consequence of her partially impaired Structural Encoding.

In order to distinguish between these two hypotheses, C was assessed with two direct (forced-choice familiarity and forced-choice cued) and one indirect (priming) covert face recognition tasks. Furthermore we interpreted her performance on these tasks in the context of a cognitive model of face processing. In line with the some cases from the AP literature (Schweinberger & Burton, 2003), C showed dissociations between these tasks. Our results underline the importance of using different tasks, and

in particular tasks that involve name cues (as they seem to be the most sensitive tasks for covert recognition investigation, see Barton et al., 2001; 2004).

If we consider the way that different covert recognition tasks access the face recognition system, it seems clear that the priming task and the forced choice familiarity task access FRUs in a "direct" way via structural encoding, whereas the forced choice cued task accesses the FRUs "indirectly" via the NRUs and PINs. The result that covert face recognition was found only in the forced choice cued task implies that only the convergence of both face and semantic information (cued by the name) can trigger covert recognition. This suggests that the main locus of C's impairment is not necessarily at the level of the FRUs, but could be at an earlier stage of face processing. Hence, C's case illustrates how the assessment of covert recognition can be a *more sensitive tool* for the localization of impairment within the face processing system than more traditional overt face recognition assessment tasks.

How could it be possible that individuals with CP have (at least partially) intact FRUs despite impaired structural encoding? A comparison between CP and AP may help to answer this question. People with AP have lost a previously normal ability: the ability to recognise people by the face. This means that, as a consequence of a stroke or other neurological problems, they have specific cognitive impairments (e.g. selective problems at the FRUs or at the structural encoding). People with CP experience a developmental problem that prevents them the acquisition of normal face recognition abilities. The literature seems to show that people with AP have usually a serious face recognition problem, where they can recognise closely to 0% of faces (De Haan, Young & Newcombe, 1987; Riddoch et al., 2008), whereas people with CP have usually some spared (residual) face recognition skills (Avidan et al., 2008; Bate et al., 2008).

This, in our opinion, indicates that people with CP can use compensatory strategies and that they must have some form of FRUs because without FRUs it is theoretically impossible to recognise (even few) faces. This raises the possibility that C has FRUs (formed from repeated exposure to faces of personally familiar and famous people over the years) for many - maybe all - familiar faces, but because of a partially damaged structural encoding system they cannot be easily and directly accessed every time she sees a familiar face. We do not claim that C has "normal" representations of faces within the FRUs, but it is clear that C has representations that allow a minimal level of overt recognition (e.g., to allow 30% of famous faces to be recognized in the Face naming task) and covert recognition when names and PINs boost activation in the FRU.

Why do some individuals with prosopagnosia show covert recognition in some but not other tasks? As mentioned above, differences in performance between different covert recognition tasks have been reported in the AP literature (Barton et al., 2001; 2004; Sergent and Signoret, 1992; Young and DeHaan, 1988). These differences have mostly been proposed to reflect the variability of the severity of overt face recognition impairments in prosopagnosic individuals. More specifically, it has been suggested that there is a correlation between overt face recognition abilities and behavioural covert recognition, i.e., the more severe the overt face recognition impairment, the less likely covert recognition will be observed. In the current study we have attempted to shed further light on the reasons underlying the dissociations between performance on covert processing tasks, and argue that these can be explained by postulating specific impairments within the face processing system.

As stated in the introduction, little research has been conducted into covert recognition in CP, with only five studies published to date. In our opinion, the main

weakness of these studies is that covert recognition is generally assessed with only one task (with the exception of DeHaan & Campbell, 1991) and, no studies have investigated covert recognition using the forced-choice cued task, which seems to be the most sensitive tool for the investigation of covert face recognition in acquired prosopagnosia. As illustrated by C's case, we believe that the through assessment with multiple tasks, and the analysis of differential patterns of performance between them, one can shed light on the specific mechanisms underlying covert face recognition.

We note that C, like other CPs tested in our lab, could overtly recognise approximately one-third of the famous faces used in our covert recognition tests. We do not know whether C is consistently unable to recognise the other two-thirds, or whether she is able to recognise other images of these famous faces. However, we are confident that C was unable to overtly recognise the face images classified as "covert" in our study because C was administered all the covert and control tests in the same session and the covert and control tests contained the exact same face images. The fact that many CPs can recognise some famous faces opens up an important avenue for future research; which would be to determine whether there is a subset of famous faces that the CP consistently fails to recognise over multiple test images/test sessions and assess covert recognition of this subset of faces. The results of the present study suggest that covert recognition would be apparent if the individual was tested with a forced-choice cued task, but this remains to be examined.

CONCLUDING COMMENTS

The present study represents the first investigation of behavioural covert recognition in CP which:

1. Assesses covert recognition with multiple direct and indirect tasks, including one using name cues,

2. Explains the dissociations between performances on these tasks using a cognitive model of face recognition as a frame of reference,

3. Uses covert recognition as an assessment tool aimed at pinpointing the localization of impairment within the face processing system.

Further studies with larger numbers of individuals will be of great interest in order to investigate whether the dissociations found in C will also be found in other cases with CP. We believe that the assessment of covert face processing with multiple tasks holds great promise for shedding light on the specific deficits underlying face processing impairments in CP as well as AP.

Chapter 2

ETHICS DECLARATION

The current study was approved by the Ethics Committees of Macquarie University, and has therefore been conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. Informed consent was obtained from all participants.

Chapter 2

ACKNOWLEDGMENTS

Thank you to C. Ellie Wilson for designing and programming the famous face recognition task, Alan Taylor for his statistical advice, and to C for her time and patience. Thank you also to A. Mike Burton and Brad Duchaine for helpful comments on this work.

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Appendix

List of the 148 famous people adopted for the assessment of covert face recognition in CP.

Adam Glichrist
Adam Sandler
Al Pacino
Alexander Downer
Andrew Johnes
Anthony Hopkins
Arnold Schwarzenegger
Barack Obama
Barbara Streisand
Ben Affleck
Bette Midler
Bill Clinton
Bill Gates
Billy Joel
Bob Hawke
Bono Vox
Brad Pitt
Brendan Nelson
Britney Spears
Bronwyn Bishop
Bruce Willis
Cameron Diaz
Cate Blanchett
Celine Dion
Charlize Theron
Cher
Christina Aguilera
Christopher Reeve
Claudia Shiffer
Collin Farrell
Danii Minogue
Danny DeVito
David Beckham
David Caruso
David Duchovny
Delta Goodrem
Demi Moore
Denzel Washington
Diane Keaton
Dolly Parton
Drew Barrymore
Dustin Hoffman
Eddie Murphy
Elijah Wood
Elizabeth Hurley
Elle McPherson
Elton John

Elvis Presley
Eva Longoria
Fidel Castro
George Bush
George Clooney
George Michael
Grant Hakett
Greg Norman
Gwen Stefani
Gwyneth Pathrow
Harrison Ford
Heidi Klum
Helen Clark
Henry Winkler
Hillary Clinton
Hugh Grant
Hugh Jackman
Ian Thorpe
Jack Nicholson
Jennifer Aniston
Jennifer Hawkins
Jessica Alba
Jessica Biel
Jessica Simpson
Jim Carrey
Jodie Foster
John Fitzgerald Kennedy (JFK)
John Howard
John Travolta
John Wayne
Johnny Depp
Judi Dench
Julia Gillard
Julia Roberts
Kate Hudson
Kate Moss
Kate Richie
Katherine Heigl
Katie Holmes
Keanu Reeves
Keira Knightley
Kevin Rudd
Kurt Cobain
Kylie Minogue
Lee Karnaghen
Leonardo Di Caprio
Linsday Lohan
Liv Tyler
Liz Taylor
Luciano Pavarotti
Madonna
Malcom Turnbull
Margaret Thatcher

Mark Philippousis
Matt Demon
Megan Gale
Mel Gibson
Melanie Griffith
Meryl Streep
Michael Bolton
Michael Douglas
Michelle Pfeiffer
Mick Jagger
Miranda Kerr
Morgan Freeman
Names
Naomi Campbell
Natalie Imbruglia
Nicholas Cage
Nicole Kidman
Olivia Newton Jones
Orlando Bloom
Owen Wilson
Pamela Anderson
Paris Hilton
Pat Cash
Patrick Dempsey
Paul Keating
Paul McCartney
Paul McDermott
Penelope Cruz
Peter Costello
Peter Garrett
Piers Brosnan
Pope Benedict XVI
Pople John Paul II
Prince Charles
Prince Harry
Prince William
Princess Diana Spencer
Queen Elizabeth II
Rene Zellweger
Robbie Williams
Robert De Niro
Robert Redford
Robin Williams
Rod Stewart
Russell Crowe
Saddam Hussain
Sandra Bullock
Sarah Jessica Parker
Scarlett Johansson
Sharne Warne
Sharon Stone
Simon Crean
Sinead O'Connor

Steve Irwin
Steve Waugh
Sting
Sylvester Stallone
Tiger Woods
Tom Cruise
Tom Hanks
Tony Blair
Uma Thurman
Victoria Beckham
Vladmir Putin
Will Smith
Wynona Ryder

Chapter 3

Covert face recognition in congenital prosopagnosia: A group study

Manuscript accepted for publication in *Cortex*

The reference for this publication is:

Rivolta, D., Palermo, R., Schmalzl, L. & Coltheart, M. (2011). Covert face recognition in congenital prosopagnosia: A group study. *Cortex*, doi: 10.1016/j.cortex.2011.01.005.

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Rivolta, D., Palermo, R., Schmalzl, L., & Coltheart, M. (2012). Covert face recognition in congenital prosopagnosia: A group study. *Cortex*, *48*(3), 344-352.

DOI: 10.1016/j.cortex.2011.01.005

Chapter 4

The face-specificity of the M170 correlates with behavioural performance: Insights from congenital prosopagnosia

Chapter 4

The face-specificity of the M170 correlates with behavioural performance: Insights from congenital prosopagnosia

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Abstract

It is known that face perception generates specific neural activity as early as 170 ms post-stimulus onset, which is called M170 when measured with Magnetoencephalography (MEG). We examined the M170 in six people with life-long severe deficits recognising faces (congenital prosopagnosics; CPs) and 11 typical controls. Individuals with CP showed face-selective M170 responses within the right lateral occipital area (rLO) and right fusiform gyrus (rFG), which did not differ in magnitude to those of the controls. To examine possible links between neural activity and behaviour we correlated the CP's MEG activity generated within rLO and rFG with face perception skills. The rLO-M170 correlated with holistic/configural face processing (i.e. the ability to process relationships between features), whereas the rFG-M170 correlated with featural processing (i.e. the ability to process individual face features), suggesting that early responses in the rLO and rFG code for different aspects of face processing

Keywords: congenital prosopagnosia, face processing, M170, MEG, prosopagnosia, scene processing.

Introduction

Faces are ubiquitous in our environment, and most humans are extremely efficient in determining their identity. Facial identity recognition is mediated by specific cognitive and neural mechanisms. In particular, upright face processing is mediated by both *holistic/configural mechanisms*, which involve an analysis of the whole face rather than just individual features, and by *featural mechanisms*, that code for specific facial features (Maurer, Le Grand, & Mondloch, 2002; McKone & Yovel, 2009; Tanaka & Farah, 1993; Young, Hellawell, & Hay, 1987). Neurally, specific brain areas within the ventral visual pathway respond preferentially to faces compared to other categories of visual stimuli (Haxby, Hoffman, & Gobbini, 2000). Within these regions, the "core" regions for face identification include the lateral part of the occipital cortex (Gauthier, et al., 2000), and the fusiform gyrus on the ventral surface of the temporal lobe (Kanwisher, McDermott, & Chun, 1997). Larger neural responses to faces than non-face objects also occur rapidly, approximately 170 ms post stimulus onset as measured with Event Related Potentials (ERP; labeled as the N170, Bentin, McCarthy, Perez, Puce, & Allison, 1996) and Magnetoencephalography (MEG; labeled as the M170; Liu, Higuchi, Marants, & Kanwisher, 2000). These N/M170 responses are sensitive to manipulations that disrupt holistic/configural face processing, such as face inversion, which delays the N/M170 by ~ 10-13ms (Bentin, et al., 1996; Itier, Herdman, George, Cheyne, & Taylor, 2006; Liu, et al., 2000; Rossion, et al., 2000). The N/M170 have also been shown to be sensitive to variations of both face features and configuration in adaptation paradigms (Eimer, Kiss, & Nicholas, 2010; Harris & Aguirre, 2008; Harris & Nakayama, 2008).

Given the evidence that the N/M170 reflects early face-sensitive processing, it has been of considerable interest to ascertain whether people suffering from prosopagnosia,

a specific inability to recognize faces, show typical N/M170 responses. Prosopagnosia can be *acquired* via neurologic conditions such as stroke or a head injury, or can be *congenital*, where the inability to recognize faces is apparently life-long but not associated with brain injury (Behrmann & Avidan, 2005; Duchaine, 2000; Duchaine & Nakayama, 2006; Lee, Duchaine, Wilson, & Nakayama, 2010; Rivolta, Schmalzl, Coltheart, & Palermo, 2010; Schmalzl, Palermo, & Coltheart, 2008).

The results of only two published single-case investigations of the N170 in acquired prosopagnosia (AP) were contradictory. One prosopagnosic patient showed lack of face-selective neural processing (i.e., objects generated an N170 as large as the one generated by faces) (Eimer, 2000), whereas a second prosopagnosic showed, like controls, a greater N170 for face than object perception, indicative of face-selective neural processing (Bobes, et al., 2004). The face-sensitivity of the N/M170 has also been examined in at least fourteen individuals with congenital prosopagnosia (CP) (see Supplementary Table 1 for a summary). The results vary; five individuals showed face-selective neural activity, whereas nine did not (Bentin, DeGutis, D'Esposito, & Robertson, 2007; Bentin, Deouell, & Soroker, 1999; DeGutis, Bentin, Robertson, & D'Esposito, 2007; Harris, Duchaine, & Nakayama, 2005; Kress & Daum, 2003; Minnebusch, Suchan, Ramon, & Daum, 2007). The reason for this heterogeneity is not clear, as previous investigations have failed to find any correspondence between the magnitude of the CPs behavioural impairment on face memory tasks assessing both familiar and unfamiliar face processing, and face-selectivity of the N170 (Harris, et al., 2005; Minnebusch, et al., 2007).

Here, we wished to re-examine the face-sensitivity of early neural responses in CP, with the aim of using the variation in CPs' face perception ability to learn more about the M170. Our study varied from previous MEG research (both in normal and

clinical populations) in two ways. First, there is evidence that the M170 is generated from two neural areas, the lateral occipital cortex and fusiform gyrus (Itier, Alain, Sedore, & McIntosh, 2007; Wantabe, Kakigi, & Puce, 2003). However, no previous study has differentiated the neurophysiological activity within these two cortical regions crucial for face processing. By coupling the recording of MEG activity with structural brain images (MRIs), we can potentially record and separate the two M170s. This is important since it has been suggested that neural activity (as measured with Transcranial Magnetic Stimulation, TMS) within the lateral occipital cortex mainly mediates processing of features (Pitcher, Walsh, Yovel, & Duchaine, 2007), whereas fusiform gyrus activity (as measured with fMRI) mediates both features and holistic/configural processing (Maurer, et al., 2007; Yovel & Kanwisher, 2005).

Second, we investigated whether there was a relationship between neural activity and behavioral performance. Previous behavioural studies have indicated that holistic/configural mechanisms might play a role in typical face processing (Rotshtein, Geng, Driver, & Dolan, 2007, but see Konar, Bennett, & Sekuler, 2010). Here, we correlated MEG activity, as indexed by the face-specific M170, with CPs' holistic/configural and featural processing skills. Given the variability in CPs behavioural performance on measures of holistic/configural processing, combined with the heterogeneity of face-selective N/M170, this approach is suited to the analysis of data from CPs.

Method and Results

This study received ethical approval from the Macquarie University Ethics Committee. All participants provided written consent.

Congenital Prosopagnosics (CPs)

Six CPs (3 female) with a mean age of 42.7 years (Range: 21-57, SD: 13.78) completed a behavioural diagnostic assessment session, and then approximately 8-12 months later a MEG test session. None of the CPs reported any psychiatric or neurological conditions, and all reported normal or corrected-to-normal vision (see Table 1).

Table 1. Biographical information for the six CPs, z-scores on the MACCS Famous Face Task 2008 (MFFT-08), the Cambridge Face Memory Test (CFMT) adjusted for age (see Bowles et al., 2009 for normative data), and z-scores for the face inversion effect on the spacing and features sets of the Jane task. In italics are z-scores 2 SD below, or above, the control mean.

					"Spacing"	**"Features"**
CPs	**Age**	**Sex**	**MFFT-08**	**CFMT**	**Inversion-effect**	**Inversion-effect**
LL	40	F	-2.43	-2.16	-0.14	-0.33
GE	22	M	-2.04	-1.89	*-2.05*	1.79
OJ	53	M	-2.46	-2.72	-1.33	1.18
GN	47	F	-4.05	-1.81	-0.62	0.27
SD	57	M	-3.1	-2.83	-0.38	*2.7*
MG	33	F	-3.49	-2.09	0.57	0.27

Behavioural diagnostic assessment session

Non-face processing assessment

All CPs displayed normal contrast sensitivity as assessed by the *Functional Acuity Contrast Test* (FACT, Vision Sciences Research Corporation, 2002) and normal color perception with the *Ishihara Test for Colour Blindness* (Ishihara, 1925). Performance on the length, size, orientation and picture naming (long version) subtests of the *Birmingham Object Recognition Battery* (BORB) (Riddoch & Humphreys, 1993) confirmed that basic object recognition skills were intact. The *Raven Coloured Progressive Matrices* (Raven, Raven, & Court, 1998) further indicated that the IQ of all

participants with CP was within the normal range. None of the CPs scored within the autistic range on the *Autism-Spectrum Quotient* (AQ, Baron-Cohen, Wheelwright, Skinner, Martin, & Clubley, 2001). As such, the every day face recognition difficulties reported by the CPs (and confirmed on the two tests of face memory reported below) are not due to general visual recognition difficulties, low IQ, or impaired social functioning.

Face memory: Famous faces

Memory for familiar faces was assessed with the *MACCS Famous Face Test 2008* (MFFT-08). The MFFT-08 contains the faces of 20 people who are famous to the Australian population, and 20 who are unfamiliar. On each trial, a face was presented and participants judged whether it was familiar or not. If the face was that of a famous person, participants were then asked to identify the face by providing the name or specific autobiographical information (i.e., an answer like "she is an American actress" was considered incorrect). Participants were then shown the name of the famous person, accompanied by relevant autobiographical details, and participants were asked to report whether the famous person was actually known to them. The face of any person that was unknown was excluded from further analyses.

For each participant with CP, the percentage of correctly recognized faces of known famous people was calculated, and then transformed to an age-adjusted z-score (using age-based norms reported in Bowles, et al., 2009). The CPs scored between -4.05 to -2.04 below Australian norms (see Table 1).

Face memory: Unfamiliar faces

Memory for unfamiliar faces was assessed with the *Cambridge Face Memory Test* (CFMT) (Duchaine & Nakayama, 2006). On this task participants were asked to learn to identify six individuals and then recognize the previously seen faces when shown in novel views and/or degraded by noise. Total scores on the upright CFMT of CPs were transformed to age-adjusted z-scores (using age-based norms reported in Bowles, et al., 2009), with the CPs scoring between -2.83 and -1.81 below the Australian norms (see Table 1).

Holistic/configural processing

Perceiving the identity of faces is more difficult when they are upside-down than upright (Yin, 1969), and the effects of inversion are larger for faces than non-face objects (Robbins & McKone, 2007). The *face-inversion effect* has generally been attributed to a disruption of holistic/configural processing mechanisms with inversion (McKone, 2010). Here, we assessed holistic/configural face processing by investigating the effect of face inversion on the discrimination of sequential pairs of faces that varied in their *features* (i.e., the eyes, nose and mouth of the original face were replaced with features from a different face) or the *spacing* of their internal features (i.e., eyes were either moved in or out; eyes and mouth were moved either up or down)[1]. Spacing processing has been considered as an index of holistic/configural mechanisms (Maurer, et al., 2002; McKone & Yovel, 2009). This task, known as the "Jane task" has been used in numerous studies with typical participants, who show a greater effect of inversion for faces that vary in spacing as compared to those that vary by feature,

[1] A contour condition was also included, in which the internal portion of the original face was combined with the outer contour of a different face (data not reported here).

indicating a greater role of holistic/configural processing for detecting "spacing" rather than "feature" changes (Le Grand, et al., 2006; Mondloch, Le Grand, & Maurer, 2002)[2]. Thus, in the current investigation the magnitude of the inversion effect on the spacing set was considered an index of primarily holistic/configural processing whereas the magnitude of the inversion effect on the feature set was considered an index of primarily feature processing.

The Jane task has been also adopted for the assessment of face processing skills in clinical populations. Groups of individuals with early visual deprivation caused by bilateral congenital cataracts show impairments in spacing but not feature processing (Le Grand, Mondloch, Maurer, & Brent, 2001). Some, but not all, individuals with CP show impairments in spacing, and some also show impairments with feature processing as assessed with the Jane task (Le Grand, et al., 2006; Schmalzl, et al., 2008)[3]. This variability of CPs on the Jane task makes it ideal for the analysis of the correlation between behavioural performance and neurophysiological activity.

On each trial of the Jane task, a face was shown for 200 ms, followed by a 300 ms interval, and then a second face was shown until participants made a response as to whether the faces were the same or different. The trials were blocked (upright spacing, upright feature, inverted spacing, inverted feature), with 30 trials in each block. For each participant, a face inversion effect (upright minus inverted) was calculated for the spacing and feature conditions.

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[2] McKone and Yovel (2009) suggest that the dissociation between the two sets may be consequence of the characteristics of the "features set", where stimuli change not only in the shape, but also in the brightness of their features. However, equivalent face inversion effects have recently been demonstrated for *shape only* versus *shape and brightness* changes on the "feature set" of the Jane task (Mondloch, Robbins, & Maurer, 2010)

[3] Yovel and Duchaine (2006) however showed that eight CPs were, as a group, impaired both on the spacing and feature processing when assessed with a different task (i.e. "The Albert task").

To provide a normative dataset for comparison, fifty-five people without face recognition difficulties (38 female, Mean age = 25 years, range: 19-62 years, SD = 8.9) completed the Jane task (see supplementary material for a complete analysis of the Jane task in controls). For both the spacing and feature sets, upright face processing was more accurate than inverted face processing, $F(1,54) = 144$, $p < .001$). The face inversion effect (as expressed in % of accuracy reduction) was greater for spacing (M = 20%, SD = 14.10) than features (M = 6.7%, SD = 11.06), ($F(2, 108) = 18.43$, $p < .001$), replicating previous studies.

As there were no sex differences (also see Le Grand et al., 2006), and performance did not decline with age, we used the whole control sample as a reference for our participants with CP. For CPs, inversion scores on the spacing and feature sets of the Jane task were transformed to z-scores, with the prosopagnosics scoring between -2.05 to 0.57 on the spacing set and from -0.33 to 2.70 on the feature set (Table 1). Such variability on performance of tests of spacing and features in CP is consistent with previous findings (Le Grand, et al., 2006; Lee, et al., 2010; Schmalzl, et al., 2008).

Magnetoencephalography (MEG) session

Participants

The six CPs and 11 typical adults (5 Female, Mean age: 37.3, Range: 23-55, SD: 11.21) participated.

Experimental design

The MEG activity was recorded while participants performed a “Target task”. In this task, 240 faces and 240 places were shown, where 120 faces and 120 places were famous. Each trial consisted of a pair of stimuli (S1 and S2), either two faces, or two

places, shown for 1000 ms with an inter-stimulus interval (ISI) of 1000 ms during which only a central red fixation cross was present. The fixation cross was also superimposed on all stimuli to avoid saccades and facilitate central fixation. On the face trials, each pair consisted of either two familiar or two unfamiliar faces, while on the place trials each pair consisted of either two familiar or two unfamiliar places. The pairs of stimuli were either "Repeated", where S2 depicted the same picture as S1, or "Unrepeated" where S2 was a different face/place to S1 (Fig. 1).

Participants were not informed that they were viewing pairs of stimuli but were instructed to fixate centrally and press a button whenever they saw one of the two previously specified target stimuli (one face and one place). Each of the two target stimuli was shown 48 times during the task. The task was divided into 8 blocks of 120 trials, each including the presentation of 12 targets, for a total of 960 trials (half face pairs and half place pairs). All stimuli were shown in the centre of a screen (size: 38 x 35 cm; resolution: 800 x 600 pixels) installed inside the magnetically shielded room, and placed at a distance of approximately 40 cm from the participant's head. The MEG experiment was programmed and delivered with Presentation software (Neurobehavioral Systems, Albany, CA).

Stimuli

Familiar faces included famous actors, politicians and athletes. Unfamiliar faces were matched to the familiar faces for sex, age and approximate level of attractiveness. Familiar places included famous landscapes or famous buildings. Unfamiliar places were matched to the familiar places for category and visual similarity (for example the Eiffel Tower was matched with an unfamiliar tower). One additional face and one additional place were used as target stimuli.

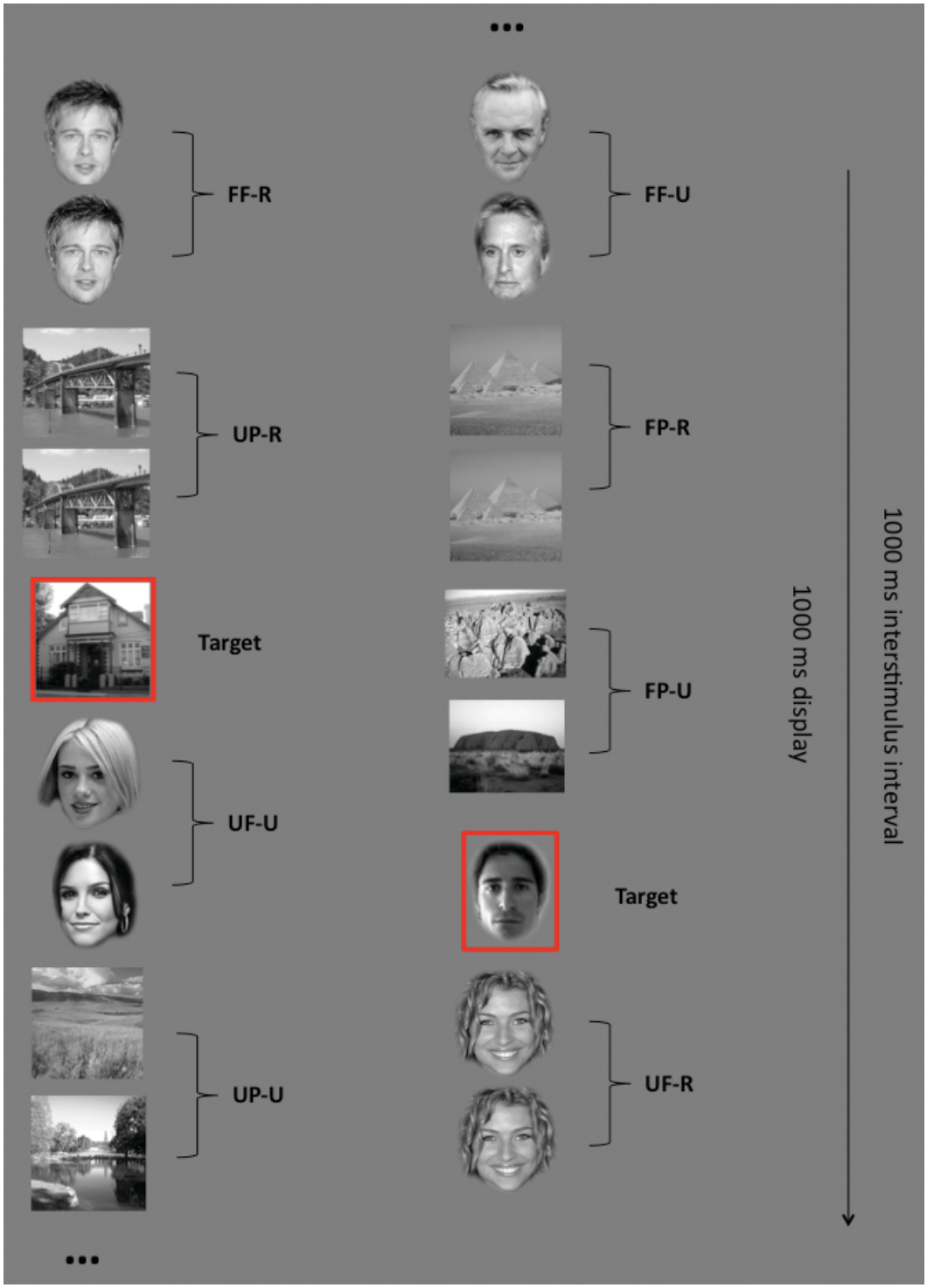

Figure 1. Experimental design. Participants had to press the button whenever they saw a previously selected target (either a face or a place). Stimuli were shown in pairs. Each pair consisted of faces or places. Both faces and places could be familiar or unfamiliar and could be repeated or unrepeated (FF-R: familiar face repeated; FF-U: familiar face unrepeated; UF-R: unfamiliar faces repeated; UF-U: unfamiliar face unrepeated; FP-R: familiar place repeated; FP-U: familiar place unrepeated; UP-R: unfamiliar place repeated; UP-U: unfamiliar place unrepeated). The superimposed red fixation cross is not indicated in this picture for representation purposes.

All stimuli were converted to grayscale using Adobe Photoshop software (Adobe Systems Incorporated). Places were presented within a 7.5 cm x 5 cm frame. Faces were edited so that the internal facial configuration (but not hair) fitted into a 6 x 4 cm oval template. On average, places covered a visual angle of 10.7° X 7.2°, whereas faces subtended 5.7° X 8.6°. The mean luminance of the places and faces did not differ ($t(238) = -1.82$, $p = .070$).

MEG data acquisition

A 160-channel whole-head first-order axial gradiometer system (50 mm baseline; sampling rate: 1000 Hz) was used to record MEG activity. A digital head-shape was recorded for each participant before entering the magnetically shielded room. Five head position indicators (HPI) coils were attached to a tightly fitting elastic cap, and the 3D locations of three cardinal landmarks (the nasion and bilateral preauricular points), as well as approximately 400 randomly selected points on the participant's head surface, were digitized using a Fastrak system (Polhemus, Colchester, VT). This allowed subsequent registration of the MEG data to the structural MRI. To correct for movement errors, the participants' head position within the MEG system was determined at the start of each recording block from the five HPI coils.

MEG Data Processing

The minimum-norm estimate (MNE) was used for the estimation of the source current distribution at each cortical location (Hamalainen & Sarvas, 1989). The cortical surfaces were reconstructed from MRI of each participant using FreeSurfer software (Fischl, Sereno, & Dale, 1999). The MEG source space was constrained to a cortical surface that comprised 4098 sources per hemisphere with an average of 7 mm spacing

between adjacent source locations. MEG signals were segmented into time epochs spanning from 200 ms before stimulus onset to 800 ms following stimulus onset, with the pre-stimulus epoch of -200 to 0 ms as baseline. Movement less than 5 mm was tolerated and noisy MEG channels (individuated offline in the raw data) were excluded in the analysis. Event-related magnetic fields were digitally filtered (50 Hz high-pass filter). MEG data associated with the target stimuli were ignored in the analysis to avoid motor artefact from responses. Automated filtering excluded neuromagnetic activity caused by eye blinks and gross eye movement artefacts.

The single-layer boundary element method (BEM) (Hamalainen & Ilmoniemi, 1994) was implemented to calculate forward solutions from estimated source configurations. The noise-covariance matrix, computed from the 200 ms pre-stimulus activity, and the forward solution were together used to create a linear inverse operator (Dale, et al., 2000). At each cortical location, the current estimate was normalized to the estimated baseline variance, resulting in z-scores. This noise-normalized solution provides a dynamic Statistical Parametric Map (dSPM), which indicates the signal-to-noise ratio (SNR) of the current estimate at each cortical location as a function of time (Dale et al., 2000).

MRI data acquisition

A 3D-MPRAGE (magnetization prepared rapid gradient echo) sequence was adopted to acquire high-resolution anatomical MRI scans for each participant. Scanning was performed with a 3 Tesla Philips Scanner at St Vincent's Hospital, Sydney, Australia.

Regions of Interest (ROIs) selection

We utilized an *a-priori* approach to define Regions of interest (ROIs). First, we focused our analysis on the right hemisphere due to converging evidence positing for its dominant role in face processing (Barton, Press, Keenan, & O'Connor, 2002; Barton, 2008; Eimer, et al., 2010; Gainotti, Barbier, & Marra, 2003; Sergent & Signoret, 1992). Second, our investigation focused on the *right lateral occipital cortex* (rLO) and the *right fusiform gyrus* (rFG), because, within the right hemisphere, these two regions are critically involved in face recognition, (Haxby, et al., 2000; Kanwisher, et al., 1997; Kanwisher & Yovel, 2006; Rossion, 2008; Rotshtein, Henson, Treves, Driver, & Dolan, 2005).

For each participant, the rLO and rFG were selected by manually drawing a mask on the inflated brain surfaces reconstructed from individual structural MRIs. In particular, rLO was selected by drawing the mask within the lateral surface of the right occipital lobe. The rFG was selected by drawing the mask on the ventral surface of the temporal lobe, including the fusiform gyrus. On average, masks had a mean area of 1066 mm^2 (SD = 86.05). MEG activity within rLO and rFG were then averaged between participants within each of the two groups[4].

Results: Magnetoencephalography (MEG) session

Behavioural data showed that performance on the Target task did not differ between controls (M = 96.03%, SD = 3.12) and CPs (M = 94.96%, SD = 2.41), (Mann-Whitney, p = .311), suggesting that all participants were paying attention to the task (Fig. 2a). This was consistent with expectations, as CPs can typically perform easy

[4] There were no differences between the sizes of the two ROIs within or between groups.

discrimination tasks. However, we do not know whether CPs were identifying the target face in the same way as controls - they could have focused on low-level characteristics of the target face.

The analysis of MEG data focused on the M170. For each participant, the M170 was computed by averaging MEG amplitude on the 24 ms around the biggest peak recorded between 130-180 ms post stimulus onset generated by S2. We performed a three factor (Category: face, place; Familiarity: face, place; Repetition: face, place) repeated measures ANOVA for each ROI and for each group separately (for total of four ANOVAs). We did not run a single ANOVA for each ROI, considering the "group" as the between factor, because we did not want to inflate Type I error by considering unequal group size (11 controls Vs 6 CPs). Instead, we first determined the presence/absence of a face specific M170 within both ROIs and both groups (by running four separate ANOVAs), and second, compared the face-selectivity of the M170 between controls and CPs by using a non-parametric test (Mann-Whitney).

In the rLO, controls showed a category effect for faces (M = 10.36, SEM = 0.83) generating greater activity than for places (M = 4.87, SEM = 0.70) ($F(1,10) = 60.41$, $p < .001$), and a repetition effect, with unrepeated stimuli (M = 7.75, SEM = 0.69) showing greater MEG activity than repeated stimuli (M = 7.45, SEM = 0.67) ($F(1,10) = 5.96$, $p = .035$). No other main effects or interactions were statistically significant (all *p*s > .05). In the rFG, controls showed a category effect for faces (M = 8.16, SEM = 1.06) generating greater activity than for places (M = 5.10, SEM = 0.94) ($F(1,10) = 6.88$, $p = .026$). No other main effects or interactions were statistically significant (all *p*s > .05).

The group of CPs also showed a category effect within the rLO, with faces (M = 6.32, SEM = 1.35) generating greater activity than places (M = 2.62, SEM = 0.57) ($F(1,5) = 14.03$, $p = .013$). The same category effect (i.e., activity greater for faces than

places) was found within rFG (Face: M = 3.05, SEM=1.16; Place: M = 2.74, SEM = 1.08) ($F(1,5) = 6.58$, $p = .05$). For both rLO and rFG no other main effects or interactions were statistically significant (all ps > .05).

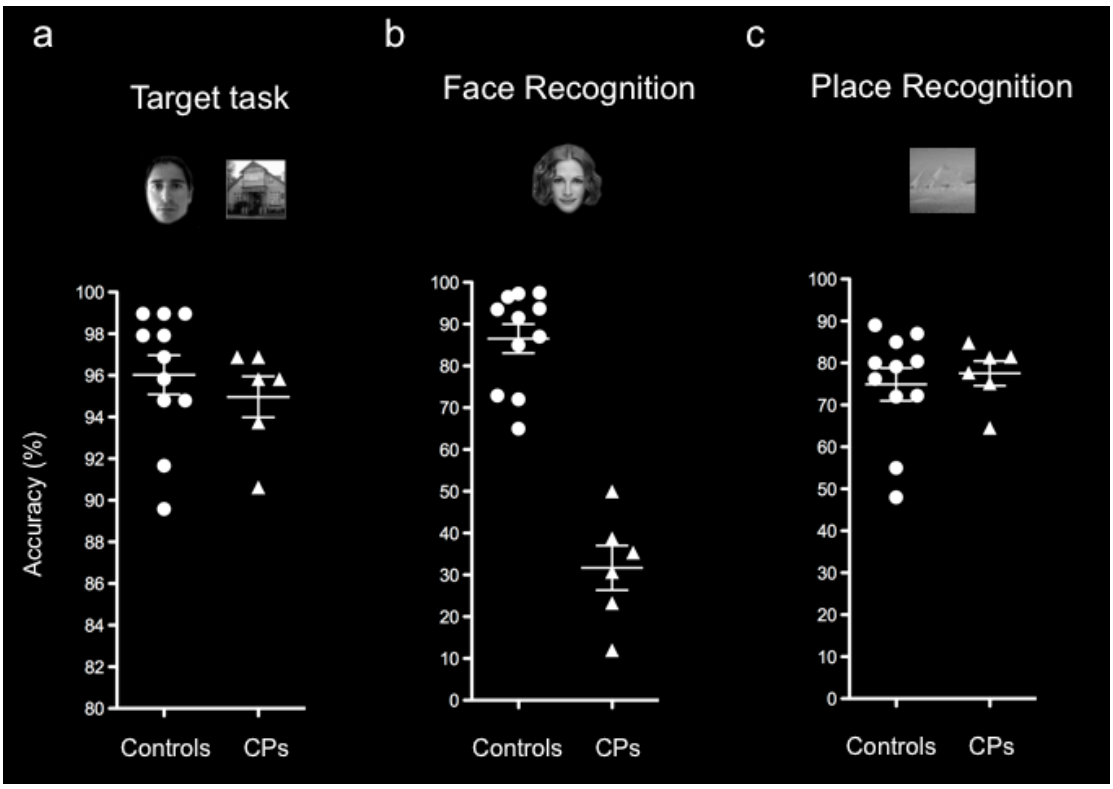

Figure 2. Behavioural performance of healthy controls and participants with CP on the (a) Target task, (b) Face recognition block, and (c) Place recognition block of the Picture recognition task. Indicated are means and standard errors of the mean (SEM). Results show that CPs (triangles) and controls (circles) show similar accuracy on the Target task and on the Place block of the Picture recognition task. The two groups differ in their ability to recognize familiar faces as shown on the Face block of the Picture recognition task.

Both controls and CPs showed neural activity that was greater for faces than places in both the rLO and rFG. To further demonstrate that the M170 in CPs shows typical characteristics, we calculated for each participant the "Face-selectivity" effect (Bentin, et al., 1999; Harris, et al., 2005). The Face-selectivity effect refers to the difference between the average MEG activity generated for faces and the average MEG activity generated for places. It is an indication of the face specificity of the M170. The

determination of the face-selectivity effect is important, since just the finding of an M170 within CPs may not be sufficient to demonstrate differences between groups. CPs may show an M170 for faces, but this might have smaller amplitude than in controls. This was not the case in these data. A Mann-Whitney test showed that the face-selectivity of the M170 did not differ between controls and CPs, both when recorded within the rLO (M ± SEM: Controls = 5.48 ± 0.70; CPs: 3.70 ± 0.99; p = .159) and rFG (Controls: M = 3.05, SEM = 1.16; CPs: M = 2.74, SEM = 1.08; p = .688) (Fig. 3). In summary, the group of individuals with CP show a normal M170.

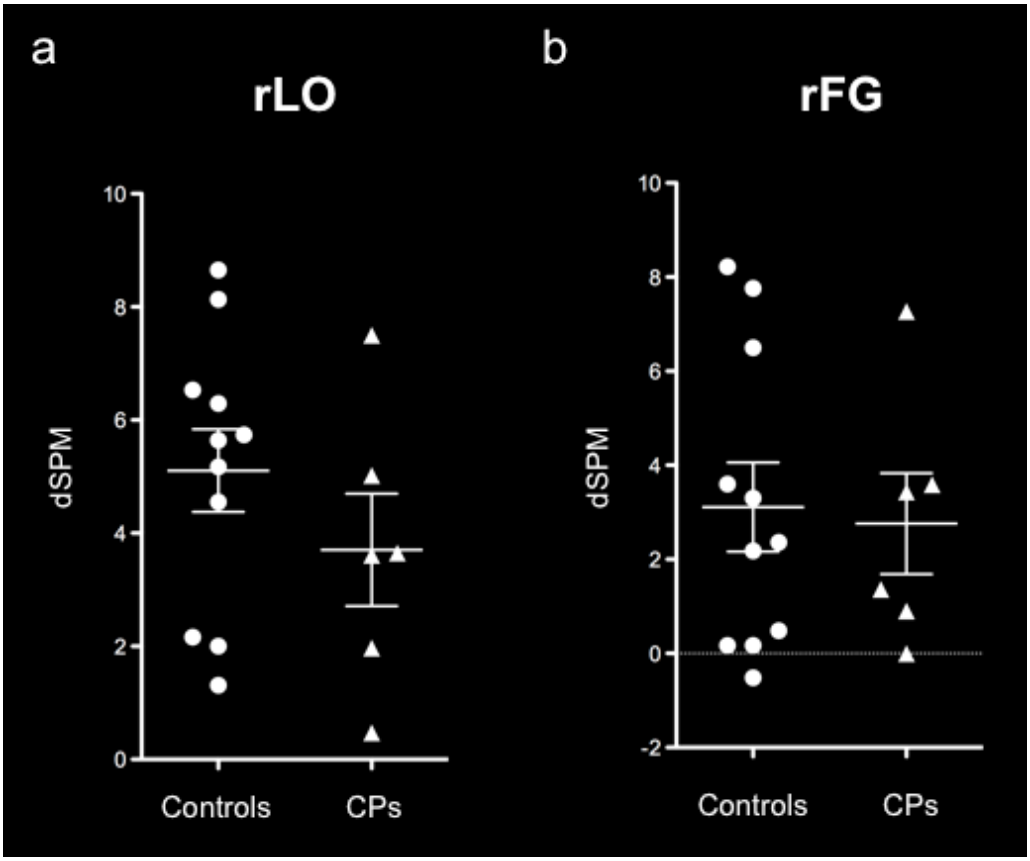

Figure 3. M170 face-selectivity effects (Face-Place MEG activity) within (a) rLO and (b) rFG show no difference between healthy controls (circles) and individuals with CP (triangles). On each graph the mean and the standard error of the mean are represented.

Picture recognition task and Name familiarity task

Following the MEG experiment, we assessed the ability of each participant to recognize the famous faces and places that were shown on the Target task. The aim was to test whether: (i) CPs (as expected) were poorer than controls in recognizing famous faces; and (ii) whether CPs' poor performance was general (i.e. involves both face and place recognition) or face specific.

In the "Picture recognition" task participants were instructed to type the name and/or specific semantic information about the person or place (a general description like "He is an actor" or "This tower is somewhere in Europe" was considered incorrect). The first block (Face recognition block) consisted of the 120 famous faces from the MEG experiment, the second block (Place recognition block) the 120 famous places. The task was programmed using SuperLab (Cedrus Corporation, 2007), and administered on a 15-inch Macintosh Power Book G4. In the "Name familiarity" task participants were asked whether they were familiar with the names of the 120 famous faces (Face block) and the names of the 120 famous places (Place block). Names belonging to Faces/places that were not familiar to participants were excluded from further analysis. Names were presented on a Microsoft Excel spreadsheet.

Control subjects were familiar with 90.10% (SD = 8.40) of the famous individuals, and recognized *86.54*% (SD = 11.51) of these faces, whereas prosopagnosics were familiar with 87.36% (SD = 8.54) of the famous individuals, but recognized only *31.70*% (SD = 13.10) of them. There was a statistically significant difference (Mann-Whitney, $p = .001$) between the recognition accuracy of control subjects and CPs, further confirming the difficulties people with CP have in face recognition (Fig. 2b).

Control subjects were familiar with 78.48% (SD = 12.52) of famous places, and recognized *74.90*% (SD = 12.88) of them, whereas people with CP were familiar with 82.22% (SD = 16.84) of the famous places, and recognized *77.53*% (SD = 7.18) of them. Controls and CPs did not differ in their ability to identify famous places (Mann-Whitney, p = .920) (Fig. 2c).

Overall, these results confirmed that: (i) people with CP were poorer than typical subjects in famous face identification; and (ii) the visual recognition difficulties in this group of CPs were not general, but specific to faces[5]. This is consistent with reports of difficulties people with CP experience in everyday life.

Correlating behavioural performance and MEG

The correlation between brain activity and behavioural performance represents a very important and sensitive procedure for neuroimaging investigations (Rotshtein, et al., 2007). Since CPs show variability in holistic/configural and featural processing (see Table 1), people with CP represent a unique opportunity to shed light into the coupling between brain activity and behaviour.

To understand the role the M170 plays in face processing, we investigated the correlation between the amplitude of the M170 face-selectivity effect in the rLO and the rFG, and the inversion effect in the spacing and feature conditions of the Jane task. Results showed a correlation between the face-selectivity effect of the M170 within rLO (rLO-M170) and inversion effect z-scores on the "spacing" set of the Jane task (r = 0.82; p = .044), indicating a relation between holistic/configural processing and MEG activity in the lateral occipital cortex. There was also a correlation between the face-

[5] Note however that CPs can show variability in the face-specificity of their recognition problems (Duchaine, Germine, & Nakayama, 2007; Wilson, Palermo, Schmalzl, & Brock, In press).

selectivity effect of the M170 recorded within rFG (rFG-M170) and inversion effect (z-scores) on the "feature" set of the Jane task (r = -0.89; *p* = .017) (see Fig. 4), indicating a relationship between feature processing and MEG activity in the lateral occipital cortex[6]. Both statistically significant correlations indicated a similar pattern: the more the M170 was face-sensitive, the more behavioural performance approached normal (typical) values[7].

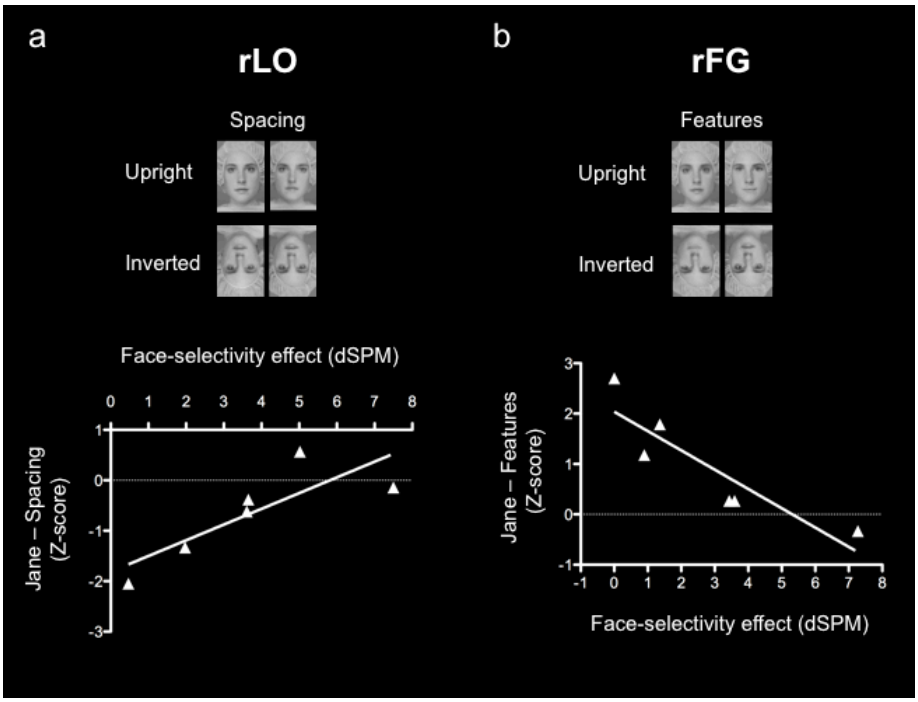

Figure 4. Correlations between the face-selectivity of the M170 in CP and the face inversion effect (z-scores) on the Jane task. Each triangle represents one participant with CP. Results show a) a positive correlation between the face-selectivity of the M170 and inversion effect on the *spacing* subset of the Jane task within the rLO and a b) negative correlation between the face-selectivity of the M170 and inversion effect on the *features* subset of the Jane task within the rFG.

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[6] There was no correlation between rLO-M170 and features processing (r = 0.48, *p* = .335), nor correlation between rFG-M170 and holistic/configural processing (r = -0.65, *p* = .165).

[7] There was no correlation between face memory (for both familiar and unfamiliar faces) and MEG activity recorded within either rLO or rFG. Even though the lack of relation between M170 and face memory is in agreement with Harris et al. (2005), it could however be the consequence of the small variability shown by CPs on the CFMT and the MFFT-08 and/or of the small number of CPs (see supplementary Table 2).

Discussion

People with congenital prosopagnosia (CP) have never acquired typical face processing skills despite normal cognitive functioning, and despite no obvious sign of brain lesion (Behrmann & Avidan, 2005; Duchaine & Nakayama, 2006). Although CPs have clear behavioural impairments in face processing, the current results demonstrated that early M170 responses do not differ between individuals with CP and healthy control subjects. We were able, however, to use the individual variation in behavioural performance on the Jane task among our CPs to explore the functions reflected by the M170 in detail. The correlation between the M170 and behavioural performance demonstrates that the M170 generating within the lateral occipital cortex (rLO-M170) codes for holistic/configural processing, whereas the M170 generating within the right fusiform gyrus (rFG-M170) codes for featural processing.

This study has shown, both in controls and CPs, the existence of face-selective neural activity (M170) within rLO (rLO-M170) and rFG (rFG-M170). This is consistent with previous evidence describing two anatomical generators (i.e. the inferior lateral occipital lobe and the fusiform gyrus) for the M170 (Itier, et al., 2007; Wantabe, et al., 2003). Furthermore, the results revealed that, on average, the face-selectivity of the M170 in CP does not differ from typical subjects. These findings indicate that neuromagnetic activity generated within rLO and rFG at around 170 ms post stimulus onset is face-selective even in people with lifelong difficulties in face identification. The M170 therefore does not represent the neurophysiological correlate of CP.

The lack of familiarity effects for face stimuli in both controls and CPs agrees with findings indicating familiarity effects occur later (e.g., 400 ms) than the M170 (Eimer, 2000; Harris & Aguirre, 2008). Our study indicated that in typical subjects the rLO-M170 showed a repetition effect, with reduced amplitude for repeated than

unrepeated stimuli. This may reflect a general adaptation phenomenon potentially leaded by low-level features of the stimuli. Unlike controls, people with CP did not show a general repetition effect of the rLO-M170. The reasons for this are not completely clear, but could be due to reduced power for the CP group (6 CPs compared with 11 controls). For both controls and CPs however, repetition did not affect the rFG-M170. This lack of a repetition effect in the FG seems to be in disagreement with previous findings that found repetition effects within this region (Williams, Berberovic & Mattingley, 2007). There is however a possible reason behind this apparent discrepancy. Previous research mainly used functional Magnetic Resonance Imaging (fMRI), which represents an indirect measure of neural activity with a low temporal resolution. In contrast, the current study adopts MEG, which represents a direct measure of brain activity and has an excellent temporal resolution. The discrepancies between fMRI and MEG findings might be due to the proprieties of the technology adopted. Due to its poor temporal resolution, it might be the case that previous repetition effects found using fMRI reflect neural activity that occurs after 170 ms post stimulus onset. In fact, it is likely that neural activity within the rFG may be mediated by repetition only after around 250 ms post stimulus onset, since at that timecourse, interactions between stimuli repetition and familiarity have been shown, indicating that access to specific identities occurs after the M170 (Schweinberger, Pickering, Jentzsch, Burton, & Kaufmann, 2002). Future research will need to clarify whether different MEG components (i.e. M250, M400), sensitive to the familiarity of face stimuli (Eimer, 2000; Harris & Aguirre, 2008; Schweinberger, et al., 2002), may show abnormal features in CP.

One of the ultimate goals of neuroimaging is to establish the relationship between behaviour and neural activity. In fact, much information about neural coding can be

missed if the relation between behavioural performance and neural activity is not taken into account (Rotshtein, et al., 2007). The current study sheds light on the coupling between brain activity and behavioural performance by correlating face perception performance with MEG component amplitude. The most important finding of this investigation is that the two neural generators of the M170 reflect two different roles in face processing: the rLO-M170 codes for holistic/configural processing, whereas the rFG-M170 codes for feature processing. The M170 is therefore not a single component. Our results are generally in line with previous MEG findings showing the engagement of the M170 in both holistic/configural and feature processing (Harris & Aguirre, 2008). The improved spatial resolution in this MEG study due to coregistration of MEG data with structural MRIs allowed us to demonstrate the differential role played by the rLO and the rFG in face processing. This result is in agreement with previous work showing that holistic/configural and feature processing are coded by different neural populations in monkeys (Freiwald, Tsao, & Livingstone, 2009).

Previous research using fMRI has also investigated the neural correlates of holistic/configural versus feature processing in humans. Some authors suggest that the lateral occipital lobe, and in particular the occipital face area (OFA) (Gauthier, et al., 2000), is mainly engaged by feature processing (Yovel & Kanwisher, 2005), whereas others suggest this region is involved in both holistic/configural and feature processing (Harris & Aguirre, 2008; Rotshtein, et al., 2007; Schiltz & Rossion, 2006). There is general agreement, however, on the role played by the fusiform gyrus, and in particular the fusiform face area (FFA) (Kanwisher, et al., 1997), in both holistic/configural and feature processing (Harris & Aguirre, 2008; Rotshtein, et al., 2007; Schiltz & Rossion, 2006; Yovel & Kanwisher, 2005). The current results are at least partially inconsistent with the fMRI research. One reason may be that MEG and fMRI measure different

neural signals (Logothetis, 2008; Singh, 2006), and it may be therefore misleading to directly compare fMRI with MEG findings. For example, it has been shown that face inversion causes a larger N170, but a smaller fMRI signal (Yovel and Kanwisher, 2004). To shed light on these issues, future investigations will need to compare MEG and fMRI activity generated by performing the same task.

Conclusions

In summary, we have demonstrated that both the rLO and the rFG are sources of a face-sensitive M170 signal. Interestingly, people with CP, who experience selective lifelong difficulties in face recognition showed a typical M170 within both these brain regions. The main finding of this study is that the M170 is not a single component. By considering the behavioural variability of CPs we demonstrated that the rLO and the rFG code for different aspects of face processing: the rLO is crucially involved in holistic/configural processing, whereas the rFG is crucially involved in featural processing. Despite much previous research on the M170, this result provides the first evidence of the relationship between this reliable face-sensitive component and behavioural performance, by indicating that the neural activity generating at around 170 ms post stimulus onset within the lateral occipital cortex and the fusiform gyrus mediate different behaviours.

Acknowledgments

We wish to thank members of the Kanwisher Lab, Anina Rich, Patrik Vuilleumier and Rachel Robbins for their insightful comments on this work. We wish to also thank Loes Koelewijn, Graciela Tesan, Melanie Reid and Christopher Sewell for the support provided in the MEG data acquisition and processing, and C. Ellie Wilson for the support given in participants' recruitment. Stimuli for the Jane task were provided by Daphne Maurer (McMaster Visual Development Lab). This work was supported by the Macquarie University Research Excellence Scholarship (iMQRES) to D.R. M.A.W. is supported by the Australian Research Council Fellowship Schemes (DP0984919).

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Supplementary material

Supplementary Methods

Jane task analysis (control subjects)

A 2 X 3 repeated measures ANOVA on accuracy, with orientation (upright, inverted) and set (spacing, features, contour) as within-subject factors, revealed an orientation effect ($F(1, 54) = 144$, $p < .001$), a set effect ($F(2, 108) = 75.81$, $p < .001$), and an orientation by set interaction ($F(2, 108) = 18.43$, $p < .001$). In the upright condition a set of pairwise comparisons (Bonferroni corrected for multiple comparisons) showed that accuracy was greater on the feature set (M = 90% SD = 9.60) than on the spacing (M = 76.7% SD = 12.83) ($p < .001$) and contour (M = 80%, SD = 10.30) ($p < .001$) sets, whereas the spacing and contour conditions did not differ ($p = .226$).

In the inverted condition, accuracy on the feature set (M = 83.3%, SD = 11.50) was significantly higher than on the spacing (M = 60%, SD = 10.40) ($p < .001$) and contour (M = 66.7%, SD = 10.40) ($p < .001$) sets. Accuracy on the contour condition set was significantly higher than the spacing set ($p = .002$). Additional planned contrasts were calculated to investigate the effect of inversion on all the three sets. Results showed that the inversion effect of the feature set (M = 6.7%, SD = 11.06) was significantly smaller than the inversion effect on the spacing set (M = 20%, SD = 14.10) ($p < .001$) and the contour set (M = 16.7%, SD = 12.93) ($p < .001$). There was no difference between the inversion effect of the spacing and contour conditions ($p < .085$).

Supplementary tables

Supplementary Table 1. Studies investigating the face-selectivity of the N170 and/or the M170 in different case studies of congenital prosopagnosia. "Face-sensitive" N/M170 indicates a component that shows bigger activity for face compared to object perception. "Not-selective" indicates an ERP/MEG component that has similar amplitude for face and object processing (i.e. object perception generates a component that is as strong as the one generated by face perception).

Study	Participant	N170	M170
Bentin, Deouell & Soroker (1999)	YT	not-selective	n.a.
Kress & Daum (2003)	GH	not-selective	n.a.
	SO	not-selective	n.a.
Harris, Duchaine & Nakayama (2005)	EB	n.a.	not-selective
	KNL	n.a.	not-selective
	NM	n.a.	not-selective
	ML	face-selective	face-selective
	KL	face-selective	face-selective
Bentin, DeGutis, D'Esposito & Robertson (2007)	KW	not-selective	n.a.
DeGutis, Bentin, Robertson & D'Esposito (2007)	MZ	not-selective	n.a.
Minnebusch, Suchan, Ramon & Daum (2007)	ET	not-selective	n.a.
	LT	face-selective	n.a.
	NN	face-selective	n.a.
	TP	face-selective	n.a.

Supplementary Table 2. Correlation between MEG activity (M170 face-selectivity) and performance on the face memory tasks. Results showed no correlation between famous face memory (as assessed with the MACCS famous face task-2008; MFFT-08) and MEG activity within both rLO and rFG. Furthermore there was no correlation between memory for unfamiliar faces (as assessed with the Cambridge face memory test; CFMT) and MEG activity within both rLO and rFG.

	Face memory			
	MFFT-08		CFMT	
	r	*p*	r	*p*
rLO	-0.263	.615	0.037	.944
rFG	-0.062	.908	0.499	.313

Chapter 5

Multi-voxel pattern analysis of fMRI data reveals abnormal anterior temporal lobe activity in congenital prosopagnosia

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Multi-voxel pattern analysis of fMRI data reveals abnormal anterior temporal lobe activity in congenital prosopagnosia

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Abstract

The typical ability to identify faces is mediated by a network of cortical and subcortical brain regions. It is still a matter of debate which of these regions represents the functional substrate of congenital prosopagnosia (CP), a condition characterized by the lifelong impairment in face recognition. Here, using multi-voxel pattern analysis of fMRI data, we demonstrate that the pattern of neural activity within the right anterior temporal cortex is less face-selective in people with CP than healthy controls. Therefore, the right anterior temporal region appears to be the neural locus of face-specific difficulties in CP. These data indicate that the right anterior temporal cortex represents a crucial node for typical face processing.

Keywords: body perception, congenital prosopagnosia, face perception, fMRI, object perception.

Most of us are able to recognize thousands of familiar faces with ease. The fusiform gyrus (FG) and the anterior temporal lobe (AT) are part of a neural network that supports this extraordinary ability (Haxby et al. 2000; Ishai 2008; Kanwisher 2010). Neural activity (as measured with fMRI) within the FG and the AT correlates with the behavioural measures of face recognition ability (Furl et al. in press; Kriegeskorte et al. 2007; Yovel and Kanwisher 2005) and brain injuries encompassing one or both of these regions often result in debilitating problems in face identification (i.e. acquired prosopagnosia) (Barton 2008; De Renzi et al. 1991; Evans et al. 1995; Gainotti 2007; Williams et al. 2006).

Although the majority of humans have normal face recognition ability, about 2-3% of the general population have specific difficulties in recognizing faces in the context of otherwise intact sensory, neurologic and intellectual functioning (Bowles et al. 2009; Kennerknecht et al. 2006; Wilmer et al. 2010). This condition is known as developmental or *congenital prosopagnosia* (CP) (Behrmann and Avidan 2005; Duchaine 2000; Duchaine and Nakayama 2006; McConachie 1976; Rivolta et al. 2010; Schmalzl et al. 2008). Recent research has found evidence for a volume reduction within the anterior temporal lobe (Behrmann et al. 2007; Garrido et al. 2009) and reduced connections (white matter tracts) between posterior and anterior brain regions (Thomas et al. 2009).

While there have been advances in the elucidation of the structural (anatomical) characteristics of CP, the neuro-functional correlates of the condition are far from clear. Various investigations of CP report typical face-selective response to faces in the FG (Avidan and Behrmann 2009; Avidan et al. 2005; Hasson et al. 2003). In addition, studies investigating "repetition suppression" (Grill-Spector and Malach 2001), which refers to a diminished fMRI signal to the repeated presentation of face stimuli,

demonstrate normal neural suppression to repeated faces in CP (Avidan and Behrmann 2009; Avidan et al. 2005; Furl et al. in press). Taken together, these findings indicating normal FG activity in CP suggest that this area may be necessary, but not sufficient, for normal face recognition (Avidan and Behrmann 2009; Rossion 2008). As such, regions other than the FG, such as the AT, may play an important role in the behavioural face recognition difficulties underlying CP.

We examined the neuro-functional aspects of CP by investigating the pattern of neural activity elicited by the processing of different categories of visual stimuli within the AT and the FG. We adopted a multivariate-pattern analysis (MVPA) approach of fMRI data (Cox and Savoy 2003; Haynes and Rees 2006; Norman et al. 2006). MVPA enables the investigation of neural representations by looking at the pattern of voxel activity within the brain (Mur et al. 2009). We performed MVPA on four regions of interest (ROIs): the right and left anterior temporal lobe (R-AT; L-AT), and the right and left fusiform gyrus (R-FG; L-FG).

The selection of these four ROIs reflects previous evidence showing their functional involvement in face processing (Gorno-Tempini et al. 1998; Kanwisher et al. 1997; Kriegeskorte et al. 2007; Rajimehr et al. 2009; Sergent et al. 1992; Sergent and Signoret 1992; Sugiura et al. 2001; Tsukiura et al. 2006; Williams et al. 2006). Even though previous univariate fMRI studies showed typical FG functioning in CP, MVPA may potentially show differences in the neural activity between controls and CPs that previous research was not able to detect. Since there is a volume reduction of the AT regions in CP (Behrmann et al. 2007), and injury to the AT causes face-specific difficulties (Williams et al. 2006), we hypothesized functional differences between typical subjects and CP in this region.

Method

Participants

Ten typical subjects (4 Females, Mean age = 34, Range: 27-55, SD = 9.47) and seven people with CP (4 Females, Mean age = 39, Range: 22-58, SD = 9.40) completed the experiment. All participants but one with CP were right handed, all had normal or corrected to normal vision, and none had any history of neurological or psychiatric conditions. All participants provided written consent after the experimental procedure was explained.

All participants with CP were recruited through the MACCS prosopagnosia database (https://www.maccs.mq.edu.au/research/projects/prosopagnosia/register). All CPs registered on the database because they were experiencing recognition difficulties in everyday life. Details about CPs' behavioural difficulties and selection criteria are specified in the supplementary material.

Experimental tasks

During the experiment participants were presented with visual stimuli belonging to four different categories: faces, headless bodies, individual body-parts (hands and feet) and objects. All stimuli were greyscale photographs edited with Adobe Photoshop editing software and matched for brightness and contrast. The set of stimuli included a total of 240 images, 60 for each of the four stimulus categories (half of the "face" and "body" stimuli were females and half males). Stimuli covered approximately 4.1° of visual angle.

The presentation of stimuli during the fMRI acquisition was programmed with Presentation software (Neurobehavioral Systems, Albany, CA; http://www.neurobs.com/) and run on a 15-inch Macintosh Power Book with screen

resolution set to 1280 x 854 pixels. Stimuli were back-projected via a projector onto a screen positioned 1.5 m behind the fMRI scanner, and participants viewed the screen through a mirror mounted on the headcoil and positioned at 10 cm distance from their head. An optic fibre button box was used to record the participants' responses.

Participants' brain activity was recorded in 8 functional runs with the duration of 336 sec each. During each run, 114 functional scans (TRs) were acquired. The stimulus categories were presented in a blocked design with a total of 32 blocks of 16 sec each. Each of the 32 blocks contained 16 stimuli of a specific category. Stimuli were presented in the centre of the screen for 500 ms with a 500 ms inter-stimulus interval (ISI). The maintenance of attention to the stimuli was ensured by presenting participants with a standard "one-back" task. The task required pressing a button whenever a particular image was repeated consecutively (10% of the trials was a repeat). The order of blocks was counterbalanced across subjects. In addition, a fixation block (where a fixation cross was presented in the middle of the white screen) was presented at the beginning of each block and at the end of each fourth block (which corresponded to the end of the functional run).

MRI data acquisition

Functional images were acquired with a 3 Tesla Philips scanner at St Vincent's Hospital (Sydney, New South Wales, Australia). At the beginning of the experimental session a high-resolution anatomical scan was acquired for each participant using a 3D-MPRAGE (magnetization prepared rapid gradient echo) sequence. Subsequently, high-resolution functional scans were obtained using an 8-channel head coil and a gradient echo planar imaging (EPI) sequence (114 time points per run; Inter-scan interval: 2 sec, TR = 3000 ms, TE = 32 ms, voxel size = 1.4 x 1.4 x 2.0 mm). Each volume contained

24 slices with a thickness of 1 mm and an interslice gap of 0.2 mm. The 24 oblique axial slices were aligned approximately parallel to the anterior / posterior commissure line.

ROI selection

We selected four regions of interest (ROIs) for each participant: the left midfusiform gyrus (L-FG), the right midfusiform gyrus (R-FG), the left anterior temporal lobe (L-AT) and the right anterior temporal lobe (R-AT). The selection procedure for these ROIs was based on participants' structural MRIs and was performed by using MRIcro (http://www.cabiatl.com/mricro/). Both the midfusiform and anterior temporal ROIs were selected by masking voxels with a spherical mask of 2 cm radius. The L-FG and R-FG were selected by placing the mask in the centre of the temporal lobe (including the fusiform gyrus). The L-AT and R-AT regions were selected by placing the mask in the centre of the temporal poles (rostral to the ears canals) (Fig. 1).

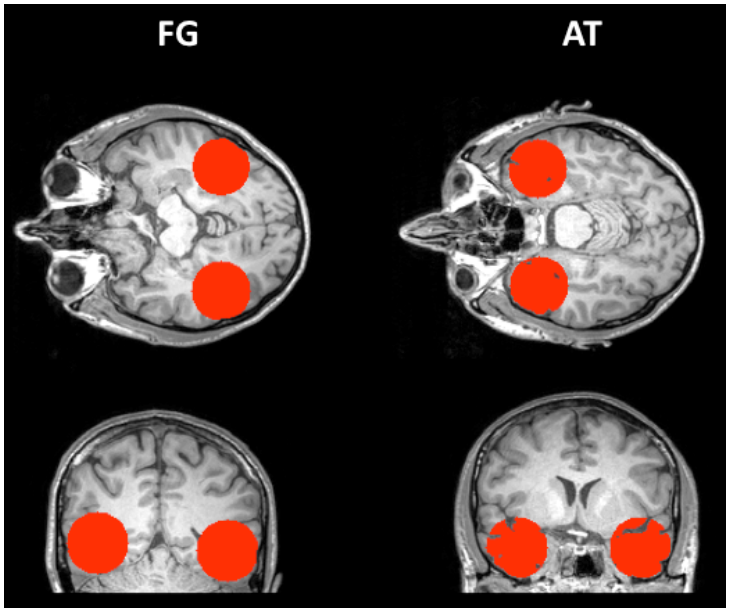

Figure 1. Regions of interest (ROIs) selection. The fusiform gyrus ROIs (FG) are shown on the left and the anterior temporal ROIs (AT) are shown on the right.

The adoption of the same mask for all participants guaranteed that all ROIs were made of the same number of voxels. Controlling for this factor is important since MVPA performance is affected by the number of voxels included in the analysis (Cox and Savoy 2003).

Data processing and Pattern classification analysis

Functional scans were converted into "image files" with MRIcro. No normalization, spatial smoothing or other transformation were applied before multivariate analysis (Haxby et al. 2001). We then used a multivariate-pattern analysis (MVPA) method to investigate the pattern of responses across voxels in each of the four ROIs. MVPA enables the investigation of neural representations by considering the blood-oxygen-level-dependent (BOLD) signals distributed over a large number of voxels. MVPA was carried out using the MVPA toolbox for MATLAB (MathWorks, Inc., Natick, MA, USA) created by the Princeton Computational memory lab (http://code.google.com/p/princeton-mvpa-toolbox/wiki/Main). This toolbox involves the use of neural networks to determine how patterns of multiple voxels fMRI activity relate to different experimental conditions.

We adopted a three layers neural network with input, hidden and output units. The number of input units was determined by the "feature selection" (see below), whereas output units were 4 (one for each stimulus category). We added 10 hidden units to increase the sensitivity of the classifier (Norman et al. 2006). The neural network implemented the "backpropagation" algorithm for the weights updating. The dependent factor of our analysis was the *accuracy* of a neural network (classifier) to determine the category of a test item. Accuracy is taken as an index of voxels-pattern distinctiveness for a particular category in a particular ROI. As such, high accuracy values suggest a

distinctive voxel pattern for a specific category, whereas lower accuracy suggests non-distinctive (or less distinctive) voxels pattern for a particular class of stimuli.

We applied MVPA to the fMRI data of each individual subject, and results were then averaged within and between groups. The following steps were carried out for MVPA analysis: First, for each subject, we applied a *feature selection* procedure to select, within each ROI, the voxels to use for training the classifier (and to consequently reduce the number of uninformative voxels). This was achieved by performing an ANOVA on each voxel and for each ROI. Voxels showing a *p* value below .05 (not corrected for multiple comparisons), indicating a general effect of Category, were selected for the training (these voxels represented the input units of the classifier, see above), whereas voxels showing a *p* value above .05 were discarded. This procedure represents a key step in machine learning since it has been shown that uninformative voxels (redundant voxels) decrease classifier accuracy (Norman et al., 2006).

We then applied a *N-minus-one (leave-one-out) cross validation procedure*. This procedure consists in running a separate classifier for N times, where N is the total number of runs. Each time a separate classifier is run, it is trained using the pattern of activity (determined by the feature selection, which, in turn, is run N times) of N -1 runs and tested on the remaining - never shown to the classifier - run. Given that the number of runs in our experiment was 8, the cross validation was performed eight times for each participant.

On each iteration, the classifier was trained using the pattern of voxel activity shown by the TRs of seven runs and tested on the remaining one, thus guaranteeing the independence between TRs used for training and TRs used for testing / generalization. For each participant, the classifier's performance for each of the four categories was calculated by averaging the performance of the eight iterations. This resulted in a

"confusion matrix", which indicated the classifier's performance for each of the four categories of interest. Comparisons of performance between and within groups were performed using SPSS 18.0 (SPSS Inc., Chicago, IL, USA).

Results

Behavioural performance

Ten healthy controls and seven people with CP were presented with visual stimuli from four different categories (faces, headless bodies, body parts and objects) while their blood oxygen level dependent (BOLD) activity was recorded using a 3T Phillips fMRI scanner and a 12-channel head coil. Participants had to press a button whenever a stimulus was repeated twice (one-back task). The one-back task was administered to ensure that participants were paying attention to the stimuli.

Performance on the one-back task was analyzed by running a repeated measures ANOVA with Group (controls, CPs) as a between-subject factor and Category (face, body, body part, object) as a within-subject factor. The absence of the main effect of Group showed that typical subjects (M = .771, SEM = .185) and CPs (M = .722, SEM = .221) performed similarly on the one-back task ($F(1,15) = 2.9$, $p = .109$). In addition, overall performance was not affected by the Category of the stimuli ($F(3,45) = 1.79$, $p = .163$), and there was no Category by Group interaction ($F(3,45) = 1.32$, $p = .277$) (Table 1). These results showed that behavioural performance on the one-back task did not differentiate between typical subjects and CPs. This is not surprising, since it was a simple task, which could be completed by simply attending to only part of the image.

fMRI analysis

The processing of fMRI data was completed by using MVPA, which consisted in training a classifier to differentiate between the neural activity associated with the perception of different categories of visual stimuli (see Methods Section). For each participant and for each ROI (see Methods Section for selection details), we tested whether the performance of the classifier for each of the four categories was above chance (chance = 0.25) using a series of one-sample *t*-tests (1-tailed). Results showed that, for both controls and CPs, and within all ROIs, the classification of all stimuli categories was above chance (all Ps < .001). These results indicated that both the fusiform gyrus and the anterior temporal cortex contain visual representations of face, objects, bodies and body parts.

Next, for each of the four ROIs, we ran a repeated measure ANOVA with Category (face, body, body part, object) as a within-subject factor and Group (controls, CPs) as a between-subject factor. Post-hoc comparisons (with alpha corrected for multiple comparisons) were calculated to investigate the significant interactions.

MVPA in left fusiform gyrus (L-FG)

In L-FG there was no difference between controls (M = .726, SEM = .033) and CPs (M = .668, SEM = .039) in their overall accuracy ($F(1,15) = 1.30$, $p = .273$). There was a significant main effect of category ($F(3,45) = 35.98$, $p < .001$), where face classification (M = .760, SEM = .028) was more accurate than body (M = .621, SEM = .025) ($p < .001$) and body part (M = .673, SEM = .029) ($p < .001$) classification, but was similar to object classification (M = .773, SEM = .026) ($p = .331$). Body part classification was higher than body classification ($p = .042$) and object classification was higher than both body ($p < .001$) and body part ($p = .004$) classification (Fig. 2).

These results agree with previous research showing face, object and body sensitive neural populations within the L-FG (Kanwisher 2010), and typical L-FG activity in people with CP (Avidan and Behrmann 2009).

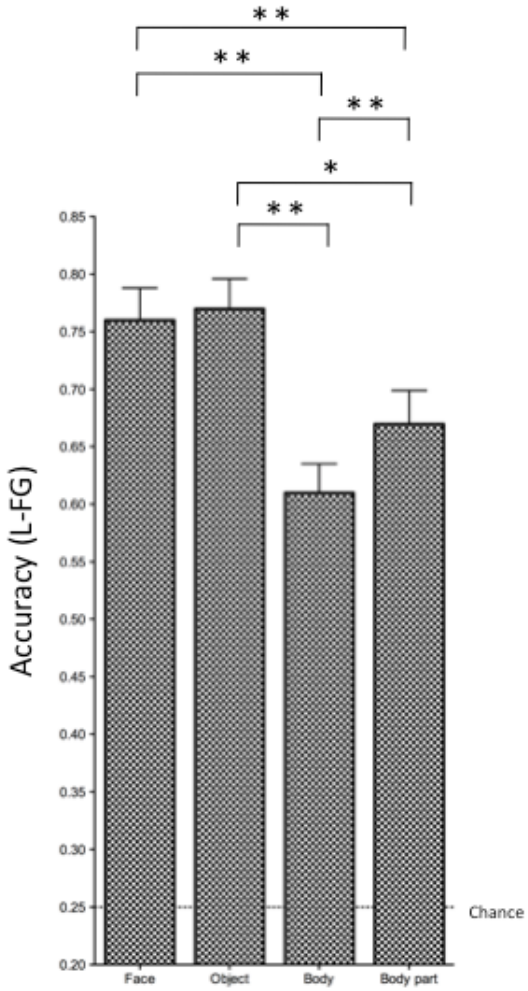

Figure 2. Classifier performance on the left fusiform gyrus (L-FG). Performance indicates the accuracy collapsed between controls and CPs. Means as well as and standard errors of the means (SEM) are displayed (∗∗ p ≤.001; ∗ *p* ≤ .05).

MVPA in right fusiform gyrus (R-FG)

The overall classification in controls (M = .776, SEM = .025) and CPs (M = .728, SEM = .029) did not differ ($F(1,15) = 1.59$, $p = .226$) in the R-FG. There was a category effect ($F(3,45) = 49.25$, $p < .001$), with face classification (M = .838, SEM = .020) being significantly more accurate than the classification of body (M = .694, SEM = .023) ($p < .001$), body part (M = .685, SEM = .023) ($p < .001$) and object (M = .789,

SEM = .020) (p = .028). Object classification was higher than body (p = .001) and body part (p < .001) classification. There was no difference between body and body part classification (p = 1) and there was no category by group interaction ($F(3,45) = .195$, p = .899) (Figure 3).

These results are in agreement with previous works showing the pivotal role played by R-FG in face processing (Kanwisher 2010), its typical functioning in CP (Avidan and Behrmann 2009), and the presence of object and body representations within the fusiform gyrus (Bar et al. 2006; Peelen and Downing 2007).

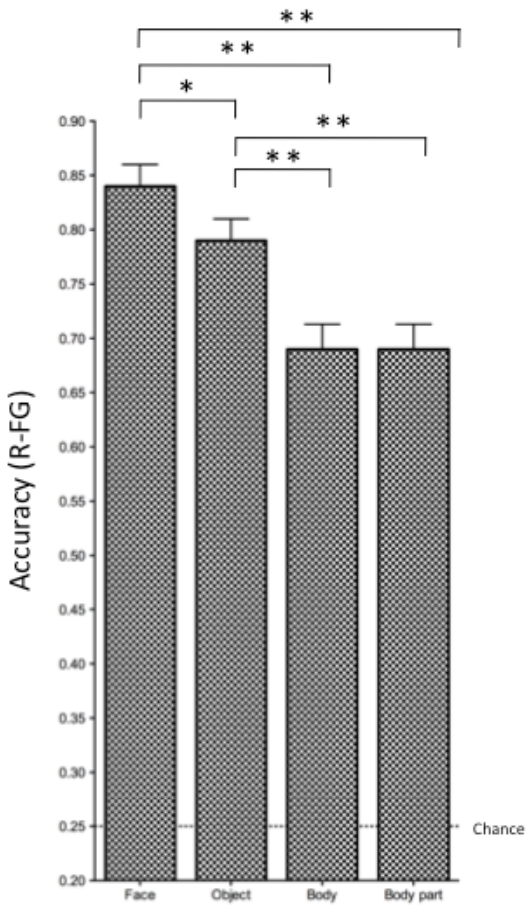

Figure 3. Classifier performance on the right fusiform gyrus (R-FG). Performance indicates the accuracy collapsed between controls and CPs. Means as well as and standard errors of the means (SEM) are displayed (** p ≤.001; * p ≤ .05).

MVPA in left anterior temporal lobe (L-AT)

Analysis of L-AT showed that, overall, classification accuracy was similar between CPs (M = .512, SEM = .024) and controls (M = .530, SEM = .020) ($F(1,15) = .720$, $p = .409$). There was a Category effect ($F(3,45) = 16.26$, $p < .001$) with face classification (M = .591, SEM = .019) showing better accuracy than body (M = .493, SEM = .018) ($p < .001$) and body part (M = .473, SEM = .020) ($p < .001$) classification, but similar accuracy to object classification (M = .544 , SEM = .020) ($p = .357$). There was no difference between body and body part ($p = 1$) classification. Furthermore, there was no difference between object and body classification ($p = .057$) or between objects and body parts ($p = .056$). There was no Category by Group interaction ($F(3,45) = 2.30$, $p = .09$) (Figure 4).

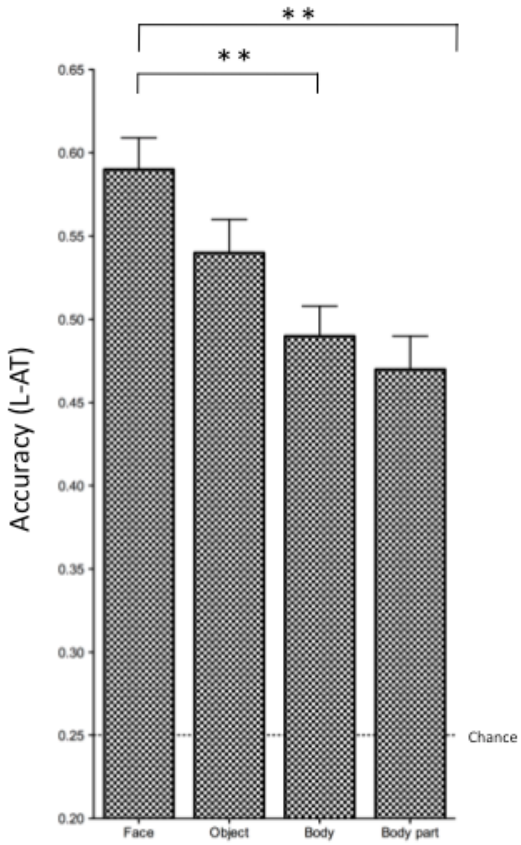

Figure 4. Classifier performance on the left anterior temporal (L-AT). Performance indicates the accuracy collapsed between controls and CPs. Means as well as and standard errors of the means (SEM) are displayed (** p ≤.001).

In summary, these results show that the pattern of neural activity within the L-AT did not differentiate between typical subjects and CPs. Since people with CP do not have problems in identifying people by their names, this result is in agreement with previous findings showing L-AT involvement in name rather than face processing (Glosser et al. 2003; Snowden et al. 2004).

MVPA in right anterior temporal lobe (R-AT)

Analysis within the R-AT showed that the overall classification accuracy in controls and CPs did not differ. Importantly however, we found a Category by Group interaction ($F(3,45) = 2.80$, $p = .05$) in the R-AT. The analysis of contrasts showed that the difference between face and body part classification (Controls: M = .144, SEM = .011; CPs: M = .106, SEM = .012) ($F(1,15) = 8.46$, $p = .001$) and the difference between face and object classification (Controls: M = .050, SEM = .011; CPs: M = .034, SEM = .011) ($F(1,15) = 4.86$, $p = .043$), was larger in controls than in CPs (Fig. 5). No other contrasts were statistically significant (all Ps > .05).

Additional ad-hoc comparisons showed that, in controls, face categorization (M = .648, SEM = .026) was significantly higher than the classification of body (M = .508, SEM = .026) ($p < .001$), body part (M = .463, SEM = .028) ($p < .001$) and object (M = .577, SEM = .025) ($p = .001$) classification. In addition, object classification was bigger than body ($p = .022$) and body part classification ($p < .001$). There was no difference between body and body part classification ($p = .357$) (Fig. 6). In CPs, face classification performance (M = .575, SEM = .031) was only bigger than body part classification (M = .479, SEM = .034) ($p < .006$). There was no statistical difference between the classification of face and the classification of body (M = .493, SEM = .031) ($p = .067$) or object (M = .555, SEM = .030) ($p = 1$). Object classification was similar to body ($p =$

.125), but bigger than body part (p = .026). Body and body part did not differ (p = 1) (Fig. 6).

The ease typical individuals show in face processing was reflected in the greater face classification than non-face classification performance. In contrast, CPs' poor face identification ability was reflected in the face classification that did not differ from object and body classification performance[1].

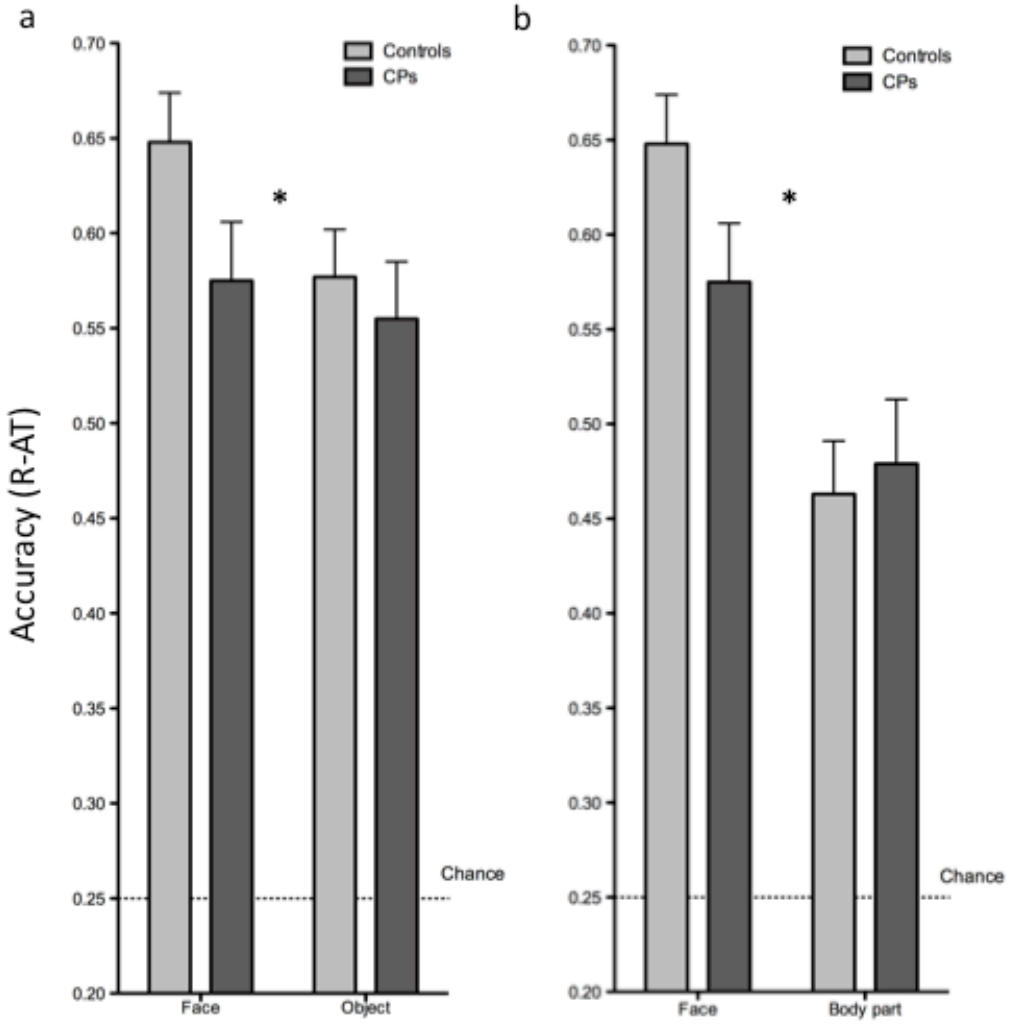

Figure 5. Category by Group interaction in the R-AT. (a) The difference between face and object classification is bigger in controls than in CPs. (b) The difference between face and body part classification is bigger in controls than in CPs. Means as well as and standard errors of the means (SEM) are displayed (∗ $p \leq .05$).

[1] For each ROI we calculated whether there was any correlation between classifier performance and accuracy on the One-back task. Results did not show any correlation between the two measures (all P's > .05).

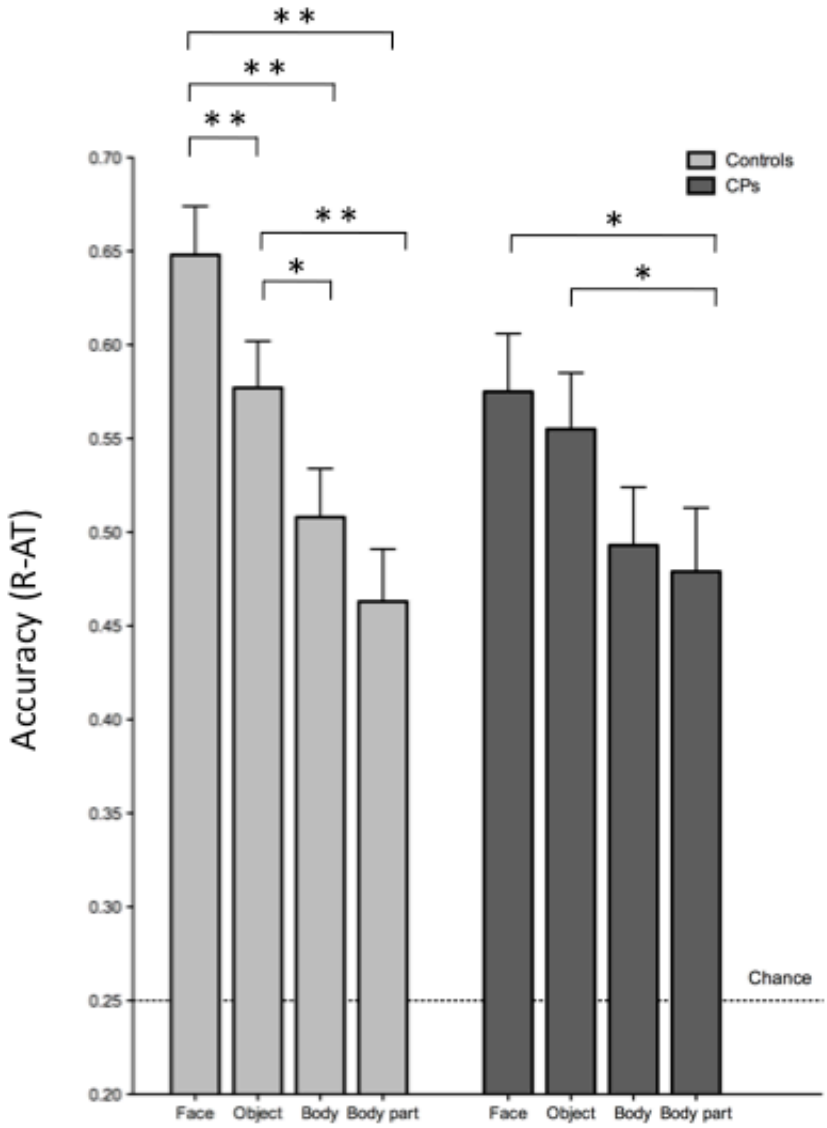

Figure 6. Classification performance for controls (left – light gray) and CPs (right – dark gray). Columns represent means and error bars represent standard errors of the means (SEM) (∗∗ $p \leq .001$; ∗ $p \leq .05$).

Discussion

We investigated the neural characteristics of CP by examining the pattern of activity using MVPA within four ROIs. Results demonstrated that the pattern of neural activity within the right anterior temporal lobe (R-AT) was less face-specific in CPs than in controls. In contrast, the two groups did not differ in regard to the pattern of voxel activity within the left anterior temporal lobe (L-AT), nor within the left and right

midfusiform gyri (L-FG and R-FG). These results demonstrated that the R-AT represents a neural correlate of face-specific difficulties in CP, and therefore a critical node for normal face processing.

Face processing relies on a network of cortical and subcortical brain regions (Haxby et al. 2000). Both neuroimaging and lesion studies have shown that, within this network, the midfusiform gyrus (FG) and the anterior temporal lobe (AT) play a pivotal role in face recognition (Kanwisher et al. 1997; Rajimehr et al. 2009). Previous investigations on the neural (functional) substrates of CP indicate that, despite their clear behavioural difficulties in face identification, people with CP usually show typical (face-specific) fMRI activity and typical repetition suppression within the FG (Avidan and Behrmann 2009; Avidan et al. 2005; Furl et al. in press)[2]. However, despite much evidence pointing to the AT as an important node in the face perception network (Evans et al. 1995; Gainotti et al. 2003; Williams et al. 2006), previous investigations have not specifically tested the functioning of this region in CP. The reason may be technical in nature. It is known that the change in density due to the ear canals and sinuses causes a signal distortion and dropout in regions of the anterior temporal lobes (Ojemann et al. 1997). As such, typical univariate activation-based analysis may not be sensitive enough for the fine investigation of face-selective activity within the AT. Here, we were able to explore this question because the multivariate analysis of the pattern of BOLD activity within clusters of voxels (MVPA) is less susceptible to signal degradation (Mur et al. 2009).

[2] Within the FG, Furl et al. (in press) showed differences in peak activity and in number of face-voxels between CPs and controls when considering an fMRI analysis focused on specific (functionally localized) ROIs, but not when performing a whole-brain analysis. In addition, CPs and controls did not differ in the "repetition suppression" of the FG both when considering the ROI and the whole-brain analysis.

The current result supports previous research demonstrating volume (structural) reduction of the anterior temporal cortex in CP (Behrmann et al. 2007) and R-AT atrophy resulting in acquired prosopagnosia (Williams et al. 2006). At this stage, it not clear whether atypical functioning of the R-AT in CP seen in this study is the consequence of poor inputs from the FG (Thomas et al. 2009) or damage to the AT itself. It will be an interesting avenue for future research to explore the connectivity between the FG and the AT. In addition, future investigations should take advantage of the sensitivity of MVPA for the assessment of the neural functioning of other important face areas such as the occipital face area (OFA) and the superior temporal sulcus (STS) (Haxby et al. 2000). This, potentially coupled with the analysis of the connectivity between multiple face areas in controls and CPs, will shed further light on the neural aspects of both typical and atypical face recognition skills.

In the current study we found face representations also within the L-AT, R-FG and L-FG. Intriguingly however, typical subjects and CPs did not differ in their pattern of voxel activity within these three regions. These results support previous evidence of typical face-selective activity within the fusiform gyrus in CP (Avidan and Behrmann 2009). In addition, in agreement with previous research (Gorno-Tempini et al. 1998), our results show that the L-AT is also a face sensitive region; however its functioning is not affected in CP.

Our finding of object, body and body part representations within the fusiform gyrus are consistent with previous studies (Bar et al. 2006; Peelen and Downing 2007). However, the novel finding of nonface representations within anterior temporal regions indicates that object representations can be found outside the lateral occipital complex (LOC, Grill-Spector et al. 2001) and the fusiform gyrus (Bar et al. 2006). Similarly,

body representations can be found outside the extrastriate body area (EBA, Downing et al. 2001) and the fusiform body area (FBA, Peelen and Downing 2005).

Conclusions

The current study demonstrates that face representations in the right anterior temporal lobe are compromised in people with CP. This effect reflects the behavioural abnormality prosopagnosics experience in everyday life and may help elucidate the biological precursor of CP. More generally, this implicates the R-AT as a very important neural substrate for normal face recognition and, intriguingly, in object and body perception as well. It will be important for future studies to further illuminate the R-AT role in both face and non-face perception.

Funding

This work was supported by the Macquarie University Research Excellence Scholarship (iMQRES) to D.R. M.A.W. is supported by the Australian Research Council Fellowship Schemes (DP0984919).

Acknowledgements

We wish to thank Regine Zopf for programming the "one-back" task and Ellie C. Wilson for helping in the recruitment of participants with CP. We wish to thank Anina Rich for the insightful comments on the manuscript.

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Supplementary material

None of the ten control participants reported face recognition difficulties in everyday life, whereas all the people with CP reported lifelong difficulties in face recognition. Further formal cognitive assessment of the CPs confirmed their face processing problems. We adopted two face memory tasks: The MACCS Famous Face Task 2008 (MFFT-08) and the Cambridge Face Memory Test (CFMT, Duchaine and Nakayama 2006). The MFFT-08 assessed famous face recognition, whereas the CFMT assessed memory for unfamiliar faces. Normative data are included in Bowles et al (2009). Individual data are reported in supplementary Table 1.

Supplementary Table 1. Biographical information of CPs and their performance (age and sex normalized z-scores) on the MACCS Famous Face Task 2008 and on the Cambridge Face Memory Test (CFMT). In italics are indicated z-scores 2 SD below the controls mean.

CPs	Age	Sex	MFFT-08	CFMT
OJ	48	M	*-2.46*	*-2.72*
SD	57	M	*-3.1*	*-2.83*
GN	47	F	*-4.05*	-1.81
NN	24	F	*-4.5*	-1.93
GE	22	M	*-2.04*	-1.89
MG	33	F	*-3.49*	*-2.09*
LL	42	F	*-2.43*	*-2.16*

The CPs showed normal contrast sensitivity as assessed by the *Functional Acuity Contrast Test* (FACT, Vision Sciences Research Corporation 2002) and normal color perception with the *Ishihara Test for Colour Blindness* (Ishihara 1925). Performance on the length, size, orientation and picture naming (long version) subtests of the *Birmingham Object Recognition Battery* (BORB) (Riddoch & Humphreys 1993)

confirmed that basic object recognition skills were intact. The *Raven Coloured Progressive Matrices* (Raven et al. 1998) further indicated that the IQ of all participants with CP was within the normal range. None of the CPs scored within the autistic range on the *Autism-Spectrum Quotient* (AQ, Baron-Cohen et al. 2001). As such, the every day face recognition difficulties reported by the CPs (and confirmed on the two tests of face memory reported below) are not due to general visual recognition difficulties, low IQ, or impaired social functioning.

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Chapter 6

An early category-specific neural response for the perception of both places and faces

Chapter 6

An early category-specific neural response for the perception of both places and faces

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Abstract

Rapid and accurate recognition of faces and places is crucial in everyday life. Faces provide clues about the identity, gender, mood, attractiveness and approachability of people surrounding us, and places help us recognize our location and navigate around our environment. Magnetoencephalography (MEG) studies have demonstrated that the human visual system can categorize an incoming visual stimulus as a face within 100 ms, as reflected by the M100. However, no similar early place-specific MEG component has been described, which is somewhat surprising as there is behavioural evidence for rapid visual categorization of places. The current study aimed to explore the existence, as well as the spatio-temporal dynamics of, a place-selective MEG component by combining MEG recordings with structural magnetic resonance images (MRI). MEG activity was recorded while 10 participants were presented with pairs of face and place stimuli. Our results show that the perception of places generates a category-specific MEG component (M100p), which occurs just as early as that seen for faces. This place specific component originates from the medial surface of the occipital lobes. Our findings suggest that early visual categorization within cortical areas does not occur exclusively for faces, but instead may be a more general phenomenon.

Keywords: face perception, M100, MEG, place perception, visual perception

The recognition of faces and places within our environment is essential for normal everyday functioning. Converging evidence indicates that places and faces represent specific categories of stimuli for the human visual system, for example, functional magnetic resonance imaging (fMRI) studies have demonstrated the existence of areas within the ventral visual cortex that selectively respond to places (Parahippocampal Place Area [PPA]) (Epstein and Kanwisher 1998) or faces (Fusiform Face Area [FFA]) (Kanwisher et al. 1997). Similarly, neuropsychological patient studies have shown that brain lesions encompassing the PPA may cause topographical amnesia (i.e. an impairment in navigating around familiar environments) (McCarthy et al. 1996), whereas lesions encompassing the FFA may cause acquired prosopagnosia (i.e. an impairment in recognizing familiar people by the face) (De Renzi et al. 1991; Barton 2008). Furthermore, behavioural studies have documented the rapidity with which our visual system can process both place and face stimuli. In fact, when stimuli are presented vey briefly (less than 100ms) humans are able to process the "gist" of a scene (Potter and Levy 1969; Greene and Oliva 2009), and can detect the presence (Purcell and Stewart 1986; Grill-Spector and Kanwisher 2005) and identity (Tanaka 2001) of faces.

MEG enables the investigation of the temporal dynamics of visual processing with millisecond resolution. Previous MEG studies have documented a face-selective response occurring as early as 100 ms after stimulus onset (Linkenkaer-Hansen et al. 1998; Halgren et al. 2000). This 'M100' response (labelled as 'M100f' here to emphasise it's face sensitivity) is generated from the medial occipital lobes (Linkenkaer-Hansen et al. 1998; Halgren et al. 2000), is significantly larger for faces than other visual stimuli, and has been proposed to be related to successful categorization rather than identification of faces (Liu et al. 2002). A similarly early

place-selective MEG response has never been reported, which is surprising given behavioural evidence for rapid processing of places. The earliest place-selective MEG responses that have been reported are 200-300 ms post stimulus onset, evident in a task where participants had to distinguish between familiar and unfamiliar places and generated within the parahippocampal gyrus (Sato et al. 1999).

However, this time window seems too late to account for the speed of reported behavioural place perception in humans. Event-related potential (ERP) data also suggests earlier responses should be evident, with frontal responses 150 ms post-stimulus onset differentiating between natural scenes with, and without, an animal (Thorpe et al. 1996). In fact, given that this study used a go/no-go task, which involves response inhibition, it is possible that 150 ms is an underestimate of rapid scene categorisation. In the current study, we therefore explored the existence, and features, of an early place-specific physiological component by combining MEG recordings with structural brain images using high-resolution MRI.

Material and Methods

Participants. We tested ten right-handed participants (3 female; mean age: 29; range: 23-40 years) with normal or corrected-to-normal vision and no history of neurological or psychiatric disorder. All participants provided written consent.

MRI data acquisition. A high-resolution anatomical MRI scan was acquired for each participant using a 3D-MPRAGE (magnetization prepared rapid gradient echo) sequence. Scanning was performed with a 3 Tesla Philips Scanner at St Vincent's Hospital, Sydney, Australia.

MEG data acquisition. MEG data acquisition was performed using a 160-channel whole-head first-order axial gradiometer system (50 mm baseline) with a sampling rate

of 1000 Hz. Before entering the magnetically shielded room, a digital head-shape was recorded for each participant. Five head position indicators (HPI) coils were attached to a tightly fitting elastic cap, and the 3D locations of three cardinal landmarks (the nasion and bilateral preauricular points), as well as approximately 400 randomly selected points on the participant's head surface, were digitized using a Fastrak system (Polhemus, Colchester, VT). This allowed subsequent registration of the MEG data to the structural MRI. To correct for movement errors, the participants' head position within the MEG system was determined at the start of each recording blocks from the five HPI coils.

Stimuli. There were 240 faces and 240 places. 120 faces depicted famous people (actors, politicians and athletes) and 120 of the places were also famous (famous landscapes or famous buildings depicted on their natural background). Unfamiliar faces were matched to the familiar faces for sex, age and approximate level of attractiveness. Unfamiliar places were matched for category and visual similarity (for example the Golden Gate bridge was matched with an unfamiliar bridge with a similar structure). One additional face and one additional place were used as target stimuli (see Figure 1 for examples). The introduction of familiarity as a factor has the aim to help understanding whether early neurophysiological components can discriminate between familiar and unfamiliar stimuli. This issue has not been previously addressed and it can help to shed light on the relation between behavioural speed in place/face processing and early neural activity. All stimuli were converted to grayscale using Adobe Photoshop software (Adobe Systems Incorporated). Places were presented within a 7.5 x 5 cm frame, whereas faces were edited so that the internal facial configuration (but not hair) fitted into a 6 x 4 cm oval template. On average, places covered a visual angle of 10.7° X 7.2°, whereas faces 5.7° X 8.6°. The luminance of the places and faces did

not differ ($t(238) = -1.82$, $p = .070$). However, the luminance of the familiar stimuli (both faces and places) was greater than that of the unfamiliar stimuli (both faces and places) (Places: $t(118) = 3.38$, $p = .001$), Faces: $t(118) = 3.74$, $p < .001$).

Experimental design. The MEG experiment was programmed and delivered with Presentation software (Neurobehavioral Systems, Albany, CA). Each trial consisted of a pair of stimuli (S1 and S2), either two faces, or two places, shown for 1000 ms with an inter-stimulus interval (ISI) of 1000 ms during which only a central red fixation cross was present (Fig. 1a). The fixation cross was also superimposed on all stimuli to avoid saccades and ensure central fixation. On the place trials, each pair consisted of either two familiar or two unfamiliar places, while on the face trials each pair consisted of either two familiar or two unfamiliar faces. The pairs of stimuli were either "Repeated", where S2 depicted the same picture as S1, or "Unrepeated" where S2 was a different face/place to S1 (Fig. 1b). Understanding the effect of repetition and its interaction with familiarity may help elucidate the nature of the representation of the first category-specific MEG components. For example, a bigger repetition effect for familiar than unfamiliar stimuli would suggest that familiarity information is coded within around 100 ms post stimulus onset (see Schweinberger, Pickering, Jentzsch, Burton & Kaufmann, 2002, for a similar methodology).

Participants were not informed that they were viewing pairs of stimuli but were instructed to fixate centrally and press a button whenever they saw one of the two target stimuli (one was a face and one was a place). Each of the two target stimuli was shown 48 times during the task. The task was divided into 8 blocks of 120 trials, each including the presentation of 12 targets at either S1 or S2, for a total of 960 trials (half face pairs and half place pairs). Participants attended to the targets, reporting 92.30% (SD = 3.71). All stimuli were shown in the centre of a screen (size: 38 x 35 cm;

resolution: 800 x 600 pixels) installed inside the magnetically shielded room, and placed at a distance of approximately 40 cm from the participant's head.

Following the MEG experiment, we assessed the ability of each to recognize the famous faces and places with two tasks programmed using SuperLab (Cedrus Corporation 2007), and administered on a 15-inch Macintosh Power Book G4. In the "Picture Recognition" task participants were instructed to type the name and/or specific semantic information about the person (a general description like: "He is an actor" was considered as incorrect) or place (a description like: "This tower is somewhere in Europe" was considered as incorrect). The first block consisted of the 120 famous faces from the MEG experiment, the second block the 120 famous places. In the "Name familiarity" task participants were asked to record whether they were familiar with the names of the 120 famous faces (block 1) and the names of the 120 famous places (block 2). Participants were familiar with 93.91% (SD = 4.00) of the famous individuals, and recognized 89.86% (SD = 9.44) of these faces. For places, participants were familiar with 74.83% (SD = 10.51), and recognized 83.83% (SD = 7.65) of these places.

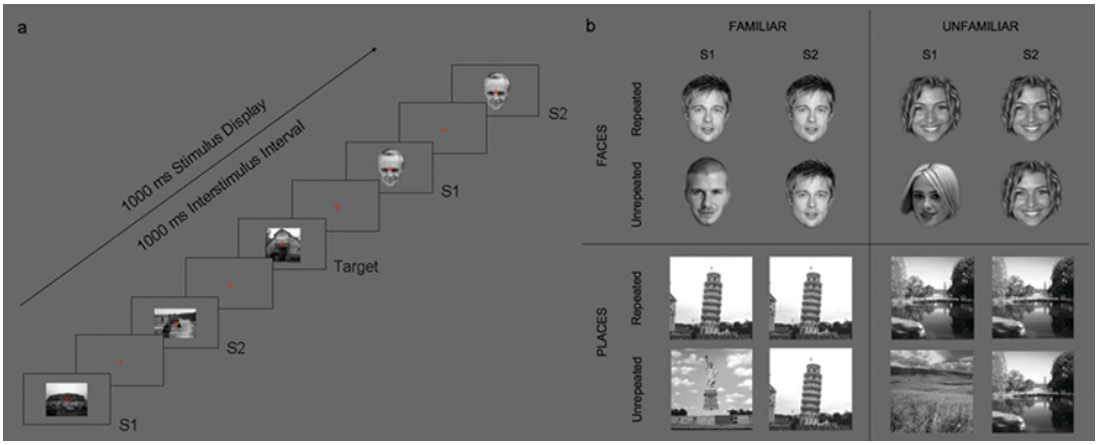

Figure 1. MEG experiment: (a) Example trial sequence; (b) Examples of stimuli from each of the three conditions: Category (face Vs place), Familiarity (familiar Vs unfamiliar) and Repetition (repeated Vs unrepeated).

MEG Data Processing. The minimum-norm estimate (MNE) was used for the estimation of the source current distribution at each cortical location (Hamalainen and Sarvas 1989) and MEG data were analyzed offline using MNE software (http://www.nmr.mgh.harvard.edu/martinos/userInfo/data/sofMNE.php). The cortical surfaces were reconstructed from MRI of each participant using FreeSurfer software (http://surfer.nmr.mgh.harvard.edu/) (Fischl et al. 1999). Movement less than 5 mm was tolerated and noisy MEG channels (individuated offline in the raw data) were excluded in the analysis. The MEG source space was constrained to a cortical surface that comprised 4098 sources per hemisphere with an average of 7 mm spacing between adjacent source locations. MEG signals were segmented into time epochs spanning from 200 ms before stimulus onset to 800 ms following stimulus onset, with the pre-stimulus epoch of -200 to 0 ms as baseline. MEG data associated with the target stimuli were ignored in the analysis to avoid motor artefact from responses. Event-related magnetic fields were then digitally filtered, with a 50 Hz high-pass filter. Automated filtering excluded neuromagnetic activity caused by eye blinks and gross eye movement artefacts.

The single-layer boundary element method (BEM) (Hamalainen and Ilmoniemi 1994) was implemented to calculate forward solutions from estimated source configurations. The noise-covariance matrix, computed from the 200 ms pre-stimulus activity, and the forward solution were together used to create a linear inverse operator (Dale et al. 2000). At each cortical location, the current estimate was normalized to the estimated baseline variance, resulting in z-scores. This noise-normalized solution provides a dynamic Statistical Parametric Map (dSPM), which indicates the signal-to-noise ratio (SNR) of the current estimate at each cortical location as a function of time

(Dale et al. 2000). Thus dSPM maps identify locations where the MNE amplitudes are above an arbitrary defined threshold that corresponds to the noise level.

ROI selection. We used the first dSPM maps (around 100 ms post stimulus onset) for the selection of face and place regions of interest (ROIs) individually for each participant. For both faces and places, ROIs were always selected based on the activity elicited by the S1. These stimuli never appeared in position S2 (which was used for the actual analysis), thus guaranteeing the independence between ROI selection and data analysis (Kriegeskorte et al. 2009). We set the dSPM threshold as 10, therefore only dSPM activity with a z-score bigger than 10 with respect to the noise level was visually shown. This threshold enables the localization (within the subjects' cortical surface) of focal areas of activity, in contrast to widespread activity. We believe that this precaution is crucial for the investigation of early and focused MEG components.

Results

Due to the high threshold adopted, not all participants showed face and place selective ROIs. In total, seven participants showed ROIs for places in both hemispheres and six showed ROIs for faces in both hemispheres. Our results showed category specific MEG activity in four different medial-occipital ROIs: two ROIs were place-specific and two were face-specific. Within each of the four ROIs, MEG responses to S2 occurring between 100-130 ms post stimulus onset (M100) were examined for each of the conditions employing a repeated measures ANOVA with three factors (Category: place, face; Familiarity: familiar, unfamiliar; Repetition: repeated, unrepeated).

We found an effect of Category, with places generating stronger activity than faces, for both left (Mean ± SEM: places = 7.03 ± .31, faces = 5.09 ± .75; $F(1,6) = 6.70$, $p = .041$) and right (Mean ± SEM: places = 8.77 ± .86, faces = 4.77 ± .49; $F(1,6) =$

77.24, $p < .001$) place-selective ROIs (Fig. 2). We will refer to the place-selective MEG component generated within the left ROI as the M100p-L and the place-sensitive MEG component generated within the right ROI as the M100p-R. For the face-sensitive ROIs, there was greater activity for faces than places, also in both left (Mean ± SEM: faces = 8.07 ± .96, places = 5.35 ± .80; $F(1,5) = 17.24$, $p = .009$) and right (Mean ± SEM: faces = 7.41 ± .78, places = 4.58 ± .78; $F(1,5) = 13.64$, $p = .014$) face-selective ROIs.

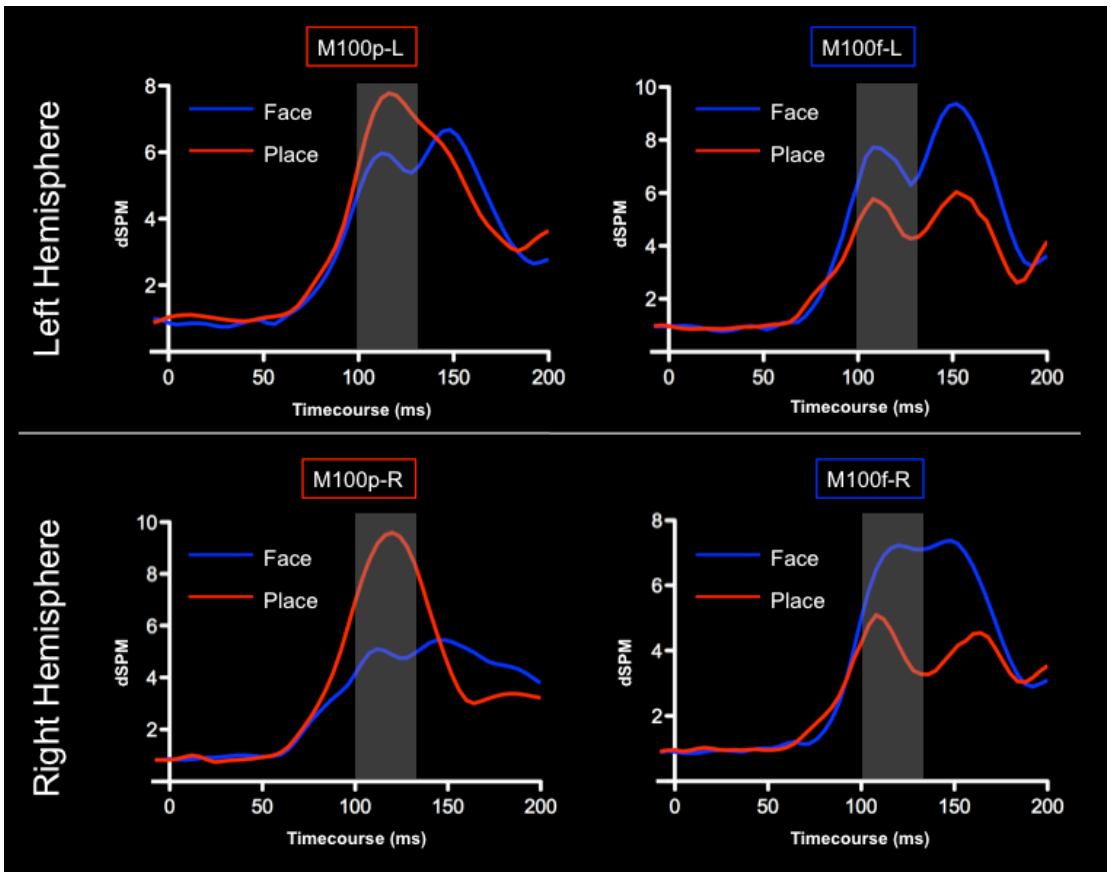

Figure 2. Results: Current estimate (dSPM) as function of the timecourse within each of the four ROIs. Grey selections underlie the activity between 100-130 ms post stimulus onset, focus of the statistical analysis.

We will refer to the face-selective MEG component generated within the left ROI as the M100f-L and the face-sensitive MEG component generated within the right ROI as the M100f-R. In addition, familiar stimuli (M = 6.90, SEM = .80) generated stronger

activity than unfamiliar stimuli (M = 6.55, SEM = .84) for the M100f-L ($F(1,5) = 8.45$, $p = .034$), and there was a Category by Familiarity interaction ($F(1,5) = 13.50$, $p = .014$), demonstrating that famous faces (M = 7.74, SEM = .76) generated stronger M100 activity than unfamiliar faces (M = 7.07, SEM = .82) in the M100f-R only. No main effects of Repetition or interactions between Repetition and other factors were observed (all Ps > .05)[1].

Discussion

In the current study we investigated the spatio-temporal dynamics of place and face perception by coupling MEG recording with structural MRIs. Our results showed that place perception generates an early and category specific MEG component (M100p) that originates within the medial occipital lobe of both the left (M100p-L) and right (M100p-R) hemispheres. In addition, in line with previous investigations, our data showed that face perception generates an early category-specific MEG component (M100f), which also originates within both the left (M100f-L) and right (M100f-R) medial-occipital lobes. Surprisingly however, our results further showed that familiar faces generated stronger MEG activity than unfamiliar faces.

As previously mentioned, there is evidence from a large body of lesion and imaging studies that both places and faces represent specific categories of stimuli for the human visual system (De Renzi et al. 1991; Kanwisher et al. 1997; Epstein et al. 1998; Barton et al. 2008). In addition, behavioural studies have also shown that both categories of stimuli are processed very rapidly (Potter and Levy 1969; Purcell and Stewart 1986; Tanaka 2001, Grill-Spector and Kanwisher 2005; Greene and Oliva 2009). In line with these behavioural demonstrations of rapid face processing, several

[1] There was not correlation between performance on the "Picture Recognition" task and M100f/M100p amplitude (all Ps > .05).

MEG studies have provided evidence for an early and face-sensitive MEG component (M100f, Liu et al. 2002). In contrast, no similarly early MEG component has previously been described for the processing of places, despite behavioural evidence for their rapid categorization. In the current study we demonstrate the existence of an early place-specific MEG component (M100p) stemming from the medial-occipital lobes. We do not know why the place-sensitive MEG component in Sato et al. (1999) is seen at 200-300ms rather than 100 ms, but there are two clear differences between the studies: the paradigms and the number of MEG sensors (160 in the current study, 74 in Sato et al.).

With regard to face processing, our study confirms an early face-specific MEG component (M100f) stemming from the medial occipital lobes (Linkenkaer-Hanses et al. 1998; Halgren et al. 2000; Liu et al. 2002). Low-level features of the stimuli are unlikely to account for these results for several reasons. First, there was a *double dissociation* between face specific (M100f) and place specific (M100p) MEG activity. Second, both places and faces were equivalent in their overall luminance. Similarly, eye movements and/or attention shifts are also unlikely to account for these results. Eye movements were filtered from the data prior to analysis, and the category specific effects shown at around 100 ms post stimulus onset occur earlier than the time required to encode the location of a target in the visual field and initiate an eye movement, which takes around 175-200 ms (see Rayner 2009 for a review).

One interesting issue regards how this very fast categorisation occurs. It is possible that the category-specificity effects shown here are related to the physical features of the stimuli. For example, it has been shown that visual areas V2/V4 in monkeys contain some neurons tuned for “arcs”, and other for “angles” (Hegde and Van Essen 2007). Thus, face selective MEG activity may be the result of “arc” sensitive

neurons, whereas place selective MEG activity may be carried by "angles" sensitive neurons. This is an interesting avenue for future research.

Our data also show that the M100f-R is greater for familiar than unfamiliar faces, suggesting that familiar faces can be discerned from unfamiliar faces very early in the visual analysis process. This early familiarity effect for faces is in line with behavioural findings showing that face identification may occur in parallel to face categorization (Tanaka 2001). It is possible that this difference is being driven by the greater luminance of the familiar than unfamiliar faces, but in this case we might also expect that processing of the familiar scenes would differ from that of the unfamiliar scenes (as the luminance of familiar scenes was greater than that of unfamiliar scenes). An intriguing challenge for future studies will be to shed further light on the nature of this early familiarity effect, its relation with low level features of the stimuli, and its relation to the familiarity effects that are associated with later face-specific MEG components (e.g., the M170 and M250r) (Bentin et al. 1996; Schweinberger et al. 2002; Kloth et al. 2006; Harris and Aguirre 2008).

In summary, we report that place perception generates a category-specific MEG component at around 100 ms post stimulus onset (the M100p) stemming from the medial surface of both the left and right occipital lobes. This is much earlier than the earliest previously reported place-specific MEG component, a parahippocampal gyral signal 200-300 ms post stimulus onset (Sato et al. 1999). This M100p demonstrates that faces do not represent the only category of visual stimuli that engage fast processing. Furthermore, the finding of the M100p fills the gap between behavioural and imaging data by providing evidence that the rapid processing of places may be explained by the coupling of place specific neural activity. Examining the mechanisms by which our visual system accomplishes the complex task of stimulus categorization within 100 ms,

and the breadth of the categories represented, will be a challenging but fascinating endeavour for future studies.

Acknowledgments

We wish to thank members of the Kanwisher Lab, Anina Rich and Matthew Finkbeiner for their insightful comments on this work. We wish to also thank Loes Koelewijn, Graciela Tesan, Melanie Reid and Christopher Sewell for the support provided in the MEG data acquisition and processing. This work was supported by the Macquarie University Research Excellence Scholarship (iMQRES) to D.R. M.A.W. is supported by the Australian Research Council Fellowship Schemes (grant number DP0984919).

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Chapter 7

General discussion

The five papers presented in this thesis have addressed a wide range of aspects of the behavioural and neural features of face processing, in individuals with congenital prosopagnosia (CP) as well as typical subjects. The purpose of this general discussion is to summarise the key findings from each of these papers and to discuss the prominent themes that emerged across them. A neuro-anatomical model of CP based on converging evidence from previous research and data shown within this thesis, and a number of fruitful avenues for future research are also discussed.

Overview of findings

Paper one: Semantic information can facilitate covert face recognition in congenital prosopagnosia.

It is known that the human brain can process information even without awareness. This form of recognition has been defined covert (implicit) recognition (Schacter, 1992). Covert recognition has been demonstrated in the face processing literature, by showing that even though people with acquired (AP) or congenital prosopagnosia (CP) can not recognize familiar faces "overtly", they can show indices of "covert" face recognition (Avidan & Behrmann, 2008; Schweinberger & Burton, 2003).

The aims of the first paper were to determine the features of covert face recognition in CP by adopting multiple behavioural tasks, and to investigate whether covert face recognition tasks are sensitive tools for pinpointing the locus of the impairment within the cognitive system in people with CP. Results of a single case investigation of CP (case "C") demonstrated covert face recognition as assessed with a Forced choice cued task when participants selected which of two faces matched a printed name, but not when assessed with a Priming task or a Forced choice familiarity

task. These results suggest that different tasks can tap into different aspects of covert face recognition. In addition, a detailed description of the cognitive mechanisms responsible for C's overall performance indicated that the assessment of covert face recognition, in addition to the assessment of overt face recognition, enables us to pinpoint the locus of the cognitive impairment better than traditional overt tasks.

Thus, the results of Paper one indicate that future investigations involving a detailed assessment of face recognition skills in both AP and CP should adopt tasks that assess covert face recognition, and include at least one covert recognition task that adopts names as cues.

Paper two: Covert face recognition in congenital prosopagnosia: A group study

Even though the first paper showed the characteristics of behavioural covert face recognition in a case of CP, it was not clear whether behavioural covert face recognition is a general feature of CP, or under which conditions it is apparent. In this second paper the three tasks adopted in Paper one were administered to a group of 11 people with CP. The results indicated that covert face processing does represent a general feature of CP.

The study also revealed that the different tasks vary in sensitivity for the detecting covert face recognition. Covert processing was found when assessed with a Forced choice familiarity task and a Forced choice cued task, but not with a Priming task. The lack of correlation between task performance and confidence ratings on the Forced choice familiarity task indicated that this task represents a "true" measure of covert recognition. Contrarily, the significant positive correlation between performance and confidence ratings on the Forced choice cued task indicated that this task taps into aspects of face processing that are halfway between "overt" and "covert" processing. By

adopting a terminology adopted by research in the AP literature (Sergent & Poncet, 1990), this form of recognition can be defined as "provoked overt recognition".

These findings have important theoretical implications for developmental models of face recognition, theories of covert recognition, as well as face processing assessment methods in both AP and CP. In particular, the results of Paper two indicated that not all behavioural tasks adopted for the investigation of covert face processing are equivalent. Some of them are sensitive enough to reveal covert face recognition in CP (i.e. Forced choice familiarity task), whereas others are not (i.e. Priming task). The finding of provoked-overt recognition demonstrated that confidence ratings must be taken into account in future investigations to monitor whether a Forced choice task is actually tapping into covert aspects of face processing in CP. In light these results, it is likely that C's above-chance performance on the Forced choice cued task (Paper one) does not represent an index of covert face recognition, but an index of provoked-overt recognition instead. This was not possible to determine at the time of C's testing, since only a group study that takes into account the correlation between performance and confidence ratings allows to underline this.

Paper three: The face-specificity of the M170 correlates with behavioural performance: Insights from congenital prosopagnosia

Papers one and two focused on the cognitive aspects of CP, by providing a wide characterization of overt and covert recognition in this population. The aim of Paper three was to investigate the neurophysiological features of CP. It is well established that the perception of a face generates a physiological component at around 170 ms post stimulus onset. This component, which shows a larger amplitude for faces compared to other categories of visual stimuli (e.g. objects, scenes), is labeled the M170 when

measured with Magnetoencephalography (MEG, Liu, Higuchi, Marants, & Kanwisher, 2000).

Since the key role the M170 has in typical face processing (Eimer, 2000b), it was of interest to ascertain whether this component shows normal features in CP. Analysis of the neuromagnetic activity (MEG) generated within the right lateral occipital cortex (rLO) and right fusiform gyrus (rFG) in six people with CP and 11 healthy controls showed that the M170 did not differ between the two groups. This indicates that, despite its key involvement in face processing, the M170 does not represent the neurophysiological correlate of CP. However, the most important result of this investigation was the demonstration of the fact that the M170 is not a monolithical component: The M170 generating within the rLO (rLO-M170) correlates with holistic/configural processing, whereas the M170 generating within the rFG (rFG-M170) correlates with featural processing.

In sum, Paper three provides important novel contributions to our current knowledge of the physiological aspects of face processing. Firstly, it demonstrates the independence of the M170 originating from the occipital lobe (rLO) and the M170 originating from the fusiform gyrus (rFG). That is, while these two components occur at the same time, they originate from two independent neural populations. Secondly, it demonstrates that the M170 does not represent the neurophysiological correlate of CP. Thirdly, and most importantly, it indicates the different roles played by the rLO and the rFG in face processing at around 170 ms post stimulus onset.

Paper four: Multi-voxel pattern analysis of fMRI data reveals abnormal anterior temporal lobe activity in congenital prosopagnosia

Paper three indicated that people with CP show typical, face-selective, neural activity at the M170 measured from the lateral occipital cortex and the fusiform gyrus. These regions have also shown normal functioning in fMRI studies of CP (Avidan & Behrmann, 2009). In contrast, volume and connectivity of the anterior temporal lobe (AT) seems to be associated with CP (Behrmann, Avidan, Gao, & Black, 2007; Kriegeskorte, Formisano, Sorger, & Goebel, 2007; Williams, Savage, & Halmagyi, 2006). The main aim of Paper four was to investigate the neural correlates of CP by adopting Multi-Voxel Pattern Analysis of fMRI data (MVPA, Norman, Polyn, Detre, & Haxby, 2006; O'Toole, et al., 2007). Seven participants with CP and ten matched controls completed an fMRI study. The results demonstrated that people with CP showed a pattern of neural activity within the right anterior temporal cortex (R-AT) that was less face-selective than that of healthy controls, suggesting that abnormal development of the R-AT represents a *neuro-functional correlate of CP.* In agreement with previous group investigations in CP (Avidan & Behrmann, 2009) the neural activity within the fusiform gyrus (FG) was within the normal range.

Furthermore, the finding of nonface representations within the AT in both typical subjects and CPs indicated that object representations can be found outside the lateral occipital complex (LOC, Grill-Spector et al. 2001) and the fusiform gyrus (Bar et al. 2006), and, similarly, body representations can be found outside the extrastriate body area (EBA, Downing et al. 2001) and the fusiform body area (FBA, Peelen and Downing 2005).

Paper five: An early category-specific neural response for the perception of both places and faces

Papers 1 to 4 described the cognitive and neural features of CP, a selective developmental impairment in face recognition. Since our sample of CPs did not show problems in low-level vision, general cognitive functioning or object recognition, the four investigations described so far support the theory that face processing is mediated by "specific" mechanisms (McKone & Kanwisher, 2005). Much evidence supports the specific status faces have for the human visual system. For example, face processing is very fast (Crouzet, Kirchner, & Thorpe, 2010; Tanaka, 2001), face perception is characterized by specific neural activity within the ventral temporal lobe (i.e. fusiform gyrus) (Kanwisher, McDermott, & Chun, 1997), and brain lesions encompassing the fusiform gyrus can selectively impair the ability to recognize people by their faces (i.e. AP, De Renzi, Faglioni, Grossi, & Nichelli, 1991; Moscovitch, Winocur, & Behrmann, 1997).

However, faces do not represent the only category of stimuli that is attributed a "special" status by the human visual system. For example, place (scene) processing shares many similarities with face processing. Like face perception, place perception takes place very rapidly (Potter, 1976), is mediated by specific neural activity (Epstein & Kanwisher, 1998), and can be selectively impaired by a brain lesion (i.e. topographical amnesia) (McCarthy, Evans, & Hodges, 1996). Even though previous research has documented the neurophysiological (MEG) correlates of early face processing (Liu, Harris, & Kanwisher, 2002), no research has yet characterised the neurophysiological correlates of early place processing.

The aim of paper five was to investigate the spatio-temporal dynamics of place and face processing by using MEG. By recording neuromagnetic activity in ten healthy

participants, results demonstrated that, similarly to face perception, *place perception generates a category-specific MEG component at around 100 ms post stimulus onset* (the M100p) stemming from medial surface of both the left and right occipital lobes. This result is important for vision research since it reveals that the early categorization of visual stimuli may be a general phenomenon and not just exclusive for faces.

Neuro-anatomical model of CP

The five studies presented in this thesis provide an important contribution to our current understanding of the cognitive and neural aspects of human face processing. Overall, these findings, coupled with previous structural and functional investigations, support a neuro-anatomical model of CP. This model will be discussed in detail below.

Much research has demonstrated that a network of cortical and subcortical brain regions mediates human face processing. Within these regions, the lateral occipital lobe (Gauthier, et al., 2000) and the fusiform gyrus (Kanwisher, et al., 1997) represent "core regions" for normal face processing (Haxby, Hoffman, & Gobbini, 2000). Previous investigations have indicated that, despite the clear behavioural impairment in face recognition, people with CP can show normal structure (volume) (Behrmann, et al., 2007) and functioning (Avidan & Behrmann, 2009; Avidan, Hasson, Malach, & Behrmann, 2005) of "posterior" face regions (i.e. LO and FG). A recent investigation in a group of CPs indicated FG differences in the peak activity and in number of face-voxels between CPs and controls when considering an fMRI analysis focused on specific Regions of Interest (ROIs), but not when performing a whole-brain analysis. In addition, CPs and controls did not differ in the "repetition suppression" of the FG both when considering an ROI and a whole-brain analysis (Furl, Garrido, Dolan, Driver, &

Duchaine, in press). As such, current research seems to posit for at least partially intact functioning of the FG in CP.

This points towards other brain regions (Avidan & Behrmann, 2009) as neural substrates of CP. Overall, the results of the current thesis support these findings. Firstly, Paper three showed that the face-sensitive neurophysiological component (M170), generating from the right lateral occipital cortex (rLO) and the right fusiform gyrus (rFG), have typical features in CP. Secondly, Paper four revealed normal neural activity (as measured with fMRI) within the fusiform gyrus (FG) in CP. Taken together, these investigations posit for typical functioning of posterior face regions in CP. We cannot however exclude that MEG activity within the rLO and the rFG will show abnormal features when considering components occurring later than the M170, such as the M400. Future research will clarify this issue.

Beyond LO and FG, a further key region involved in face processing is the anterior temporal lobe (AT) (Kriegeskorte, et al., 2007; Rajimehr, Young, & Tootell, 2009; Williams, et al., 2006). Previous investigations of anterior temporal regions in CP revealed some differences with respect to controls. For example, compared to matched healthy controls, people with CP showed a volume reduction of AT, and this reduction correlated with behavioural performance on face identification tasks, with poorer performance associated with smaller AT volume (Behrmann, et al., 2007; Garrido, et al., 2009). A recent investigation demonstrated a reduced structural connectivity (white fiber connections) between posterior and anterior brain regions in CP (Thomas, et al., 2009), possibly causing a disconnection between posterior (LO, FG) and anterior (AT) face regions. Paper four of this thesis represents the first functional brain imaging study of CP specifically investigating the functioning of the AT. The results showed that the pattern of neural activity within the right anterior temporal cortex (R-AT) was less face-

specific in CPs then controls. *Altogether, the findings summarized above strongly support a neuro-anatomical model of CP, which indicates abnormal structure, connectivity and functioning of the AT.*

Can the neuro-anatomical model of CP proposed here support the behavioural findings reported in this thesis? Despite impaired overt recognition skills in CP (e.g., difficulty in recognizing people by their faces), behavioural findings indicated covert face recognition on the Forced choice familiarity task (Paper three). No covert processing was evident in the Priming task (Papers two and three), and the above chance performance on the Forced choice cued task (Papers two and three) was considered an index of "Provoked overt" rather then covert recognition (Paper three). The neuro-anatomical model of CP proposed here can account for all these behavioural findings.

The above-chance covert discrimination between familiar and unfamiliar faces on the Forced choice familiarity task might be facilitated by normal functioning of posterior brain areas, since, as demonstrated in Paper 5, the distinction between famous vs. unfamiliar faces is mediated, at least in early processing stages, by neural activity within the occipital lobes.

In contrast, access to specific semantic/biographical information, including names, relies on anterior temporal (AT) regions (Gorno-Tempini, et al., 1998; Palermo & Rhodes, 2007; Seidenberg, et al., 2002). Converging evidence from previous investigations and findings of the current thesis demonstrate the involvement of the AT in the genesis of CP. The anatomical/functional abnormality of the AT and its disconnection with posterior face regions lead to the prediction that tasks requiring the access to semantic/biographical representations (represented within the AT) should show abnormal performance in CP.

The access to semantic/biographical information from a seen face is crucial for tasks requiring (overt) familiar face identification and on the Priming task. In overt face identification tasks such as the MACCS Famous Face Task 2008 (MFFT-08), a seen face must activate specific semantic/biographical representations in order to be identified. In the Priming task, access to semantic/biographical information about the "prime" face must take place in order for the "target" name to be categorized as an actor or politician. In agreement with the model, CPs showed impairment on the MFFT-08 and a lack of covert priming (Paper three).

Papers one and two showed that CPs performed above chance on the Forced choice cued task, showing indices of provoked overt recognition. Since on this task, similarly to the Priming task, both faces and names are shown, it would be interesting to understand the reason behind this performance. There is a crucial difference between the Priming task and the Forced choice cued task: In the former, faces and names are shown sequentially (with the faces shown first), whereas in the latter, faces and names are shown simultaneously. As indicated in Papers one and two, CPs have difficulties accessing semantic/biographical information from seen *faces*, however they can provide detailed semantic/biographical information when famous *names* are shown. This suggests that the name given as a cue in the Forced choice cued task may activate semantic/biographical information within the AT (Alvarez, Novo, & Fernandez, 2009), and these can, in turn, activate face representations within the "core face areas", thus explaining above-chance performance on the Forced choice cued task (see Paper one for an additional detailed cognitive account of the phenomenon). This is in agreement with the proposed neuro-anatomical model of CP. Even though there is reduced connectivity between posterior and anterior face regions in CP compared to normal subjects (Thomas, et al., 2009), the direction of the information flow between the two regions in

not known. It could be that poorer connectivity in CP may guarantee mainly anterior-posterior (name → face; AT → LO/FG) flow of information (thus explaining the above than chance performance on the Forced choice cued task, where the name cues face recognition) but not the posterior-anterior (face → name; LO/FG → AT) flow necessary for the Priming task and for normal "overt" recognition.

Taken together, the results summarized above strongly support the neuro-anatomical model of CP proposed in this thesis. The model indicates that CP is the consequence of the abnormal structure, connectivity and functioning of the AT, and not (or to lesser extent) of posterior face regions.

What to expect in the future?

Not only does this thesis provide a substantial contribution to our current understanding of the cognitive and neural mechanisms of human face processing, it also provides a platform for a series of future investigations. The first two papers focused on the cognitive aspects of CP and described the characteristics of covert face recognition. Future intriguing issues include, for example, the exact mechanisms underlying behavioural covert face recognition in CP. Previous research has indicated that covert face recognition in CP might be mediated by the emotional valence of the seen faces, with faces associated with positive valence recognized better than faces with a negative valence (Bate, Haslam, Jansari, & Hodgson, 2009). It is unknown whether behavioural covert recognition shown in this thesis was mediated by emotional valence. To clarify this issue, future group studies of CP will have to monitor whether, for instance, deciding which of two faces represents a famous person (i.e. Forced choice cued task) correlates with the valence (positive/negative) associated with each face.

Along with behavioural measures, previous research in AP also adopted physiological indices (e.g., Skin Conductance Responses, SCRs) to assess covert face recognition (Bauer, 1984; Tranel & Damasio, 1985). It has been proposed that different cognitive and neural routes mediate behavioural and physiological covert recognition in AP (Schweinberger & Burton, 2003). It is still not clear whether this is the case in CP. The only investigation of physiological covert face recognition in CP involved a single case (a 5-year old child). Despite results showing covert recognition as measured with SCRs, the study did not correlate physiological and behavioural covert recognition (Jones & Tranel, 2001). As such, the relation between different types of covert face recognition in CP remains a topic for future investigations.

Even though covert recognition has been described multiple times in CP, the anatomical base of this phenomenon has never been investigated. There is no direct evidence indicating which brain regions are involved in determining, for instance, a performance above chance on the Forced choice cued task, or the neural correlates of the lack of priming in CP. Future fMRI and/or MEG investigations that correlate neural activity with behavioural (covert) performance would represent an invaluable tool for this purpose. In particular, they would represent a good way to directly test the neuro-anatomical model of CP proposed in this thesis.

Paper three focused on the neurophysiological aspects of CP. Results surprisingly showed that the face-specific M170 in CP does not differ from healthy controls. This raises the question of whether different MEG components, maybe later in the timecourse, can differentiate between CPs and controls. In other words, what is the neurophysiological correlate of CP? Previous research has suggested that differences between people with AP and healthy controls may involve components peaking at around 400 ms post stimulus onset (Eimer, 2000a; Harris & Aguirre, 2008). Since this

M400 is highly affected by the familiarity of face stimuli, and since CPs show problems in famous face recognition, future research investigating the neurophysiological correlates of CP should monitor the MEG activity peaking at around 400 ms post stimulus onset.

Evidence for differential MEG activity between familiar vs. unfamiliar faces has already been shown in Paper 5, with a larger MEG activity for famous compared to unfamiliar faces at around 100 ms post stimulus onset (M100f). This familiarity effect, despite being in line with behavioural findings of very rapid face processing (Tanaka, 2001), seems to be in contrast with results of Paper 3, which failed to report familiarity effects at the M170 latencies. Given the proposal that the "depth" of information processing proceeds with the timecourse, we would have expected to observe familiarity effects at the M170 level. There are two potential accounts for this discrepancy.

The first one is that the face processing system can differentiate between familiar and unfamiliar faces as soon as a face is perceived (M100 - occipital lobes), and this information is later combined with semantic/biographical information (M400 – anterior temporal lobes) related to the person the face belongs to. The M170, occurring in between the two steps, may mediate other aspects of face processing, such as holistic/configural and featural processing, as indicated in Paper three. The second account is more parsimonious, and refers to low-level proprieties of face stimuli. In fact, as indicated in paper five, the overall luminance of familiar faces was bigger than the overall luminance of unfamiliar faces. Future investigations will have to specifically test these different accounts.

Paper four provides the first description of the neuro-functional correlate of CP, by demonstrating that people with CP show a pattern of neural activity within the R-AT

that is less face-specific than in controls. This result is important since it complements previous findings in both clinical populations (e.g., people that undergone strokes and/or have epilepsy) and healthy controls, indicating the AT is a key region for normal face processing (Seidenberg, et al., 2002; Williams, et al., 2006). Since only unfamiliar faces were adopted in Paper 4, and since converging evidence indicates that famous face representations are stored within the AT (Brambati, Benoit, Monetta, Belleville, & Joubert, 2010), future studies in CP could further investigate the neural activity within the AT by looking at differential activity generated by familiar vs. unfamiliar faces. Given their everyday life difficulties in face recognition, people with CP may show a different pattern of neural activity in the AT with respect to controls. In particular, future studies could investigate whether the AT activity correlates with behavioural performance in face recognition.

Paper five represents the first description of a place-selective MEG component (M100p) in humans, and provides the neural correlate of early place processing. I believe that future investigations will have the potential to shed further light on the M100p by focusing on the correlation between MEG activity and behavioural performance. It would be interesting, for example, to ascertain whether the amplitude of the M100p correlates with the psychophysical function describing whether a visual stimulus is perceived as a place or not.

Ideally, future research should also focus on multimodal brain imaging. For example, it would be of great interest to combine the spatial resolution of fMRI with the temporal resolution of the MEG (or EEG) to investigate face processing in CP as well as individuals with normal face processing skills. Furthermore, as supported by previous research (Rotshtein, Geng, Driver, & Dolan, 2007) and Paper three of this thesis, I strongly believe that a main focus of future neuroimaging investigations should

be the investigation of the correlation between behavioural performance and neural activity.

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