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Clinical and Cognitive Aspects
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Foreword

Together with the four articles listed below, this summary report forms a PhD dissertation in Psychology, submitted to the Faculty of Social Sciences, University of Copenhagen.


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The work presented in this PhD would not have been possible without the help from a great number of people.

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Abstract

In this thesis, work from two research projects is presented. The first section concerns the Back of the Brain (BoB) project and the second concerns the Danish Oxford Cognitive Screen (OCS-Dansk) project.

Face recognition and word recognition have traditionally been thought to rely on highly specialised, largely lateralised and independent cognitive processes. More recently, it has been suggested, that face and word recognition are instead supported by common and highly overlapping networks that are more bilaterally distributed. The debate relies highly on findings from studies of patients selected according to their highly category-selective deficits. The BoB project takes a different approach and aims to shed new light on the processes and cerebral architecture underlying the visual recognition of complex stimuli such as faces, objects and words. A large group of patients (aim: N=70) recruited according to lesion localisation (posterior cerebral artery stroke) are tested with the same large battery of sensitive behavioural tests covering lower-level, intermediate and higher-level visual perceptual functions.

Reports of patients with pure prosopagnosia and pure alexia have been considered as key evidence in favour of the position that face recognition and reading rely on processes that are highly independent and lateralised. However, it has more recently been suggested that, if tested properly, all patients with prosopagnosia should have visual word processing deficits, and all patients with pure alexia should have face recognition deficits. In Article 1: Face And Word Recognition Can Be Selectively Affected By Brain Injury Or Developmental Disorders, studies investigating whether face and word recognition can be selectively affected by acquired brain injury or developmental disorders, are reviewed. It is concluded that there is strong evidence that reading can be preserved in acquired and developmental prosopagnosia, and also evidence, though weaker, that face recognition can be left unimpaired in acquired or developmental dyslexia.

When identifying associations and dissociations between face processing and reading abilities, the same levels of processing needs to be assessed across categories. There is an abundance of face processing tests available assessing different levels of processing, making test selection for studies challenging. In Article 2: Tests Of Whole Upright Face Processing In Prosopagnosia: A Literature Review, literature is reviewed to identify tests that have been used to assess the processing of whole upright faces in acquired and developmental prosopagnosia. This resulted in a visual overview of tests classified according to the level of processing that they assess (perception, recognition and identification), as well as their experimental design. The overview is particularly useful when selecting face processing tests for a studies that compare performance across visual categories.

Article 3: Similar incidences of visual face and word processing deficits in patients with left and right posterior stroke, concerns a study assessing face and word recognition deficits in 32 patients with unilateral left and 21 patients with unilateral right lesions, respectively. The incidence of face recognition deficits and word recognition deficits were similar following lesions in either hemisphere, suggesting that face and word recognition may be supported by processes that are more bilaterally distributed than previously assumed. There was stronger evidence for impaired word recognition with preserved face recognition than the opposite pattern, a findings that stands somewhat in contrast to findings from Article 1. Findings are discussed in the context of the Many-to-Many Hypothesis.

The OCS-Dansk project, that is presented in Article 4: A Danish Version Of The Oxford Cognitive Screen: A Stroke-Specific Screening Test Providing A Useful Alternative To Currently
Used Tools, involves the collection of reference material for a Danish version of the Oxford Cognitive Screen (OCS). 91 neurotypical Danish-speaking controls were assessed with the OCS-Dansk as well as the Montreal Cognitive Assessment, and cut-offs were calculated for both tools. The study identified problems related to the MoCA cut-off currently used in Denmark, and concluded that the OCS may provide a useful alternative when screening for cognitive deficits in stroke patients in Denmark. Methodological considerations related to creating the normative material are discussed in the dissertation.
Resumé

Denne Ph.d.-afhandling vedrører to forskningsprojekter. Den første del af afhandlingen omhandler The Back of the Brain (BoB) projektet, og den anden del af afhandlingen omhandler Oxford Cognitive Screen (OCS-Dansk) projektet.

Ansigtsgenkendelse og ordgenkendelse er traditionelt blevet set som understøttet af processer, der er højt specialiserede, i høj grad lateraliseret og uafhængige af hinanden. Men de seneste år er det blevet foreslået, at ansigtsgenkendelse og ordgenkendelse er understøttet af fælles processer og overlappende netværk, der er bilateral medfølgende. Debatten har primært været baseret på fund fra studier af enkelte patienter, der er blevet udvalgt, fordi deres udfald, i høj grad er katgori-specifikke. BoB-projektet bruger en anden tilgang. Målet med projektet er, at bidrage med ny viden om de processer og den cerebrale arkitektur, der understøtter genkendelsens af komplekse stimuli som ansigter, objekter og ord. En stor gruppe patienter (N=70), som er rekrutteret ud fra lokalisationen af deres læsioner (arterie cerebri posterior), bliver udredt med det samme store batteri af sensitive tests af basale, mellemliggende og komplekse visuelle perceptuelle funktioner.


Når man ønsker at identificere associationer og dissociationer mellem evnen til at forarbejde ansigter og ord, så er det afgørende, at man udreder samme forarbejdningsevnen på tværs af kategorier. Der findes et hav af anisognatikseresvanskelighedstests tilgængeligt, der tester forskellige forarbejdningsevner, hvilket gør det svært at vælge tests ved planlægning af et nyt studie. Artikel 2: Tests Of Whole Upright Face Processing In Prosopagnosia: A Literature Review gennemgår litteraturen for at identificere tests, der er blevet brugt til at evaluere evnen til at forarbejde ansigter hos personer med erhvervet- eller udviklingsprosopagnosi. Dette resulterede i en oversigt, hvor tests er kategoriserede ud fra det forarbejdningsevne, de fokuserer på (perception, genkendelse og identifikation), samt ud fra deres eksperimentelle opsætning. Oversigten er særlig brugbar, når man skal udvælge en anisognatikseresvanskelighedstest, som skal bruges i et studie, der sammenligner præstationer på tværs af visuelle kategorier.

Artikel 3: Similar Incidences Of Visual Face And Word Processing Deficits In Patients With Left And Right Posterior Stroke, vedrører et studie, der sammenligner anisognatikseresvanskeligheder og ordgenkendelsesvanskeligheder hos 32 patienter med unilateral venstresidig skade og 21 patienter med unilateral højresidig skade. Der var lige stor andel af patienter med anisognatikseresvanskeligheder og ordgenkendelsesvanskeligheder i den højresidige og den venstresidige patientgruppe. Dette tyder på, at anisognatiksel og ordgenkendelse understøttes af processer, der er mere bilateral distribuerede end tidligere antaget. Der var stærkere evidens for at ordgenkendelse kan være bevaret ved anisognatikseresvanskeligheder, end det modsatte, hvilket ikke svarer helt overens med, hvad der
blev fundet ved artikel 1. Resultaterne bliver diskuteret inden for hypotesen: the Many-to-Many Hypothesis.

CHAPTER 1: The Back of the Brain Project
1. Introduction

A couple of years ago, we were contacted by an 80-year-old man, LB, who, after having a stroke, had lost the ability to recognise faces. He could no longer recognize celebrities on TV, struggled to recognise friends at social events, and had even failed to recognise his wife on numerous occasions. One particular episode illustrated elegantly his newly acquired deficit. He had gone to the local department store to buy clothes. When making his way towards the exit of the store, he walked down a corridor and saw someone coming towards him from the other direction. The two of them got closer until they finally were standing opposite each other. Trying to avoid each other, they both took a step in one direction and then in the other. Finally, hoping the other person would move, LB barged straight ahead and … smashed his head into the mirror. It turned out that the person he had been trying to avoid was not a stranger but his own reflection in a mirror. He had not been making his way down a corridor but rather had made his way into a fitting room. What makes LB particularly interesting is that, having had prominent positions in various large firms, he used to be an expert in recognising customers and business partners. Prior to his stroke, he could easily recognise people that he had only shortly met once, even if twenty or thirty years had passed.

While his brain injury had affected his face recognition, his knowledge about people was still intact. Despite only being able to recognize 4 out of 30 famous Danish and International people when presented with pictures of their faces, he could provide extremely detailed information about them, when provided with their names. He knew their approximate years of birth, which political parties they were involved in or, which songs they were famous for having made.

LB’s visual perceptual problems were not restricted to face recognition. His reading was slower and he made many mistakes, which was extremely frustrating for him as an avid reader. He also had total colour blindness (achromatopsia), wayfinding difficulties, a mental imagery deficit (aphantasia), as well as problems with getting a visual overview of his surroundings.

Vision is the perceptual sense that is considered to be the most highly developed in humans, nevertheless, we have a tendency to take our ability to perceive the world visually for granted. When compromised, the importance of vision becomes blatantly apparent. LB’s visual perceptual deficits have had a dramatic impact on his mood and quality of life. LB avoids social events to avoid embarrassing situations arising from his inability to recognise people. His interest in nature has also diminished now that he sees the world in shades of grey. He used to be an enthusiastic reader, but now that reading is so slow and arduous, he rarely opens a book.
Though the devastating consequences of brain injury cannot be stressed enough, patients like LB provide researchers with a unique insight into how the brain is organised. Indeed, by studying which functions are impaired and preserved in patients with acquired brain injury, conclusions can be made about how cognitive functions are organised in the neurotypical brain, and about which brain regions are involved in which cognitive processes (Shallice, 1988). Typically, researchers from the field of Cognitive Neuropsychology carry out in-depth investigations of patients with seemingly selective deficits, and use the principle of double dissociations to make conclusions about cognitive architecture. *Double dissociations* are defined as occurring if one individual has an abnormal performance on task X but performs within the normal range on task Y, and if a different individual shows the opposite pattern with a normal performance on task X but an abnormal performance on task Y (Coltheart, 2001). Based on such patterns, one can conclude that task X and Y rely on processes that are at least partially independent.

Findings from Cognitive Neuropsychology have had a particularly strong impact on the field of visual perception. There have been many reports in the literature of patients with visual perceptual disorders selectively affecting the recognition of specific visual categories. These different patterns of preserved versus impaired functions have been used to make inferences about the functional and cerebral organisation of visual recognition. Farah (1991) provided one of the first systematic reviews of patients with associative visual agnosia. 99 case reports were reviewed and patterns of co-occurrence of associative agnosia for faces, objects and words were analysed. The review reported that there were many patients with deficits in all three categories, and many patients with either co-occurring face and object processing deficits (spared reading) or with co-occurring word and object processing deficits (spared face processing). There were, however, no well-documented cases of patients with co-occurring deficits in face and word processing that also had preserved object processing. And there was only one patient with a possible pure object recognition deficit (sparing face and word processing). These patterns of deficits led Farah (1991) to propose that the visual recognition of complex stimuli is supported by two underlying capacities that are differentially involved in the processing of faces and words respectively. It was suggested that face recognition relies more strongly on the capacity to represent complex parts, and word recognition relies more strongly on the capacity to represent numerous parts simultaneously. Object recognition was, on the other hand, suggested to be supported by both capacities.
Chapter 1: The Back of the Brain project

2. Background of the Back of the Brain project

The findings from Farah’s (1991) review contributed to the view that face processing\(^1\) and word processing\(^2\) must rely on highly specialised, largely lateralised and independent cognitive processes. While this view still constitutes textbook knowledge (Gazzaniga, Ivry, & Mangun, 2013), it has been widely debated over the past decade. Indeed, it has more recently been suggested that face and word recognition are supported by common and highly overlapping networks that are more bilaterally distributed (Behrmann & Plaut, 2013). This debate constitutes one of the central questions of the BoB project and will therefore be described more in detail in the following section. Empirical findings from cognitive neuropsychology, functional magnetic resonance imaging (fMRI) studies and electroencephalography studies that are related to the debate are described, as well as key theoretical standpoints.

2.1. Face and word processing rely on highly specialised, largely lateralised and relatively independent cognitive processes

There are examples in the literature of patients with “pure” prosopagnosia, who have selective face recognition deficits (with preserved reading and object recognition), as well as examples of patients with “pure” alexia, who have selective reading deficits (with preserved face and object recognition). Most cases of pure prosopagnosia have bilateral lesions, or lesions in the right hemisphere (Barton, 2008b; Rossion, 2014), and most cases with pure alexia, have left hemisphere lesions (Leff, Spitsyna, Plant, & Wise, 2006; Starrfelt & Shallice, 2014). The two patterns of deficits have been considered as some of the strongest evidence that face and word recognition rely on processes that are, at least partially, independent.

Early studies using fMRI were initially interpreted as additional evidence of functional independence and lateralisation of face and word processing. A region in the left occipitotemporal gyrus, the visual word form area (VWFA), was shown to be more responsive to words than other visual stimuli (Cohen et al., 2000; Dehaene & Cohen, 2011; Kleinschmidt & Cohen, 2006; Puce, Allison, Asgari, Gore, & McCarthy, 1996) and a region in the right occipitotemporal gyrus, the

\(^1\) In this thesis the term “face processing” is preferred to the term face recognition, as it is more broadly encompassing. The term face processing is used to refer to aspects related to the processing of the identity of a face, spanning from the detection of a facial stimulus to the access of semantic information based on a facial stimulus, and not aspects related to for example emotion processing.

\(^2\) In this thesis the term “word processing” is used to refer to the visual processing of written word and not aspects related to the auditory processing of words.
fusiform face area (FFA), was shown to be more responsive to faces than other visual stimuli (Kanwisher & Barton, 2011; Kanwisher, McDermott, & Chun, 1997). Similar results were found using electroencephalography (EEG). Studies report that both faces and words give rise to a N170 component (an Event-related potential (ERP) wave), but that greater activity is provoked by orthographic stimuli in the left hemisphere and by faces in the right hemisphere (Bentin, Allison, Puce, Perez, & McCarthy, 1996; Schendan, Ganis, & Kutas, 1998).

2.2. Face and word processing rely on common and highly overlapping processes

While fMRI and EEG studies have indeed shown that face and word processing are lateralised, this lateralisation is far from complete. Both faces and words lead to bilateral activation, but with variable degrees of asymmetry, with the left hemisphere lateralisation for words being stronger than the right hemisphere lateralisation for faces (Bentin et al., 1996; Bentin, Mouchetant-Rostaing, Giard, Echallier, & Pernier, 1999; Dien, 2009; Harris, Rice, Young, & Andrews, 2015; Kanwisher et al., 1997; Urs Maurer, Rossion, & McCandliss, 2008; Nestor, Behrmann, & Plaut, 2013; Rossion, Joyce, Cottrell, & Tarr, 2003). These results suggest that face and word processing may rely on common functions and overlapping cortical areas.

There are also findings from cognitive neuropsychology providing evidence that face recognition is not fully right lateralised, and that reading is not fully left-lateralised. Indeed, prosopagnosia has been observed following damage restricted to the left hemisphere, and pure alexia has been described following damage restricted to the right hemisphere (Barton, 2008a; Davous & Boller, 1994; Mattson, Levin, & Grafman, 2000). Also, a study investigating reading and face recognition in patients with pure prosopagnosia and pure alexia reported that when assessed with sensitive tests, the patients with prosopagnosia also had reading deficits, and that patients with alexia also had face recognition deficits (Behrmann & Plaut, 2014). This led the authors to question previous findings of dissociations between reading and face recognition. It also led the authors to propose the Many-To-Many Hypothesis that holds a more distributed understanding of visual recognition (Behrmann & Plaut, 2013)(see Section 2.4 for a description of the Many-to-Many Hypothesis).
2.3. The lateralisation of face and word processing are related to one another

A series of studies have investigated how the lateralisation of face and word processing emerge respectively, and whether the lateralisation of face processing and the lateralisation of word processing could be associated. As they are not described in detail in any of the articles of this thesis, a more detailed description of these studies follows.

Reading proficiency has been shown to affect the degree of lateralisation of visual word processing (Kast, Elmer, Jancke, & Meyer, 2010; U Maurer, Brem, Bucher, & Brandeis, 2005; McCandliss, Cohen, & Dehaene, 2003; Mercure et al., 2009). Interestingly, it has also been shown to affect the cerebral substrates for face processing. fMRI studies have reported that, before learning to read, the ventral occipital temporal cortex responds bilaterally to faces, but that increases in reading ability in children and preliterate adults are associated with a reduction of left hemisphere response to faces (Cantlon, Pinel, Dehaene, & Pelphrey, 2011; Dehaene et al., 2010). Divided visual field studies using ERP measurements have shown that while children have adult-like left lateralised word processing, face processing in children is not lateralised. Face processing might only become right lateralised at a later time, and it has been suggested that it could be linked to reading proficiency. It has even been suggested that this may result from learning to read (Dundas, Plaut, & Behrmann, 2013, 2014).

There is, however, evidence from studies of small infants, that face processing is right lateralised prior to literacy. An EEG study using Fast Periodic Visual Stimulation investigated faces and objects processing (animals, plants, man-made objects) in four to six-month old infants. It reported that face images generated a face-specific right lateralised response that was not seen in response to non-face stimuli (de Heering & Rossion, 2015). However, in a study using the same procedure, 5-year old pre-schoolers did not show any right hemisphere lateralised face-selective brain response. These findings led the authors to suggest that the development of the right hemispheric specialisation for human face perception might be non-linear (Lochy, de Heering, & Rossion, 2017).

A couple of studies have shown that handedness impacts the lateralisation of face recognition. These studies have shown that the FFA is either bilateral or left-lateralised in left-handed individuals. Based on the results, it has been hypothesised that face processing may experience weaker competition against word processing in the left hemisphere in left-handers, as language is less left-lateralised in left-handed individuals (Bukowski, Dricot, Hanseeuw, &
Rossion, 2013; Willems, Peelen, & Hagoort, 2010). Similarly, an EEG study found that more right-handed individuals displayed more pronounced right lateralisation of the N170 for words. The study also found that the degree of lateralisation of the N170 for words was directly related to the degree of lateralisation of the N170 for faces (Dundas, Plaut, & Behrmann, 2015).

The Neuronal recycling Hypothesis and the Many-to-Many Hypothesis are two theories that have sought to account for these findings.

2.4. The Neuronal Recycling Hypothesis

According to the Neuronal Recycling Hypothesis, it is unlikely that humans have developed cerebral mechanisms that are genetically dedicated to reading as reading is such a recent invention that is acquired through specific learning. It is more likely that reading reuses pre-existing brain systems that have evolved genetically for other uses. The areas that are to be re-used must be plastic enough and must be in close proximity to associated functions (e.g. language for reading). The hypothesis proposes that various factors make the ventral occipital temporal cortex an optimal region for reading to “take over”. The ventral occipital temporal cortex is organised according to “increasingly invariant hierarchical coding” and the region has been shown to have a preference for high-resolution foveal shapes and to be well-adapted to extracting line configurations, making it well-suited for word recognition (Dehaene & Cohen, 2007). Regarding the hemispheric lateralisation of reading, the hypothesis has two plausible explanations as to why left-lateralisation is preferential. The first possibility is that left lateralisation enables shorter connections to language areas. The second possibility is that there could be intrinsic hemispheric differences in visual processing that give the left hemisphere an advantage for word processing (e.g. the left hemisphere could be better at analytic processing) (Dehaene & Cohen, 2007, 2011). Due to the constraints described, the cerebral areas that are optimal for word processing are the same areas in the left ventral occipital temporal cortex that have evolved for face processing. In other words, the authors suggest that word processing may reuse areas previously dedicated to face processing in the left hemisphere. Due to competition for cerebral space, as reading proficiency increases, face processing becomes more right lateralised (Dehaene & Cohen, 2011). According to this hypothesis, reading can be preserved in developmental prosopagnosia, but face recognition cannot be fully preserved in dyslexia. The Neuronal Recycling Hypothesis may indeed explain why neuropsychological studies have provided strong evidence of preserved reading in developmental or
acquired prosopagnosia, but only weaker evidence of preserved face processing in dyslexia and alexia (Robotham & Starrfelt, 2017; see section 2.6 for details).

2.5. The Many-To-Many Hypothesis

According to the many-to-many hypothesis, visual recognition in general, including the recognition of faces and words, is mediated by distributed cortical networks rather than circumscribed and independent modules. The hypothesis rejects the proposition that visual recognition is supported by neural regions that are specialised according to stimulus category. According to the hypothesis, hemispheric specialisation is graded rather than absolute, and normal face recognition is thought to be dependent on the integrity of a distributed circuit involving multiple cortical regions (core areas: fusiform face area, occipital face area, lateral occipital sulcus superior temporal sulcus, as well additional as areas such as the anterior temporal lobe, amygdala, inferior frontal and orbitofrontal cortex), as well as these regions’ connectivity. Normal word recognition also depends on the integrity of a network of areas (the posterior to anterior left ventral cortex, left superior temporal gyrus, right ventral cortex, inferior longitudinal fasciculus), and their connectivity (Behrmann & Plaut, 2013). These circuits overlap, in the sense that there are several regions that encompass the representation of faces and words. The authors suggest that face and word recognition are supported by bilaterally distributed networks that are not specialised for specific categories but involved in the processing of a whole range of visual categories. That face recognition problems should be found in all patients with pure alexia, and that reading deficits should be found in all patients with pure prosopagnosia, is a key prediction of the original proposal of the many-to-many hypothesis (Behrmann & Plaut, 2013). Regarding previous accounts of patients with pure prosopagnosia or pure alexia, the authors suggest they have suffered from methodological problems. In these single case studies of patients with so-called pure deficits, the function that is severely affected is typically assessed in depth, whereas functions that are described as preserved have typically not been assessed using sensitive enough tests.

The findings described above, suggesting that the acquisition of reading leads to the lateralisation of face processing, have been used as additional evidence in support of the many-to-many hypothesis (Behrmann & Plaut, 2015). The authors suggest that reading relies more on the left ventral occipital temporal areas than the right because of its proximity to language areas. Consequently, because of competition for resources, face processing that initially is bilateral,
becomes more right lateralised. Behrmann and Plaut (2015) argue that the findings represent additional evidence against the position that face and word processing rely on processes that are largely lateralised and highly independent. Instead, they provide evidence that both categories rely on bilateral processing but with one hemisphere contributing more strongly than the other. Hemispheric lateralisation is therefore considered graded rather than binary, a key feature of the Many-To-Many Hypothesis.

2.6. Dissociation or no dissociation between visual face and word processing?

As described earlier, one of the original key predictions of the Many-To-Many Hypothesis was that patients with prosopagnosia should have reading deficits, and that patients with pure alexia should have face recognition deficits. Following Farah’s seminal work (1991), a substantial amount of research was carried out to investigate whether face processing and object processing, on the one hand, and word processing and object processing, on the other hand, were dissociable. And while it was widely acknowledged for decades that face and word processing were dissociable, very little research had investigated the direct relationship between deficits in face and word processing (e.g. Gazzaniga, Ivry, & Mangun, 2013). Times have changed, and over the past decade, there has been a surge in research projects investigating directly, whether there is a double dissociation between face and word processing. Much of this research has come in direct response to the controversial prediction made by the Many-to-Many Hypothesis.

Many studies have now been carried out to investigate whether dissociations between face and word processing can indeed be found in individuals with acquired brain injury and developmental disorders (see R. Starrfelt & Robotham, 2018 for a discussion on the use of cognitive neuropsychological methods in developmental disorders), when using sensitive assessment methods. We carried out a review of the literature in order to get an overview of more recent studies investigating face recognition in dyslexia and pure alexia, as well as studies investigating reading in acquired and developmental prosopagnosia (Robotham & Starrfelt, 2017; Article 1, Appendix A). As comprehensive reviews of studies of visual agnosia for faces and words prior to 2004 are already available (Farah, 1990, 2004), only studies published after 2004 were reviewed. Only studies focusing on whether face or word recognition can be selectively affected by acquired brain injury or developmental disorders were included in the review and in total, 15 relevant studies were identified and analysed (Robotham & Starrfelt, 2017). Additional studies have
been published since the review was carried out and these are now included in the results described below (Albonico & Barton, 2017; Burns et al., 2017; Gabay, Dundas, Plaut, & Behrmann, 2017; Sigurdardottir, Fridriksdottir, Gudjonsdottir, & Kristjánsson, 2018). Overall, there is evidence that reading and face recognition can be affected selectively. Indeed, a series of studies have provided convincing evidence of normal performances on sensitive reading tests in patients with acquired prosopagnosia (Barton et al., 2010; Bukach, Bub, Gauthier, & Tarr, 2006; Hills, Pancaroglu, Duchaine, & Barton, 2015; M Jane Riddoch, Humphreys, et al., 2008; Susilo, Wright, Tree, & Duchaine, 2015) and in individuals with developmental prosopagnosia (Burns et al., 2017; Collins, Dundas, Gabay, Plaut, & Behrmann, 2017; Rubino, Corrow, Corrow, Duchaine, & Barton, 2016; Starrfelt, Klargaard, Petersen, & Gerlach, 2018). Some studies have also provided evidence, though weaker, that face recognition can be preserved in acquired alexia (Gaillard et al., 2006; Turkeltaub et al., 2014) and in developmental dyslexia (Smith-Spark & Moore, 2009). However, a couple of large studies that have assessed face processing using sensitive tests in dyslexic individuals, provide evidence that some aspects of face identity processing are impaired in these individuals, at least when investigated on a group level (Sigurdardottir et al., 2018; Sigurdardottir, Ivarsson, Kristinsdottir, & Kristjansson, 2015). Similar findings have been reported in studies of patients with acquired pure alexia (Albonico & Barton, 2017; Behrmann & Plaut, 2014).

Taken together, the results of the review suggest that face recognition is, at least in part, supported by processes that are not involved in the visual recognition words. Results also suggest that, while identifying the meaning of a word is highly left-lateralised, some other aspects of word processing, such as font and style recognition, may be supported by the right hemisphere (Barton et al., 2010). At last, results suggest that the left and the right hemisphere may contribute differentially to the recognition of facial identity (Albonico & Barton, 2017).

Taken together, these results do not fit with one of the original key predictions of the Many-To-Many Hypothesis described above: that face recognition problems should be found in alexia and that reading deficits should be found in prosopagnosia. The results fit better within the frame of the Neuronal Recycling hypothesis that predicts that reading can be preserved in developmental prosopagnosia and face recognition cannot be fully preserved in dyslexia.

The debate regarding whether the visual processing of faces and words rely on shared processes that are bilaterally distributed, or processes that are largely lateralised and independent, is
far from settled. The BoB project, that is the main focus of this thesis, aims to provide novel contributions to the debate by taking a slightly different approach. Much of the knowledge described above is based on single case studies that involve detailed investigations of patients with rare and seemingly selective deficits. In the BoB project, a large group of patients, selected according to lesion localisation rather than symptom profile, are recruited and tested with the same large battery of behavioural tests. Imaging data is also collected.

In the following sections, the objectives and hypotheses of the BoB project are first described. Then, the methods behind the study are presented. Special attention is given to the behavioural test battery as it constitutes one of the key contributions of this PhD to the BoB project. One of the key challenges related to the design of the test battery is discussed in depth. Finally, a study analysing preliminary data from a sub-set of tests from the BoB project is described. The findings, comparing face and word recognition in patients with left and right hemisphere lesions, are discussed in the context of the Many-To-Many Hypothesis.

3. Objectives and key hypotheses of the Back of the Brain project

The overarching aim of the BoB project is to acquire greater knowledge about the processes underlying the visual processing of different categories such as words, objects, and faces, and to investigate the cerebral organisation of these processes. Some of the theoretical questions that the BoB project intends to address are:

- Do face and word processing rely on processes that are largely independent, or processes that are highly distributed and shared?
- Which common processes do the visual processing of faces, words and objects rely on and which processes are selectively involved in the visual processing of specific categories?
- Is it possible to have selective deficits in visual face and word processing following brain injury, or are they always associated with other subtle deficits in visual perception?
- Can reading be spared after a lesion in the left fusiform gyrus and can face recognition be spared after a lesion in the right fusiform gyrus?
- Do the left and right hemispheres contribute differentially to the processing of different visual categories, and if so, how?
What is the relationship between deficits in object, word, or face processing and lower-level and intermediate visual perceptual deficits?

How do visual field defects affect higher-level visual perception?

Is there a relationship between premorbid reading skills or premorbid face recognition abilities, and type and severity of alexia and prosopagnosia following stroke?

Is there a systematic relationship between reading, writing, and non-reading visual deficits following injury in posterior cortical regions, and the underlying lesion location and extension?

This thesis focuses primarily on the following hypotheses that are predicted by the Many-to-Many Hypothesis:

1) Reading deficits are not only common following unilateral left hemisphere lesions, they are also common following unilateral right hemisphere lesions.

2) Face recognition deficits are not only common following unilateral left hemisphere lesions, they are also common following unilateral right hemisphere lesions.

3) In patients where reading is affected (writing spared), there will also be deficits (although perhaps subtler) in face recognition.

4) In patients where face recognition is affected, there will also be deficits in (although perhaps subtler) in word recognition.

In the following section, a more detailed description of the methods of the BoB project is provided.

4. Methodology of the Back of the Brain project

Single case studies have been the most commonly used method for investigating visual recognition following brain injury, and have provided a central contribution to the independent/distributed debate. In these studies, patients are selected according to their symptom profiles and in-depth investigations are carried out. By using principles of associations and dissociations, conclusions are made about how the brain functions. Single case studies, however, have their limitations. First, patients are included based on their symptoms and, typically, only patients with very rare patterns of deficits are studied. Therefore, single cases in the literature represent a very selective and non-representative sample of patients, and we cannot be sure that the results can be generalised to humans at large (Shallice & Buiatti, 2011). Conclusions about cerebral localisation based on the single case literature alone, are likely to be biased (Gerlach, Marstrand,
Starrfelt, & Gade, 2014). Second, single case studies often seek to prove that a patient has a pure deficit. However, one can argue that it is theoretically impossible to establish that a deficit is pure. Indeed, one can only assess a patient’s performance in a limited number of domains, so one can never exclude the possibility that a patient has another deficit (Plaut & Behrmann, 2011; see Rossion, 2018 for a counter-argument to this). Third, as patients are assessed with different tests in the different studies, comparisons across studies are difficult, if not impossible.

To overcome some of these limitations, the BoB project adopts a different approach. Patients are recruited according to their lesion location (within the regions supplied by the Posterior Cerebral Artery; PCA) rather than their symptomatology. And all patients are assessed with the same battery of sensitive tests of visual perception, making direct comparisons across participants possible. While single case studies are well suited to investigate dissolutions between deficits, investigations of larger groups of patients are better suited to investigate associations between deficits predicted by a distributed model (Starrfelt & Robotham, 2018). By selecting patients according to lesion rather than symptomatology, novel insights are expected. For example, this method may lead to the identification of patients with lesions in the Fusiform Face area, who have preserved face recognition, or patients with lesions in the Visual word form area, who have normal reading; patterns that would not be identified using the single case approach.

There are already examples of studies that have assessed a group of patients with PCA lesions. These studies have, for example, shown that category-specific deficits are not as common as one might expect from the single case literature (Gerlach et al., 2014; Kraft et al., 2014; Martinaud et al., 2012). One study investigated a wide range of visual perceptual abilities in 31 patients with stroke in the PCA (Gerlach et al., 2014). However, the tests included, lacked somewhat in sensitivity. The same can be said of a study investigating 128 patients with occipital, occipito-temporal, and occipito-parietal infarctions (Kraft et al., 2014). Another study that was more specifically interested in face, object and word processing, recruited and assessed 31 patients with stroke in the PCA. The study included very sensitive tests but only a small range of functions were assessed (Martinaud et al., 2012). Taken together, these studies provided evidence that the visual processing of faces and words are supported by processes that are more distributed than what could be expected, based on findings from single case studies alone.

The BoB project takes the lesion-based approach one step further than previous studies (for a simple overview of the BoB project, see Poster 1, Appendix F). A large group of patients (initial
aim: N=100) are recruited based on their lesions (located in the areas supplied by the Posterior Cerebral Artery) and are assessed with the same large battery of sensitive tests of lower-level, intermediate, and high-level visual perception, and associated functions. Control participants (initial aim: N=50) matched for age and education, are also included in the study and assessed with the same battery (for more details on inclusion and exclusion criteria see Article 3, Appendix C). By using the type of in-depth assessment that is used in neuropsychological single case studies in a large sample selected according to lesion location, novel insights in the processes underlying human visual perception are expected. High resolution brain imaging is also collected on all patients to provide additional anatomical insights.

To ensure recruitment of a large number of patients, the BoB project involves a collaboration between three universities. The core team consists of Principal Investigator, Professor (MSO) Randi Starrfelt, Department of Psychology, University of Copenhagen, Dr. Alexander P. Leff, Institute of Cognitive Neuroscience, University College London, and Professor Matthew Lambon-Ralph, Neuroscience and Aphasia Research Unit, University of Manchester (now Director at the MRC Cognition and Brain Sciences Unit, Cambridge University). A PhD student at University of Copenhagen (me) and a postdoc at each of the UK sites (Sheila Kerry and Grace Rice) are also involved in the project. The Copenhagen team is primarily responsible for the experimental design of the study and the UK teams are primarily responsible for subject recruitment and data collection.

Currently, 63 patients and 33 healthy control participants have been assessed, making it the largest study to date investigating visual perceptual functions in a group of patients with lesions in the areas supplied by the PCA. Data collection will stop at the end of 2018 and the current aim is to include in all 70 patients and 50 control participants.

The design of the battery is described briefly below, as it represents a central contribution of this PhD to the BoB project and as it will provide the basis for discussions in Sections 5. The imaging protocol, on the other hand, will not be discussed further, as it is not within the scope of this PhD project.
4.1. Behavioural test battery

The behavioural test battery was designed to answer the key questions of the BoB project and to test the key hypotheses. The test battery had the following key constraints:

   a) Maximum nine hours completion time for a typical patient with brain injury.
   b) Distributed over maximum three sessions (on three separate days).

First, functions of interest were identified. Then, an extensive literature search was carried out to identify available tests that could be used to assess the functions of interest. Tests that were in English, short (limit fatigue), validated and/or previously used in research were prioritised. Also, to limit the effects of hemianopia on performance, central/vertical presentation of stimuli was preferred. For assessment of non-visual functions, tests that were as visually simple as possible, were selected. An overview of the specific tests that were included in the final version of the BoB behavioural test battery, is provided in Figure 1. For a more detailed description of the behavioural battery and the tests included in the BoB project, see Supplementary material in Appendix E (a short description of the imaging protocol is also provided). The process of searching the literature for visual perceptual tests also resulted in a an overview of tests that are useful in a clinical context (see Poster 2, Appendix G).

As the main focus of the project concerns visual perceptual functions, many of the tests included in the study focused on visual perceptual abilities. Visual perception can be thought of as a process that ranges from the processing of low-level characteristics of stimuli (such as colour, motion, orientation and contrast), to the processing of complex high-level aspects of visual perception (involving the processing of faces, words and objects). Intermediate visual perceptual processes are the processes situated between the two. The ability to group visual elements into meaningful representations, to segregate overlapping figures and to segregate stimuli from their background are typically conceptualised as intermediate visual perceptual processes (see Wagemans et al., 2012 for a review).

The aspects of visual perception that were included in the BoB test battery are described in the following sections.
4.1.1. **High-level visual perception: face, word and object processing**

Many of the central research questions of the BoB project focus on relations between visual *face processing*, *word processing* and *object processing* abilities. Therefore, the test battery needed to include satisfactory assessment of these high-level aspects of visual processing. There are many tasks available that can be used to assess face, object and word processing, and these tasks assess different levels of processing. While some tasks focus on more perceptual aspects of processing,
others put higher demands on the semantic system. Bruce & Young (1986) conceptualised face processing as involving the following sequential stages: structural encoding, face recognition, retrieving biographical information and generating the name of a person. And most face processing tasks can be categorised according to the level of processing that they assess: perceptual level, recognition level and identification level. Indeed, perceptual tests focus on basic perceptual abilities that do not require participants to build a cohesive representation of the stimulus. Recognition tasks, on the other hand, involve the “matching of a currently viewed stimulus to a stored representation, affirming that one has encountered the stimulus before” (Barton and Corrow, 2016b, p. 136). Identification tasks require matching a representation to associated semantic/biographical information. In Article 2 (Robotham & Starrfelt, 2018, in press; Appendix B): Tests Of Whole Upright Face Processing In Prosopagnosia: A Literature Review, we reviewed the literature over the past five years to identify tests that had been used to evaluate upright face processing in prosopagnosia. Tests were classified according to the stages of processing that they assess. Object processing tests and word processing tests can also be categorised according to these three levels of processing (perception, recognition, and identification). Ideally, we wanted the test battery to enable conclusions to be made about the integrity of each of these levels of processing. Due to time constraints, however, the final test battery only included assessment of face, word and object recognition and identification and not perception.

4.1.2. Intermediate level visual perception

The integrity of intermediate visual perceptual processes had to be determined in order to make conclusions about face, word and object processing abilities. It has previously been hypothesised that dissociations between face and word processing abilities could potentially be explained by deficits in lower-level visual perception such as spatial frequency (e.g. Roberts et al., 2012; Woodhead et al., 2011), that affect the processing of some stimuli types more than others. Intermediate visual perceptual abilities such as: figure-ground segmenting, local/global processing, basic shape perception, perceptual grouping, evaluation of co-linearity and proximity or closure, could also explain differences in performances between different visual stimuli and are therefore relevant to assess. Additionally, identifying patients with selective deficits in intermediate visual perception would provide a useful contribution to the literature. Indeed, single case descriptions of patients with relatively selective deficits at this level following brain injury in the posterior regions do exist (e.g. patient with integrative visual agnosia described in Riddoch and Humphreys, 1987 and patient with visual form agnosia described in Milner et al., 1991), but they are rare.
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4.1.3. **Low-level visual perception**

A visual field test was included as *visual field defects* are common following posterior cerebral artery stroke, and as they can have an impact on the performance on many visual perceptual tasks (Zihl, 2011). *Visual acuity* also needed to be assessed, as it can affect performances on visual tasks. Stroke patients are often in the older age range and can be expected to have acuity problems.

4.1.4. **Semantic abilities**

A basic assessment of *semantic processing* was included in order to determine whether abnormal performances on recognition and identification tasks could be explained by general semantic deficits. A non-visual synonym task was included for this purpose.

4.1.5. **Associated functions**

Deficits such as *topographical disorientation* and *achromatopsia* have been shown to be highly associated with prosopagnosia, however, little is known about these associations. Assessment of these functions was included, as it enables further investigation of these associations. As preserved writing is a key criteria for pure alexia, assessed of *writing abilities* was included. *Handwriting recognition* was also assessed, as some studies suggest that it may be supported by processes that are right lateralised (Barton et al., 2010; Hills et al., 2015).

4.1.6. **Background information**

*Handedness* was assessed using the Edinburgh Handedness-Short (Veale, 2014); *Depression*, using the Geriatric depression scale-short (Sheikh & Yesavage, 1986), *General cognition*, using the Oxford Cognitive Screen (Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015), and *Basic motor response*, using an experiment that we designed specifically for the BoB project (see Supplementary material, Appendix E). As prosopagnosia and alexia exist as developmental disorders, premorbid abilities were evaluated (Duchaine & Nakayama, 2006; Iaria & Barton, 2010).

In the following section, one of the key challenges faced when designing the test battery is described and discussed, namely, finding tests that enable direct comparison of face, word and object processing abilities.
5. Comparing Face And Word Processing: An Insoluble Conundrum (Poster 3, Appendix H)

As discussed above, the relationship between visual face processing and the visual processing of words has received substantial attention over the past decade. A key question concerns whether face and word processing rely on processes that are largely independent, or whether they rely on processes that are highly distributed and shared. This is also a key question of interest for the BoB project. Typically, conclusions are made on the basis of a comparison between performance on one or more tests of face processing on the one hand, and word processing on the other. A visual object processing task is sometimes included as a control task (see supplementary material for Article 1, Appendix A, for an overview of tests used in neuropsychological studies comparing face and word processing).

5.1. Importance of comparing the same stages of processing across categories

As described above, the visual processing of these types of complex stimuli can be conceptualised as involving a series of sequential stages, from the structural encoding of the stimulus, to the access of semantic information related to the stimulus (Bruce & Young, 1986; Robotham & Starrfelt, 2017). Tests of face, word and object processing can therefore be categorised according to the stage of processing they assess: the perceptual stage, the recognition stage and the identification stage (see Figure 2). Table 1 provides an example of how face, word and object processing tests can be categorised according to level of processing.
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Table 1: Categorisation of commonly used tests of word, object and face processing according to stages of processing

<table>
<thead>
<tr>
<th></th>
<th>Word</th>
<th>Objects</th>
<th>Faces</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification</td>
<td>• Word reading (Voice-key RT)</td>
<td>• Object naming</td>
<td>• Naming familiar faces</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Word-to-picture matching</td>
<td>• Name-to-face matching</td>
</tr>
<tr>
<td>Recognition</td>
<td>• Lexical decision (word/non-word)</td>
<td>• Object decision task (object/non-object)</td>
<td>• Face familiarity tests (familiar yes/no)</td>
</tr>
<tr>
<td></td>
<td>• Old/new recognition (ex: Warrington recognition test for words)</td>
<td></td>
<td>• Old/new recognition</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Delayed matching</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>• Delayed discrimination</td>
</tr>
<tr>
<td>Perception</td>
<td>• Simultaneous matching</td>
<td>• Simultaneous matching</td>
<td>• Simultaneous matching</td>
</tr>
<tr>
<td></td>
<td>• Simultaneous discrimination</td>
<td>• Simultaneous discrimination</td>
<td>• Simultaneous discrimination</td>
</tr>
<tr>
<td></td>
<td>• Detection letter-strings</td>
<td>• Detection of objects</td>
<td>• Detection of faces</td>
</tr>
</tbody>
</table>

When investigating whether there is a dissociation between face and word processing, it is important that comparisons are made between performances on tests measuring the same levels of processing for each category (Barton, 2018; Robotham & Starrfelt, 2017). Indeed, if a patient performs normally on a face perception test but abnormally on a word recognition test, then it would be misleading to conclude that the participant has word-specific visual processing deficit. The difference in performance may have nothing to do with the differences in abilities to process specific visual categories, and may instead be caused by a deficit in short term memory (that affects performance on the word recognition task and not the face perception task).
When investigating the extent to which the visual processing of faces and words are supported by common or independent processes, distinguishing these levels of processing is highly relevant. Indeed, it is, for example, possible that the visual processing of faces, words and objects rely more strongly on common processes at the perceptual stage of processing than at the recognition or identifications stages of processing. This can only be investigated by assessing comparable levels of processing for all categories.

5.2. Strategies commonly used when selecting tests and their shortcomings

Three strategies are commonly used when comparing face and word processing abilities

Strategy 1: Use diagnostic tools for deficits in one category and commonly used experimental tests for the other category

A common approach in neuropsychological studies is to use diagnostic tests for one category and commonly used experimental tests for the other category. For example, in a study investigating face processing in participants with developmental dyslexia, Smith-Spark and Moore (2009) evaluated reading proficiency with a questionnaire, the Dyslexia Adult Screening Test (Fawcett & Nicolson, 1998), and assessed face processing with a famous-face-naming test. And in a study investigating reading in patients with acquired prosopagnosia, Hills et al. (2015) evaluated face processing abilities with a questionnaire and a couple of diagnostic tests, and evaluated reading with experimental word reading tasks. While this approach makes a lot of sense from a practical perspective, it has its limitations. As such different methods are used for the different categories (e.g. questionnaire vs performance-based test), the conclusions that can be made about dissociations between face and word processing are limited.

Strategy 2: Compare typical effects found in neurotypical participants or clinical groups with the different categories of stimuli

Patients with prosopagnosia have been shown to have a different pattern of performances to controls on tasks measuring the face inversion effect. Controls are much faster and more accurate at recognising upright faces than inverted faces. Patients with prosopagnosia, however, do not show an upright advantage (Busigny & Rossion, 2010). Patients with pure alexia, on the other hand, are characterised by having a word length effect (Barton, Hanif, Eklinder Bjornstrom, & Hills, 2014; Starrfelt & Shallice, 2014). In contrast to healthy participants, their reaction time for reading words...
increases for each additional letter. Therefore, an absence of face inversion effect is sometimes used as evidence of abnormal face processing, and a word length effect is used as evidence for abnormal reading. A study investigating face processing in patients with acquired alexia, and reading abilities in patients with acquired prosopagnosia, measured face inversion effects and word length effects to determine whether there were associations in deficits of face recognition and reading (Behrmann & Plaut, 2014). Although the word length effect has been shown repeatedly in patients with alexia, and an absence of inversion effect in patients with prosopagnosia, little is known about the perceptual mechanisms that they reflect (see Rezlescu et al., 2017 and Barton et al., 2014 for discussions about the face inversion effect and word-length effect, respectively). Even less is known about the relationships between such effects, and what conclusions can be made based on the comparisons between such affects.

**Strategy 3: Test the stimulus categories in the same experimental setup to ensure similar task demands.**

Comparing performance on a face processing task using two-alternative forced choice, to a reading task requiring verbal response, is not ideal. And this, regardless of whether standard measures like accuracy or RT, or specific effects are used as independent measures. If a participant has an abnormal performance on one task, but not the other, one cannot necessarily conclude that the participant has a category specific deficit. The difference may instead be caused by task-dependent factors. To overcome this, some studies use the same experimental paradigm to assess the processing of faces, objects and words. This ensures, that task demands are comparable across categories.

Many neuropsychological studies that have compared face processing and word processing directly in participants with acquired or developmental prosopagnosia and alexia, include the Warrington Recognition Memory test (WRMT; Warrington, 1984) for faces and words, as the same paradigm is used for both categories (Barton et al., 2010; Gaillard et al., 2006; Hills et al., 2015; Riddoch, Johnston, Bracewell, Boutsen, & Humphreys, 2008; Rubino et al., 2016). As another example, a study investigating the hemispheric superiority for faces and words in children, adolescents and adults used the same delayed matching paradigm for all three categories (Dundas et al., 2013)(Figure 3).
Using the same experimental paradigm for both categories seems like a useful solution for ensuring that the same stages of processing are being assessed. Therefore, for the BoB project, we adopted this strategy to design a novel experiment that assessed word, object and face recognition abilities: the WOF test.

5.3. The Words, Objects, and Faces (WOF) test

The WOF test was developed to assess the recognition stage of processing, as this is the stage that has received most attention in the literature. It aimed to enable the identification of potential dissociations between the processing of these three visual categories.

The WOF test is described in detail in Article 3 (Appendix C). It combines two commonly used paradigms: a delayed matching paradigm, and an old/new recognition paradigm. In the delayed matching part, participants are presented with a stimulus, followed shortly after by another stimulus, from the same visual category that is either identical to the initial stimulus or different. Participants are asked to respond as quickly and accurately as possible whether the two stimuli that they have been presented with sequentially, are the same or not. Faces, words and objects are assessed in separate blocks. In the old/new recognition part, which is run directly after the delayed matching paradigm, participants are presented with two stimuli at a time, one stimulus that they have seen in the delayed matching part of the task, and one novel stimulus. Participants are asked to indicate which stimulus they have seen before. Faces, words and objects are also assessed in separate blocks here. With its two parts, the test is designed to differentiate between difficulties in
creating a short-term representation of a stimulus and matching it with a currently viewed stimulus, and deficits in storing a representation over longer time interval.

The results from 31 British controls (collected within the BoB project, see Paper 3, Appendix C for more details on data collection) and from 43 healthy controls in Denmark (collected from some of the participants within the OCS-Dansk project; age range: 36-82, mean: 64.7, SD: 11.0; years of education: 7-23, mean: 14.8, SD: 3.6; see Article 4, Appendix D for details) suggest that the level of difficulty is relatively well matched across categories (Figure 4). Despite mean accuracy being close to ceiling for controls, preliminary patient data collected within the BoB project provide convincing evidence that the test can identify deficits in face, word and object processing.
Figure 4: Mean accuracy and mean RTs based on correct trials for whole control participants from a British (N=31) and a Danish sample (n=43)
In Article 3 (Appendix C), BoB data from 58 PCA patients and 31 healthy control participants were analysed in order to 1) evaluate whether face recognition deficits are more common in patients with unilateral right hemisphere lesions, and whether word recognition deficits are more common in patients with unilateral left hemisphere lesions, and 2) identify whether any patients had dissociations between face processing and word processing. Data from a selected subset of tests included in the BoB project were analysed: the WOF test, the Cambridge Face Memory Test and a single word reading test.

The core finding of the study was that there was no significant difference in mean performance between the group of 32 patients with unilateral left hemisphere lesions, and the group of 21 patients with right hemisphere lesions on any of the conditions (words, objects and faces) of the WOF test. A substantial proportion of patients with left hemisphere lesions had abnormal performance in the face conditions of the task, and a substantial proportion of patients with right hemisphere lesions had abnormal performance in the word conditions of the test. And interestingly, the proportions of patients with left hemisphere lesions and right hemisphere, respectively, with abnormal performance in either category, was highly similar. The Cambridge Face Memory Test, that also measures processing at the level of recognition, yielded similar results. These results suggest that face and word recognition may be supported by processes that are less lateralised than what may be expected on the basis of the single case literature, and may instead be highly distributed.

Results differed, however, between the patient groups on the single word reading test requiring naming. The left hemisphere patient group performed significantly worse than the right hemisphere patient group, and a higher proportion of patients with left hemisphere lesions had abnormally long reaction times on the test. It is possible that tasks requiring verbal output rely on processing that is more strongly lateralised.

An additional finding from the study was that there were 3 patients with LH lesions, and 1 patient with RH lesion, who had dissociations between reading and face processing. These patients all had impaired reading but preserved face recognition. These results suggest that the visual processing of written words may, at least in part, be supported by some processes that are not involved in face recognition. The results indicate, however, that patterns of dissociation between face and word recognition are rare (only 4 patients out of 58).
5.4. Discussion: An insoluble conundrum

The findings of the study described above, related to dissociations, illustrate the implications of comparing performance across tests measuring the same level of processing. When evaluating dissociations on the basis of comparisons between accuracy measured of the CFMT (measuring recognition) and the reading-out-loud task (measuring naming/identification), seven patients had impaired reading and preserved face recognition. However, only four of these patients had a pattern of dissociation when comparing their scores on a recognition task using the same experimental set-up (the WOF test). For the other three patients, the pattern of dissociation observed between the CFMT and the reading-out-loud test may be due to task dependent factors, rather than differences in abilities to process specific visual categories.

Earlier in this section, it was suggested, that using the same experimental paradigm was likely the most appropriate solution, for ensuring that the same stages of processing are being assessed across categories. It can be argued, however, that despite using the same experimental design across categories, different levels of processing may be involved for the different categories. In the WOF test described above, while the semantic system is only likely to be involved to a small degree for the face and object conditions, participants can rely more strongly on the semantic system to respond in the word condition. Both the sequential matching and surprise recognition paradigms involve creating and storing a representation, and then matching a stimulus that is being viewed to the stored representation. And while the specific items that need to be stored (e.g. “Bead”) can be verbalised for the word condition, individual items cannot be verbalised as easily in the object and face conditions of the test. So although the categories are assessed using the same experimental paradigm, task requirements and levels of processing are not identical.

Another difference between the word condition and the face and object conditions in the WOF task is the level of familiarity of the stimuli. While the examplars used in the face and object conditions are novel to the participants, the examplars used in the word condition are not. A potential solution to this, could be to use non-words rather than real words for the word condition. The disadvantage of this is, however, that patterns of reading differ highly between words and non-words. And the main focus of the project is to understand the processes underlying normal reading and not the reading of non-words.

That no study has succeeded in developing a paradigm that uses the same experimental set-ups across categories, while measuring the same level(s) of processing, might tell us something
about the nature of the entities that we are studying. Words are a unique type of visual stimulus that are symbolic in nature. They carry meaning, but in contrast to faces (and objects), there is no resemblance between the shape and form of the word itself, and what it refers to. It is possible that designing an experiment measuring the same level of processing of faces and words, while using the same experimental set-up, is impossible due to the categorical constructs of faces and words being so radically different.

Our pragmatic take on this was to 1) Develop the WOF test that assesses words, object and face recognition, using the same experimental paradigm 2) include familiarity tasks for each category: a lexical decision test (word vs non-word), a face familiarity test (famous vs non-famous) and an object decision test (object vs non-object), and 3) Include typically used measures of face recognition (e.g. CFMT) and reading (e.g. single word reading). We are, however, not fully satisfied with this solution. The paradoxes of comparing faces and words, that are two radically different constructs, deserves further attention, and new approaches enabling direct comparisons between categories are needed.

6. BoB: General discussion

The debate regarding whether face and word processing rely on processes that are independent or distributed is far from settled (Behrmann & Geskin, 2018). Indeed, some still maintain the view that there are brain regions that are fully dedicated to specific visual categories. Kanwisher et al. (1997), who published the seminal paper identifying a face-specific area in the right fusiform gyrus and who coined the term Fusiform Face Area, recently published a paper that argues that the brain is “composed of a set of distinct components, some of them specialised for solving a very specific problem” (Kanwisher, 2017, p. 1057-1058). Kanwisher (2017) specifies that by discovering the Fusiform Face Area, they had discovered “a little piece of brain that seemed to do just one thing: perceive faces” (p. 1056). The proponents of the Many-To-Many Hypothesis, on the other hand, propose that different visual categories (such as faces and words) rely on highly distributed and overlapping processes. They reject that faces and words are mediated by circumscribed “centres” that are dedicated to specific categories, and reject that there are fundamental and intrinsic differences between the right and left hemisphere (Behrmann & Plaut, 2013, 2015).

The current thesis has contributed in various ways to this discussion. First, a review was carried out of studies investigating whether face or word recognition can be selectively affected by
acquired brain injury or developmental disorders (Article 1, Appendix A; described in section 2.4). It was concluded, that there is strong evidence that reading can be preserved in acquired and developmental prosopagnosia, and also evidence, though weaker, that face recognition can be left unimpaired in acquired or developmental dyslexia.

A second contribution comes from an empirical study using preliminary data from the BoB project (Article 3, Appendix C; described in section 5.3). The performance of patients with unilateral left or unilateral right hemisphere lesions on a novel test of face, word and object recognition (the WOF test) was highly similar on a group level. Also, the frequency of patients with deficits in the word conditions and the face conditions of the WOF test did not differ significantly between left hemisphere and right hemisphere groups. Interestingly, an analysis of patterns of dissociations revealed that while there was evidence of patients with impaired reading and preserved face recognition, there was no convincing evidence of the opposite pattern (note that the review above found stronger evidence for dissociations in the other direction).

The core findings of the empirical study, namely, that face and word recognition deficits are common following lesions in either hemisphere, fit well with the Many-To-Many Hypothesis, that suggests that face and word recognition are supported by networks that are bilaterally distributed (Hypothesis 1 and 2 described in Section 3). However, the evidence of patterns of dissociation from Article 1 and Article 3 represent evidence against key original predictions of the Many-To-Many Hypothesis (hypothesis 3 and 4 described in Section 3), namely, that patients with prosopagnosia would always have reading deficits, and that patients with alexia would always have face recognition deficits (Behrmann & Plaut, 2013).

In response to Susilo and Duchaine (2013) pointing out that there is now highly convincing evidence of patients with category specific deficits, Plaut and Behrmann (2013) made a small change to their key prediction. They specified that the Many-To-Many Hypothesis does not hold that: “individuals with prosopagnosia will always have some deficits in word recognition while individuals with alexia will always have some deficits in face recognition” (Plaut & Behrmann, 2013, p. 546). They specify instead that: “patients with severe face or word impairments will, as a population, tend to be more moderately impaired in the other domain, as well” (Plaut & Behrmann, 2013, p. 546). Despite it being small, this adjustment has considerable theoretical implications. Indeed, while the original prediction was falsifiable, the new formulation is
not. It suddenly becomes unclear what testable predictions can be made based on the Many-To-
Many Hypothesis, and what evidence would be needed to reject the hypothesis.

It can also be argued, that the Many-To-Many Hypothesis lacks in detail. While it advocates
that the recognition of different categories is supported by cortical networks that are “highly
distributed” (Behrmann & Plaut, 2013), it does not refute the possibility that there could be
processes involved in word processing, that are not involved in face processing, and vice versa. But
very little detail is provided regarding the extent to which the different visual categories are
supported by common or independent mechanisms. And, it is not specified which processes are
thought to be common, and which are not. One of the few seemingly testable statements made by
the proponents of the hypothesis is that while there are regions that are more or less specialised for
particular categories, there are no regions that are fully dedicated to specific categories (Plaut &
Behrmann, 2013). But it is also debatable whether this statement can be falsified (a discussion that,
in part, relates to definitions of selectivity, see Cohen & Dehaene, 2004).

According to Rossion (2018), in order to determine that there is a specific neural system
dedicated to faces (a “face module”), clear evidence of a double dissociation between face and
object recognition would be required. While many argue that there is strong evidence of patients
with pure prosopagnosia, a selective deficit in face recognition deficits (preserved object
recognition) (Rossion, 2014), evidence of patients with pure object agnosia, a selective object
recognition deficit (preserved face recognition) is weak. One could, however, take this one step
further and argue that evidence for a double dissociation between visual face processing and visual
object processing would not be enough. Indeed, proving that there is a “face module” would require
dissociations to be shown between face recognition and all other visual categories.

Where do we go from here? What seems clear from the literature is that nobody claims that
the visual processing of categories such as faces, words and objects are supported by fully shared
processes, nor does anyone argue that the processing of such categories is fully modular. Most
would agree that faces and words share early visual processing and share some semantic processing.
However, some of the questions that remain to be answered are:
1) Where, along the ventral stream between V1 and the anterior temporal lobe, is processing more
specialised according to categories?
2) Does this differ between the hemispheres?
3) Which processes and cortical areas are common to face and word recognition, and which, if any, processes and cortical regions are selectively involved in either faces or words?

4) Are there clusters of neurons that are fully dedicated to the visual processing of a specific category?

Indeed, while the processes and cerebral areas in V1 in the occipital pole and the semantic areas in anterior temporal lobe are likely to be less category-specific, it is possible that areas responsible for the visual recognition of complex stimuli are organised with some areas being more specialised for the recognition of specific visual categories. But there is a need for novel theories of visual recognition that provide detailed and falsifiable accounts of the functional and cerebral organisation of the visual processing of complex stimuli such as faces, words and objects.

The preliminary findings from Article 3 (Appendix C), analysing data from the BoB project, indicate that face and word recognition is supported by processes that are more bilaterally distributed than traditionally thought. Also, the patterns of dissociations of impaired word recognition and preserved face recognition suggest that there are processes involved in word recognition, that are not involved in the recognition of faces. Further analysis of the full dataset from the BoB project, which enables analysis at various levels of processing in a large group of patients, will hopefully lead to novel insights into which aspects of the visual processing of faces, words and objects are shared, and which are not.
Intermezzo

And now for something completely different.

The following chapter of this dissertation concerns the OCS-Dansk project. While planning the BoB project, we discovered the Oxford Cognitive Screen (OCS): a screening tool specifically designed for identifying cognitive deficits in stroke patients. As there to date has not been a short stroke-specific cognitive screening tool available in Danish, I decided to translate the OCS into Danish. The OCS-dansk project, that is described in detail in Article 4 (Appendix D), also involved collecting reference material from healthy Danish controls and providing cut-offs for clinical use. In the following chapter, additional information regarding cognitive screening of stroke patients in a Danish context is provided, key methodological considerations of the OCS-Dansk study are discussed, and limitations are described. Thoughts regarding future directions for the OCS-Dansk are also presented.
CHAPTER 2: Oxford Cognitive Screen – Dansk
1. Introduction

Approximately 15,000 people suffer from stroke annually in Denmark (Sundhedsstyrelsen, 2015) and approximately 50% of those who have a stroke experience long-term effects. The number of people living with the consequences of stroke is expected to rise over the coming years, due to the aging population. The care and management of stroke patients is complicated, as stroke can lead to a combination of physical, cognitive, and emotional dysfunctions. Cognitive deficits are common (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009), have severe impacts on quality of life and levels of independence (Hommel, Miguel, Naegele, Gonnet, & Jaillard, 2009), and lead to a higher level of burden on caregivers and higher societal costs (Patel, Coshall, Rudd, & Wolfe, 2002). And as cognitive deficits are often subtle and can easily be overlooked in a clinical setting, systematic screening of cognitive deficits before discharge, would be helpful in planning adequate care and rehabilitation of stroke patients.

In the United Kingdom, assessment of cognition is mandatory. The guideline for Stroke Rehabilitation in Adults published by the National Institute for Health and Care Excellence, state that during hospital stay, one must perform a “full medical assessment of the person with stroke, including cognition (attention, memory, spatial awareness, apraxia, perception), vision, hearing, tone, strength, sensation and balance” (p. 17, Stroke rehabilitation in adults: Clinical guidelines, 2013). In Denmark, however, assessment of cognition following stroke is not mandatory. While working as a clinician at a stroke ward, I observed that many patients were discharged without their cognition being assessed directly. None of the cognitive screening tools available in Danish have been well-suited for quick screening of stroke patients, which has been one of the key challenges for implementing more systematic screening of cognitive deficits following stroke in Denmark.

1.1. Cognitive Screening Tools that are used in a stroke context in Denmark

The Mini Mental State Examination (MMSE) (Folstein, Folsein, & Fanjiang, 2001; Folstein, Folstein, & McHugh, 1975), the Addenbrooke’s Cognitive Examination (ACE) (Mathuranath, Nestor, Berrios, Rakowicz, & Hodges, 2000), and the Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) are dementia screening tests that are commonly used for stroke screening internationally (Burton & Tyson, 2015) and that are available in Danish.
The MMSE (Folstein et al., 2001, 1975) is the cognitive screening tool that is most commonly used worldwide. Although there is no official Danish version of the test, there are various Danish translations available. Various studies have been carried out over the past decades to collect reference material for Danish versions of the MMSE (Kørner et al., 2008; Lolk & Nielsen, 2002; Schultz-Larsen, Kreiner, & Lomholt, 2007; Vogel, Gade, Stokholm, & Waldemar, 2005). The ACE (Mathuranath et al., 2000) is a more extensive screening tool that is designed to detect mild dementia and to differentiate between Alzheimer’s disease and frontotemporal dementia. It includes the items from the MMSE as well as additional tasks. Danish norms are available for the ACE (Stokholm, Vogel, Johannsen, & Waldemar, 2009). The MoCA (Nasreddine et al., 2005) was designed to identify mild cognitive impairment and has been shown to be more sensitive to cognitive deficits following stroke than the MMSE and the ACE (Burton & Tyson, 2015; Pendlebury, Cuthbertson, Welch, Mehta, & Rothwell, 2010). I have been in contact with various stroke wards in Denmark, where the MoCA is used by physiotherapists to screen for cognitive deficits. And, as there are no published Danish norms for the test, results are interpreted either without using norms, or using the cut-offs of 25-26 provided in the original Canadian study (Nasreddine et al., 2005).

The CABPad is, to our knowledge, the only stroke specific cognitive screening tool that has been available in Denmark until now (Willer et al., 2016). It enables evaluation at the level of cognitive domain and measures the most common and significant symptoms seen after stroke. The original version of the CABPad is in Danish and the test has been validated in a Danish stroke sample (Willer, Pedersen, Forchhammer, & Christensen, 2016). The CABPad is well-designed and enables in-depth assessment of a wide range of cognitive functions. The main disadvantage of the test is, however, that it takes 40 minutes to complete, making it an unlikely choice as a standard screening tool that can be administered to all stroke patients.

None of the tools described above are optimal for quick and systematic screening of stroke patients. While the MMSE, the ACE and the MoCA enable quick screening of cognitive deficits and can be used by health care professionals with limited training, they focus on cognitive functions that are relevant for dementia (e.g. memory, language and visual construction) and fail to screen some of the functions that are commonly affected following stroke (e.g. neglect and visual perception). Also, they fail to provide assessment at the level of cognitive domain, which is an important limitation within a stroke context, as stroke can lead to highly selective cognitive deficits.
While the CABPad overcomes these limitations, it has a relatively long administration time (see Table 2 for comparison of tests).

Table 2: Comparing the OCS to screening tools currently used in a stroke context in Denmark

<table>
<thead>
<tr>
<th>MMSE</th>
<th>ACE</th>
<th>MoCA</th>
<th>CABPad</th>
<th>OCS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completion time</td>
<td>10-15 min.</td>
<td>15-20 min.</td>
<td>10-15 min.</td>
<td>40 min.</td>
</tr>
<tr>
<td>Stroke – specific</td>
<td>x</td>
<td>x</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Evaluation at domain level</td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Official Danish version available</td>
<td></td>
<td></td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Danish reference material available</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
<tr>
<td>Validated in Danish stroke patients</td>
<td></td>
<td></td>
<td></td>
<td>x</td>
</tr>
<tr>
<td>Free</td>
<td>x</td>
<td>x</td>
<td>x</td>
<td>x</td>
</tr>
</tbody>
</table>

MMSE (Folstein et al., 1975); ACE (Mathuranath et al., 2000); MoCA (Nasreddine et al., 2005); CABPad (Willer et al., 2016); OCS (Demeyere et al., 2015)

1.2. The Oxford Cognitive Screen

The OCS is a cognitive screening tool specifically designed for stroke patients that offers many advantages compared to existing screening tools currently used in Denmark (see Table 2). It is free, takes 15-20 minutes to administer and includes 10 tasks enabling the evaluation of the following cognitive domains: Attention and Executive function, Language, Memory, Number processing, and Praxis. An extra feature of the tool is the “visual Snapshot” that can be used to provide a visual overview of the patient’s cognitive profile, making communication between health care professionals, the patient, and caregivers easier (see Figure 5).

The OCS has been reported to show higher levels of sensitivity than the MoCA and the MMSE in a stroke context. A British study comparing scores of 200 acute stroke patients on the MoCA to scores on the OCS (Demeyere et al., 2016) reported that the OCS was more sensitive than the MoCA overall (87 vs 78 % sensitivity). While 76% of patients were impaired on MoCA, 86% had impairments on one of the cognitive domains assessed by the OCS. An Italian study compared the OCS to the MMSE with regards to their ability to detect cognitive impairments post-stroke in 325 stroke patients (Mancuso et al., 2018). While approximately a third of patients performed below cut-off on the MMSE, over 90% were impaired on at least one domain in the OCS, and over 80% were impaired on at least 2 domains in the OCS. All participants with impaired performance on the MMSE were also impaired on at least one test of the OCS. However, 180 out of 208 patients with MMSE scores in the normal range, showed impairment in two or more domains on the OCS.
The OCS has also been shown to have significant test–retest alternate form reliability on all subtests (Demeyere et al., 2015). It has been translated into various languages (Dutch, Greek, Putonghua, Brazilian Portuguese, German, and Spanish) and validated in various countries (see Article 4, Appendix D, and Demeyere et al., 2015, for more detailed description of the OCS and its features).

2. The OCS-Dansk study: Summary

The overreaching aim of the OCS-Dansk study was to make a cognitive screening tool available in Danish that could provide a better alternative to tools currently available. The OCS-Dansk study involved the translation of the OCS into Danish, the collection of reference material from healthy
Danish controls, and providing cut-offs for clinical use. The study also investigated the appropriateness of the MoCA cut-off currently used in Denmark (see Article 4, Appendix D, for more details about the study).

The OCS was first translated into Danish following the translation licence agreements with Oxford University Innovations and following the best practice guidelines provided in “Translation and Linguistic Validation Process” provided by Associate Professor Nele Demeyere, one of the developers of OCS. 91 healthy Danish participants were assessed with the OCS-Dansk followed by the MoCA (MoCA version 7.0, Danish translation by Kirsten Abelskov). As age and education has been reported to affect performances on OCS subtests (Demeyere et al., 2015; Mancuso et al., 2016), the study included participants representing a wide age range (36 to 87 years) and a wide range of years of education (4 to 23 years)\(^3\). For data analysis, participants were categorised into three age groups and three education groups. Mean scores for the different age and education groups were calculated for the OCS subtests. 5\(^{\text{th}}\) percentile cut-offs were also calculated for the OCS subtests and the MoCA, but only on the basis of the whole sample.

Mean scores on the OCS-Dansk were found to be similar to those provided in the larger international validation studies (Demeyere et al., 2015; Mancuso et al., 2016). Scores on some sub-tests correlated with age and education. As raw scores for most sub-tests had a very narrow range and were not normally distributed (positive skew), cut-offs for impairment were calculated using direct percentile conversions. Cut-offs also have the advantage of being easier to understand for clinicians and patients (Crawford and Garthwaite, 2009). 5\(^{\text{th}}\) percentile cut-offs (and 95\(^{\text{th}}\) percentile for specific tasks) were overall similar to those provided in the Italian study (Mancuso et al., 2016; N=489).

The median score on the MoCA was 26.5 (minimum: 19, maximum: 30), the mean score was 26.22 (SD=2.44), and the 5\(^{\text{th}}\) percentile was at 22.35. Lower age and higher education were associated with better scores. The 5\(^{\text{th}}\) percentile cut-off from the present study was lower than expected. As there are no local norms available for the test, health care professionals in Denmark commonly use a cut-off of 25/26 (1 point added to score if education \(\leq 11\)) provided in the original Canadian validation study (Nasreddine et al., 2005). 35.2% of the healthy participants from the current study performed below this cut-off, suggesting that it may be inappropriate in a Danish

\(^3\) Years of education (YOE) was calculated as total number of years of under education (no maximum). Years with part-time education are converted into corresponding number of years of full-time education (e.g. 2 years of 50% education is counted as 1 year full-time education). If a participant first took an education as a baker, then as an electrician, both educations are counted.
context. In line with international studies (e.g. Borland et al., 2017; Chertkow et al., 2011; Pereiro et al., 2017), MoCA scores correlated with age and education in the current study.

Based on the Danish study as well as international studies comparing the sensitivity of OCS to dementia screening tools, it was concluded that the OCS-Dansk might provide a useful alternative to tools currently used in Denmark. Additionally, it was concluded that the lack of Danish age and education norms for the MoCA represents a general problem related to using the MoCA in a Danish context, not only in the context of stroke screening but also in the context of dementia screening.

3. OCS-Dansk limitations

The OCS-Dansk study suffers from various limitations. A first limitation is related to the representativeness of the sample. Ideally, when creating normative material, testing a population-based sample is ideal as it ensures the best possible representation of the population at large. However, due to limitations in resources, this was not an option. Although participants were recruited in two geographical locations (Copenhagen and Aalborg), broader geographical representation would have been ideal.

A second limitation is related to the size of the normative sample size (N=91). A higher N would have provided us with stronger reference material. However, as the cut-offs from this study are highly similar to those provided in a larger Italian study (Mancuso et al., 2016), our confidence that the data presented here can be used in a clinical context is strengthened.

A third limitation is related to the distribution of participants according to age and education in the normative sample (see Table 3). The project intended to include participants with a wide range of age and years of education. As stroke happens over the age of 60 in 90% of cases and the median age for having a stroke in Denmark is 75 years, inclusion of a larger proportion of participants between 65 and 85 years was intended (see Table 3 for intended versus acquired sample distribution). We succeeded in recruiting the intended numbers of participants with high education in all age brackets except the over 85 age bracket, but despite using a wide range of recruitment channels (advertising, staff announcements, contacting hospital, and university volunteers), we failed to recruit a high number of participants in the older age range and failed to recruit to the intended number of participants with 12 or less years of education across age ranges (except the 65-
Therefore, the results presented for the group with low education and higher age in Article 4 (Appendix D) are based on relatively small groups. Due to the small sample size and limitations related to the composition of our sample, separate cut-offs for the different age and education groups were not calculated. When using the general cut-offs, there is a small risk for clinicians of over-diagnosing cognitive deficits in participants who are elderly and/or have limited education.

Table 3: Intended composition of sample and in brackets, final composition of sample according to age and education.

<table>
<thead>
<tr>
<th></th>
<th>&lt;49 years</th>
<th>50-64 years</th>
<th>65-74 years</th>
<th>75-84 years</th>
<th>&gt;85 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low education ≤11</td>
<td>10 (1)</td>
<td>10 (5)</td>
<td>15 (14)</td>
<td>15 (5)</td>
<td>10 (0)</td>
</tr>
<tr>
<td>High education ≥12</td>
<td>10 (10)</td>
<td>10 (20)</td>
<td>15 (21)</td>
<td>15 (13)</td>
<td>10 (2)</td>
</tr>
</tbody>
</table>

A fourth limitation of the study is that it did not involve validation in a stroke sample. Content validity has been shown in various international validation studies (Demeyere et al., 2015; Kong et al., 2016). However, a Danish validation study with stroke patients is needed, to acquire additional information about the Danish version of the test.

4. What is a normal sample?

A key aspect of neuropsychological assessment involves comparing a participant’s score to a normative sample. Indeed, this step is necessary to make inferences about the presence or absence of cognitive impairments. A neuropsychologist’s ability to make accurate and appropriate interpretations relies, therefore, largely on the composition of the normative sample to which scores are compared (Martin, Schroeder, & Baade, 2017; O’Connell et al., 2017).

When planning the OCS project, most criteria for enrolment in the study were relatively uncontroversial (over the age of 35, Danish as first language, no previous or ongoing neurological disorder, and no visual field deficits). There was, however, one exclusion criteria that lead to greater discussions. This concerned the extent to which participants should be screened for dementia and if yes, how this should be done. Should participants performing below a specific cut-off on MoCA be excluded from the OCS reference material? If so, what cut-off should be used? While the original British validation study (Demeyere et al., 2015) did not exclude healthy participants on the basis of a dementia screening test, the Italian study excluded healthy participants scoring lower than 22/30 on the MMSE (Mancuso et al., 2016).
By not screening for dementia, there is a risk of including participants with MCI or dementia in the normative sample and thereby, a risk of setting the cut-off too low. This can lead to a high rate of false negatives. By excluding participants with low scores on a dementia screening tool, there is a risk of excluding some participants who represent the lower end of normal curve, and thereby a risk of setting the cut-off too high. This can lead to a high rate of false positives.

According to Martin et al. (2017), there are two approaches to creating normative samples. Most norms that are provided for neuropsychological measures are based on cognitively “healthy” individuals. They exclude participants with, for example, current central nervous system diseases, known cognitive decline, or other medical conditions known to impact cognition. Other norms are based on “typical” individuals. They are less restrictive and include individuals with a variety of diagnoses. In older groups, the difference between these samples of “healthy individuals” and “typical individuals” is particularly large, as older individuals have higher incidences of medical and psychosocial issues than younger individuals. Studies have also shown that age is associated with increased variability in performances on cognitive tasks. This is related to the fact that the mean number of morbidities increases with age, and that changes in cognition are partially moderated by health factors. When using more restrictive inclusion criteria, less variability in performance can be expected. Consequently, when comparing a score to such a sample, any deviation from the norm can be interpreted as more unusual than it truly is (Martin et al., 2017).

The OCS normative material is designed to help determine whether a participant has newly acquired cognitive deficits as a consequence of a stroke. As being perfectly healthy is the exception rather than the norm in old age, comparing the patient’s performance with a “typically aging normative sample” is likely to be more informative than comparing the performance to a “perfectly healthy normative sample”. By not excluding patients with low MoCA scores in the current study, the sample is likely to be more representative of a typically ageing group. Volunteer based normative studies, like the current one, typically suffer from the limitation of reflecting a very selected group of the population that has many resources and is high functioning and therefore risk setting the bar for a normal performance too high. Excluding participants with low MoCA scores was likely to contribute further to this.

On the basis of the considerations described above, it was decided that participants would not be excluded on the basis of a low MoCA score (Robotham, Riis, & Demeyere, n.d.). To investigate the implications of the decision not to exclude participants with low MoCA scores in our
study, an alternative set of OCS cut-offs were calculated based only on the healthy controls who performed above cut-off on MoCA (see Section B, Table 4). As there are no Danish norms for MoCA available, Swedish population-based norms were used (Borland et al., 2017). Six participants who had z-scores of less than -2 (when adjusted for age, education and gender) were excluded from the analysis, leaving 85 participants. When comparing the two sets of cut-offs (Section A versus Section B, Table 4), cut-offs only differed for the Broken hearts test (acc. and RT) and the Executive score of the executive test. While scores of 40 and 41 on the Broken Hearts test are considered within the normal range when using the less restrictive inclusion criteria, they are considered to be below expected, when using the alternative set of reference material (in which participants with low MoCA scores have been excluded). On the basis of this analysis, we conclude that the consequences of not excluding participants with low MoCA scores are limited.
Table 4: Comparison of OCS-Dansk cut-offs when including participants with low MoCA scores and when excluding participants with low MoCA scores

<table>
<thead>
<tr>
<th></th>
<th>A: All included (results from Article 4)</th>
<th>B: Excluding MoCA under -2 z-scorea</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Naming</td>
<td>91</td>
<td>3.7 (0.52)</td>
</tr>
<tr>
<td>Semantics</td>
<td>91</td>
<td>3.0 (0)</td>
</tr>
<tr>
<td>Orientation</td>
<td>91</td>
<td>4.0 (0)</td>
</tr>
<tr>
<td>Visual field</td>
<td>91</td>
<td>4.0 (0)</td>
</tr>
<tr>
<td>Reading</td>
<td>91</td>
<td>15.0 (0.18)</td>
</tr>
<tr>
<td>Writing</td>
<td>91</td>
<td>3.0 (0)</td>
</tr>
<tr>
<td>Calculation</td>
<td>91</td>
<td>3.9 (0.3)</td>
</tr>
<tr>
<td>Broken hearts (Acc.)</td>
<td>91</td>
<td>47.0 (3.84)</td>
</tr>
<tr>
<td>Broken hearts (RT)</td>
<td>91</td>
<td>103.6 (29.83)</td>
</tr>
<tr>
<td>Spatial asymmetry</td>
<td>91</td>
<td>0.1 (1.33)</td>
</tr>
<tr>
<td>Object asymmetry</td>
<td>91</td>
<td>0.0 (0.39)</td>
</tr>
<tr>
<td>Praxis</td>
<td>89</td>
<td>10.8 (1.42)</td>
</tr>
<tr>
<td>Recollection</td>
<td>91</td>
<td>2.6 (1.07)</td>
</tr>
<tr>
<td>Recognition</td>
<td>91</td>
<td>3.9 (0.40)</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>91</td>
<td>3.9 (0.23)</td>
</tr>
<tr>
<td>Circles (Acc.)</td>
<td>91</td>
<td>5.9 (0.27)</td>
</tr>
<tr>
<td>Triangles (Acc.)</td>
<td>91</td>
<td>5.9 (0.28)</td>
</tr>
<tr>
<td>Alternating (Acc.)</td>
<td>91</td>
<td>12.5 (1.46)</td>
</tr>
<tr>
<td>Executive score</td>
<td>91</td>
<td>-0.6 (1.42)</td>
</tr>
</tbody>
</table>

a According to norms provided by Borland et al. (2017)

*Cut-off differs between the two methods

5. Concluding remarks and future directions

As described in the introduction, one of the key challenges in Denmark for implementing more systematic screening of cognitive deficits following stroke, has been the lack of a short cognitive screening tool that is well-suited for stroke patients. Indeed, while there are short screening tools available in Danish, they are typically designed for dementia screening and do not assess some of the common cognitive symptoms seen in a stroke. Another limitation of these tools is that they are not domain specific, which is particularly problematic, as stroke can lead to highly domain-specific deficits. There is one cognitive screening tool available in Danish, that is specifically designed for the stroke population: the CABPad. Despite it being well-designed and sensitive, it takes 40 minutes to administer, which may limit its application as a tool that can enable more systematic screening of stroke patients.
Chapter 2: The Danish Oxford Cognitive Screen

The OCS is specifically developed for stroke and therefore enables assessment of symptoms commonly seen following stroke and enables assessment at the level of the cognitive domain. It is free and only takes 15-20 minutes to carry out. The OCS fulfils the key requirements for a tool that can be used for the systematic screening of patients with acquired brain injuries. The main limitation of the OCS is that, like other short screening tools, it only enables a coarse evaluation of cognitive functions and cannot replace more in-depth neuropsychological evaluations.

Although translating the OCS and providing reference material from healthy controls constitutes a key step for clinicians to be able to use the tool in a Danish context, the Danish version of the OCS deserves further attention. First and foremost, a Danish validation study, comparing the performances of stroke patients on the OCS to their performance on currently used neuropsychological tests, is needed to ensure content validity in a Danish context. While content validity has been reported for other language versions of the OCS, one cannot be certain that the OCS-Dansk has the same content validity. Second, more research is warranted regarding the predictive validity of the test. Does the OCS taken at the acute or subacute stage predict the long-term neuropsychological outcome? The OCS is a screening tool and it will fail to identify some subtle neuropsychological deficits in the acute stages after injury. The question is therefore, does the OCS used in the acute stages ensure identification of cognitive deficits that affect the participant in the long term? Third, reference material for the parallel version of the test should be collected to avoid learning effects in follow-up assessment. As part of this Ph.D., the parallel version of the OCS was also translated into Danish, however, no reference material was collected. Fourth, more research is needed regarding the use of screening tools in clinical settings. This would enable detailed practical guidelines to be made, describing the situations in which screening tools such as the OCS are useful or not.

By making the tool available in Danish and by providing Danish reference material, this thesis may, in the long run, represent a small contribution to improving the management and care of stroke patients in Denmark. Indeed, the OCS-Dansk might enable a more systematic screening of cognitive deficits in stroke patients.
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Appendix A: Article 1
Face and Word Recognition Can Be Selectively Affected by Brain Injury or Developmental Disorders

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Department of Psychology, University of Copenhagen, Copenhagen, Denmark

Face and word recognition have traditionally been thought to rely on highly specialised and relatively independent cognitive processes. Some of the strongest evidence for this has come from patients with seemingly category-specific visual perceptual deficits such as pure prosopagnosia, a selective face recognition deficit, and pure alexia, a selective word recognition deficit. Together, the patterns of impaired reading with preserved face recognition and impaired face recognition with preserved reading constitute a double dissociation. The existence of these selective deficits has been questioned over the past decade. It has been suggested that studies describing patients with these pure deficits have failed to measure the supposedly preserved functions using sensitive enough measures, and that if tested using sensitive measurements, all patients with deficits in one visual category would also have deficits in the other. The implications of this would be immense, with most textbooks in cognitive neuropsychology requiring drastic revisions. In order to evaluate the evidence for dissociations, we review studies that specifically investigate whether face or word recognition can be selectively affected by acquired brain injury or developmental disorders. We only include studies published since 2004, as comprehensive reviews of earlier studies are available. Most of the studies assess the supposedly preserved functions using sensitive measurements. We found convincing evidence that reading can be preserved in acquired and developmental prosopagnosia and also evidence (though weaker) that face recognition can be preserved in acquired or developmental dyslexia, suggesting that face and word recognition are at least in part supported by independent processes.

Keywords: visual perception, prosopagnosia, alexia, face recognition, word recognition, reading, hemispheric specialisation

INTRODUCTION

Face and word recognition have traditionally been thought to rely on highly specialised and relatively independent cognitive processes. Some of the strongest evidence for this has come from neuropsychological case studies. There are many examples of patients suffering from pure prosopagnosia, a selective deficit in face recognition, and patients suffering from pure alexia, a selective reading deficit (for comprehensive reviews see Farah, 1990, 2004). Together, the patterns of face recognition deficits with preserved reading, and reading deficits with preserved face recognition constitute a double dissociation, which is current textbook knowledge (Gazzaniga et al., 2013).

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Citation:
The hemispheric laterisation of face and word recognition has been considered additional evidence for their functional independence. Pure prosopagnosia occurs after bilateral or right hemisphere damage, whereas pure alexia arises after left hemisphere damage (Farah, 1991; Leff et al., 2006; Barton, 2008b; Starrfelt and Shallice, 2014). Also, functional imaging studies have shown that a region in the left fusiform gyrus, the visual word form area (VWFA) is more responsive to words (Puce et al., 1996; Cohen et al., 2000) whereas a part of the right fusiform gyrus, the Fusiform Face Area (FFA) is more responsive to faces (Kanwisher et al., 1997). This aligns well with ERP-studies: The N170 component for faces has a larger amplitude in the right hemisphere while the N170 for words has a larger amplitude in the left hemisphere (Bentin et al., 1996; Schendan et al., 1998).

Imaging studies also show, however, that the lateralisation of activation for faces and words is far from complete, as both categories lead to bilateral activation with variable degrees of asymmetry, suggesting that they might rely on neural networks that are highly overlapping (Dien, 2009; Nestor et al., 2013).

Findings from neuropsychological studies have also challenged the idea of functional independence. There are a few patients on record with prosopagnosia following lesions restricted to the left hemisphere and patients with alexia following damage restricted to the right hemisphere (Davous and Boller, 1994; Mattson et al., 2000; Barton, 2008a). A greater challenge comes from a study reporting face recognition deficits in alexia patients with left hemisphere damage and word recognition deficits in prosopagnosics with right hemisphere damage (Behrmann and Plaut, 2014). This finding, combined with imaging and modelling results, led the authors to propose a distributed model of visual recognition: the many-to-many hypothesis (MTMH: Behrmann and Plaut, 2013). According to the MTMH, the cortical networks supporting face and word recognition are not specialised for specific categories but instead involved in processing a whole range of visual categories. Face and word recognition are supported by common and overlapping networks that are bilaterally distributed, rather than by independent modules. The contributions of the left and right hemisphere are, however, differently weighted for the two categories (Behrmann and Plaut, 2013). A key prediction of the hypothesis that has been described explicitly by the authors is that face recognition problems should be present in all patients with pure alexia and reading deficits should accompany all cases with pure prosopagnosia (Plaut and Behrmann, 2013). In other words, the authors question whether a dissociation between face and word recognition exists. This has led to an increase in studies specifically investigating whether face and word recognition can be selectively impaired.

Dissociations are considered as a key tool in neuropsychology for identifying independent mental processes. Double dissociations are more powerful than single dissociations as they cannot be explained by differences in task difficulty. Although double dissociations have some methodological limitations (e.g., Dunn and Kirsner, 2003), most researchers still consider them the strongest inferential tool available in neuropsychology for establishing whether two processes are separate (Shallice, 1988; Coltheart, 2001).

Associations refer to patterns where a patient’s performance is impaired in two tasks after brain injury (Coltheart, 2001). Association does not necessarily imply, however, that the two functions rely on common and overlapping processes. For example, it is possible that the functions rely on independent processes located spatially close in the brain, so that both were affected by the same lesion. Another possibility is that the two functions rely on some common and some independent processes. Abnormal performance in face recognition and word recognition following injury could for example be due to blurry vision. It does not exclude the possibility that faces and words, at a higher level, rely on independent processes.

Findings of dissociations between face and word recognition would provide strong evidence that faces and words are not supported by fully distributed processes but instead at least in part by independent processes. Also, such dissociations would constitute evidence against one of the original key predictions of the MTMH (Susilo and Duchaine, 2013).

METHODS

Farah (1990, 2004) has provided comprehensive reviews of studies of visual agnosia for faces and words up to 2004. In this paper we review 15 studies published since 2004 specifically investigating whether face or word recognition can be selectively affected by acquired brain injury or developmental disorders.

RESULTS

We start by describing studies that selected patients according to their symptoms and then describe studies that selected participants according to the location of their lesions (see Supplementary Table 1 for more details on each study).

Face Recognition in Acquired Alexia and Developmental Dyslexia

Two studies report face recognition deficits in patients with pure alexia or in patients with unilateral lesions in the left posterior fusiform gyrus (pFG), when assessed with a range of sensitive tests. Testing face and word recognition in four patients with pure alexia (Behrmann and Plaut, 2014) showed that the patients with pure alexia showed mild but significant deficits on simultaneous face discrimination tasks and had abnormal face inversion effects. A drawback of this study is that the results are only based on comparisons between very small groups and that individual test scores are not reported (but the significance level of individual scores are reported!).

A study of face processing in 19 patients with lesions in the left ventral occipito-temporal cortex and/or who had an abnormally high word-length effect (Roberts et al., 2015) reports similar findings. Patients were slower and less accurate than controls on a face naming task and slower (not less accurate) on a face-to-name matching task and half of them were also impaired when compared individually to the control group. Interestingly, longer
RTs on a simultaneous face discrimination task were associated with more severe reading deficits (higher word length effect).

In contrast, two single case studies have reported preserved face recognition in patients with acquired alexia. An epilepsy patient was shown to have unimpaired face processing following resection of a word responsive area in the occipito-temporal cortex which resulted in alexia (Gaillard et al., 2006). However, while the patient’s impaired function, reading, was assessed with various sensitive tests (RTs and Acc.), the supposedly preserved function, face processing was assessed using only accuracy in a quite crude test, the 25 item Warrington face recognition test. An interesting finding in this patient was that fMRI activation patterns for faces that were restricted to the RH before surgery did not change following surgery, while the “selective” activation elicited by visual words disappeared. Another study with similar findings (Turkeltaub et al., 2014) describes a patient who, following a selective lesion in the inferior left occipito-temporal cortex (corresponding to the VWFA), shows an abnormal word length. The patient has a normal performance on a subtest of the Philadelphia Face Perception Battery, which is a relatively sensitive, accuracy based task.

A few studies have investigated face recognition in developmental dyslexia, showing mixed results. One study report that a group of 18 participants with developmental dyslexia were not significantly slower or less accurate than a group of controls on a face naming task (Smith-Spark and Moore, 2009). The study did, however, show that there were larger age of acquisition effects in the control group compared to the dyslexia group, which the authors suggested could be related to attentional or executive dysfunctions in the dyslexia group. In contrast, in a study investigating face and complex object recognition in subjects with developmental dyslexia (Sigurdardottir et al., 2015) dyslexics were on a group level reported to perform significantly worse than controls on two face recognition tests. According to the authors, the face recognition deficits seen in dyslexics in this study do not seem to be caused by a deficit in holistic processing, which many consider a core deficit in prosopagnosic patients.

Reading in Acquired and Developmental Prosopagnosia

In addition to reporting impaired face processing in alexia, Behrmann and Plaut (2014) also reported three patients with prosopagnosia who showed abnormally long RTs and word-length effects on reading tasks. This study has, however, been criticised (Hills et al., 2015) for including a prosopagnosia patient that had previously been described in the literature as having integrative agnosia (Behrmann and Kimchi, 2003).

Other studies have provided evidence that reading can be preserved in acquired prosopagnosia. Five patients with acquired prosopagnosia were tested on seven sensitive tests of word recognition and four patients performed normally (Acc. and RT) on all tasks when compared individually to the control group (Susilo et al., 2015).

Another study investigated word processing in two patients with prosopagnosia following stroke in the right hemisphere, one patient with prosopagnosia following herpes simplex encephalitis, as well as one patient with pure alexia following stroke in the left hemisphere (Barton et al., 2010). The participants had to sort words by word identity or by style (font or handwriting). The two prosopagnosic patients were impaired in sorting words according to script style (Acc. and/or RTs) but performed normally when sorting for word identity, whereas the alexic patient had the opposite pattern. The herpes simplex patient performed normally on both tasks. The results suggest that while patients with prosopagnosia can have unimpaired reading, other aspects of word processing, such as style, might be affected in these patients.

Yet another study testing six prosopagnosia patients with unilateral right lesions and five with bilateral lesions (Hills et al., 2015) found that none of the patients with unilateral lesions showed abnormal word-length effects or RTs in word-naming. Patients also carried out the sorting task mentioned above (Barton et al., 2010), and again patients were as fast as controls in sorting the words by identity but many were slower than controls in sorting the words according to handwriting or font style.

A few single case studies have also described intact reading in acquired prosopagnosia (see Supplementary Table 1 for details). One subject with face recognition problems following traumatic brain injury had a very fast reading rate of 364 words per minute when reading text (Bukach et al., 2006). Another patient with severe face processing deficits was shown to have normal accuracy on the word part of the Warrington Recognition Memory Test (Riddoch et al., 2008).

Reading can also be unaffected in developmental prosopagnosia. In one study, 10 developmental prosopagnosics performed well within the normal range on four sensitive tests of letter, word, and text reading, and a dissociation was demonstrated statistically between impaired face and preserved word recognition (Starrfelt et al., 2016).

Similarly, Rubino et al. (2016) assessed reading in ten developmental prosopagnosics using a word-naming and word-sorting task (according to content or style, cf. Barton et al., 2010). At a group level, there was no difference between the prosopagnosic and controls group regarding errors, mean RTs and word-length effects. And at the individual level none of the prosopagnosics had elevated word-length effects. In contrast to subjects with acquired prosopagnosia assessed with the same task in a previous study, only one subject was impaired in sorting by font (Hills et al., 2015).

Large Studies Using Anatomy-Based Inclusion Criteria

Two studies included patients on the basis of lesion location rather than symptomatology. A large patient study investigated 31 patients with Posterior Cerebral Artery (PCA) stroke with sensitive experimental face, house, object, and word processing tests (Martinaud et al., 2012). Face processing deficits were observed after right and after left hemisphere damage. Word processing deficits were, however, only found in patients with left hemisphere lesions. Interestingly, although six patients had...
deficits for a single category (house, phone, word, or face), only one of these, a patient with a house processing deficit, had a truly selective deficit according to the stringent Revised Standardized Difference Test (Crawford and Garthwaite, 2005). Another study investigating visual perceptual abilities in 31 patients with unilateral, subacute stroke in regions supplied by the PCA found that many patients with left hemisphere lesions had face recognition deficits and that many patients with right hemisphere lesions also had reading deficits (Gerlach et al., 2014).

Methodological Considerations: Levels of Processing

All the studies included compare performances in word and face processing, and discuss whether these functions rely on common or selective mechanisms. In many of these studies, however, the tests used measure different levels of processing for faces than for words (see Supplementary Table 1). While some experiments tap processing at a perceptual level that requires very little semantic knowledge, others require identification of specific stimuli. Overall, there are three broad groups of tests (see Table 1): (1) Perceptual tasks like simultaneous matching that can be performed without the subject having to store a cohesive representation of the stimulus. (2) Recognition tasks that require subjects to build and store short-term or longer-term representations, such as the Cambridge Face Memory Test (Duchaine and Nakayama, 2006). And (3) Identification tasks, like famous face tests or reading out loud, which require associating the perceived stimulus with stored semantic and/or phonological representations. Some studies also use key behavioural effects like the word length effects and the face inversion effects as proxies for reading and face processing functions.

If the aim is to draw conclusions about the extent to which face and word processing rely on common mechanisms, then matching tasks to measure the same level(s) of processing is important.

DISCUSSION

The studies described show mixed results. Deficits in reading and face recognition sometimes co-occur. But this does not necessarily imply that the two functions rely on shared processes only. For example, if face and word processing were supported by independent processes closely located in the brain, a single lesion affecting both would lead to co-occurring deficits. Also, face and word processing must rely on some common processes, that if damaged, lead to abnormal performances in both types of tasks. For example, blurred vision could affect performance on a wide range of visual tasks and language deficits could affect performance on face and word tasks that require naming.

More importantly, our review shows that there is convincing evidence that dissociations between the two functions can be found, suggesting that face and word recognition, at least in part, rely on independent processes. As pointed out by Susilo and Duchaine (2013), this contradicts one of the original key predictions of the many-to-many hypothesis, that reading and face recognition deficits should always co-occur (Behrmann and Plaut, 2013).

Interestingly, at this point, the evidence for dissociation is stronger in one direction (preserved reading in prosopagnosia) that in the other. This might be for trivial reasons not related to the main question, but it is also possible that such dissociations (preserved face recognition in alexia or dyslexia) are rarer or less reliable. The most obvious explanation for a single dissociation, however, is that one task (face recognition) is simply more demanding than the other (reading) (Shallice, 1988). This seems counter intuitive here as face recognition is innate while reading is learned. Recent evidence suggests, however, that there is a systematic relationship between the two functions cognitively and cerebrally and that learning to read might directly affect the cerebral substrate for face processing. Before learning to read, ventral occipito-temporal cortex responds bilaterally to faces, but increases in reading ability in children and preliterate adults are associated with a reduced left hemisphere response to faces (Dehaene et al., 2010; Cantlon et al., 2011). Studies using divided visual field paradigms and ERP measurements in children and adults have shown similar results (Mercure et al., 2009; Dundas et al., 2013, 2014).

The neuronal recycling hypothesis (Dehaene and Cohen, 2007) explicitly describes how learning to read might affect the neural substrates of face processing. Reading recycles pre-existing brain systems that are genetically defined for other uses, specifically in the left ventral occipito-temporal (vOT). The vOT shows a preference for high-resolution foveal shapes, and is well-adapted to extracting line configurations consistent with

<table>
<thead>
<tr>
<th>TABLE 1</th>
<th>Examples of commonly used tests sorted according to level of processing.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Word processing</strong></td>
<td><strong>Face processing</strong></td>
</tr>
<tr>
<td>Perception</td>
<td>Perception</td>
</tr>
<tr>
<td>Sorting words according to content or style</td>
<td>Cambridge face perception test (Duchaine et al., 2007)</td>
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<tr>
<td>Recognition</td>
<td>Working memory tasks</td>
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<tr>
<td>Warrington recognition tests for words</td>
<td>Matching task (e.g., Plaut et al., 2014)</td>
</tr>
<tr>
<td>Lexical decision (e.g., Gaillard et al., 2008)</td>
<td>Familiarity judgement test (e.g., Bukach et al., 2008)</td>
</tr>
<tr>
<td>Identification</td>
<td>Naming words (WLE) (e.g., Starfelt et al., 2016)</td>
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</table>
requirements for word recognition (Dehaene and Cohen, 2007). The left lateralisation allows shorter connections to language areas [indeed the connectivity of the VWFA in pre-reading children predicts its location following reading acquisition (Saygin et al., 2016)]. Because of these constraints regarding localisation, word processing competes with face processing for cortical space in the left vOT, and as one becomes more proficient in reading and the left vOT is tuned for word recognition, face processing becomes more right lateralised (Dehaene and Cohen, 2011). This hypothesis could potentially account for why reading can be preserved in prosopagnosia but that face recognition problems are likely to be seen in people with dyslexia (see Ventura, 2014, for a recent review of how reading acquisition and face recognition could be related).

In conclusion, while there is convincing evidence that reading can be preserved in acquired and developmental prosopagnosia, evidence that face recognition can be preserved in acquired or developmental dyslexia is somewhat weaker. Taken together the results suggest that face and word recognition are at least in part supported by independent processes. More detailed investigations of face recognition in dyslexia are needed to determine whether face processing can be preserved when reading is impaired, and thus whether there is a reliable double dissociation between face and word recognition.

**AUTHOR CONTRIBUTIONS**

RR selected relevant articles for the review and wrote the first draft of the manuscript. RS provided a revised version of the manuscript. The manuscript was then finished in close collaboration between the authors.

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**SUPPLEMENTARY MATERIAL**

The Supplementary Material for this article can be found online at: http://journal.frontiersin.org/article/10.3389/fpsyg.2017.01547/full#supplementary-material

**REFERENCES**


<table>
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<th>Participants</th>
<th>Reading tests</th>
<th>Face processing tests</th>
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</thead>
<tbody>
<tr>
<td>Barton et al. (2010)</td>
<td>Syndrome:</td>
<td>1 acquired prosopagnosia (stroke right lateral fusiform) - 1 left-handed acquired prosopagnosia (herpes encephalitis, right roIT damage, not lateral fusiform gyrus) - 1 acquired alexia (stroke left fusiform)</td>
<td>- WRMT-words (Acc.; R) - Word-sorting task: according to content and according to style (Acc.; RT): P</td>
<td></td>
</tr>
<tr>
<td>Bohrmann &amp; Psalt (2014)</td>
<td>Syndrome:</td>
<td>4 acquired alexia (stroke left vOT) - 3 acquired prosopagnosia (stroke right vOT)</td>
<td>- Diagnosis criteria for alexia patients not described - Reading 3, 5, 7 letter words (Acc.; RT, WLE): I</td>
<td>- BTHR: P - Simultaneous face discrimination task: P - Simultaneous matching of treated and inverted faces: R</td>
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<td></td>
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<td></td>
<td>- Lexical decision (Acc.; RT, WLE): R</td>
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<td></td>
<td>- BTFR (original): P - BTFR (time cut-off version): P - WRMT (Acc.): R - Familiarity judgment (Acc.): R - Famous face recognition: I</td>
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<td>Gaillard et al. (2006)</td>
<td>Lesion:</td>
<td>1 patient pre and post-surgery (lesion: word-responsive area in left inferior vOT)</td>
<td>- WRMT-words: 25 items (Acc.; R) - Reading 3-8 letter words (Acc.; RT, WLE): I</td>
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<td>- Reading 4, 6, and 8 letter words: randomly presented in left or right hemifield (Acc.) I - Lexical decision task (Acc.; RT, WLE): R</td>
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<tr>
<td>Gerlach et al. (2014)</td>
<td>Lesion:</td>
<td>31 patients IVA stroke (13 left; 14 right)</td>
<td>- Reading of 10 words test (Acc.): I</td>
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<td>- Famous face recognition and naming (Acc.): 1 - Rivermead face recognition test (Wilson, Cockburn, &amp; Baddeley, 1985): R</td>
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<td>- Subjective complaints of impaired recognition in daily life - Famous face test (Acc.): I - CFMT (Acc.): R</td>
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<td>- WRMT-faces (Acc.): R</td>
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<tr>
<td>Martinaud et al. (2012)</td>
<td>Lesion - 12 PCA stroke (13 left, 13 right, 3 bilateral)</td>
<td>Army test: Detection of words (Martinaud et al., 2012); P - Reading 3-9 letter words (Acc., RT): I</td>
<td></td>
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<td>Army test: Detection of faces (Garrido, Duchaine, &amp; Nakayama, 2008); P - CFMT: R</td>
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<td></td>
<td></td>
<td>- Faces old vs new (B. C. Duchaine, Wendt, New, &amp; Kulomaki, 2005); R</td>
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<td>Naming 10 famous faces (Acc.): I - Face Familiarity test (Acc.): R - Delayed unfamiliar face matching task with change of view (Acc.): R</td>
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<td></td>
<td></td>
<td>- Word-list learning (interference paradigm) (Duchaine, Germine, &amp; Nakayama, 2006); I</td>
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<td>Sigurdardottir et al. (2015)</td>
<td>Syndrome - 20 developmental dyslexia adults</td>
<td>Adult Reading History Questionnaire (Leffy &amp; Pennington, 2000) - IS-FORM reading test (Sigurdardottir et al., 2015): I</td>
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<td>Starrfelt et al. (2015)</td>
<td>Syndrome - 10 developmental prosopagnosia adults</td>
<td>Reading 5-7 letter words (Acc., RT, WLE): I - Naming 3-6 letter words and Reading single letters: I - Identifying 5-letter words or letters presented 10-100ms:. I - Test reading test - 617 words long (seconds): I</td>
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<td>Face recognition part of the Focus and Emotion Questionnaire (Fremere, P., Palmer, R., &amp; Stok, 2015)</td>
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<td>Sain et al. (2015)</td>
<td>Syndrome - 3 acquired prosopagnosia right stroke or surgical lesion</td>
<td>WMFT: words: R - Reading 3-9 letter words (Acc., RT, WLE): I - Naming 10 famous faces (Acc.): I - Old-New Face Recognition Test (Acc.) (B. C. Duchaine, Yovel, Butterworth, &amp; Nakayama, 2006); R</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1 acquired prosopagnosia bilateral stroke</td>
<td>WMFT: words: R - Reading 3-9 letter words (Acc., RT, WLE): I - Naming 10 famous faces (Acc.): I</td>
<td></td>
<td></td>
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<tr>
<td>Turkshah et al. (2016)</td>
<td>Lesion - 1 acquired alexia (stroke: left inferior vOT, including VWFA)</td>
<td>Reading 3-6 letter words (Acc., RT, WLE): I - Philadelphia Face Perception Battery: Face similarity subtype (Acc.): P</td>
<td></td>
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</tr>
<tr>
<td></td>
<td></td>
<td>1 acquired alexia (stroke: left inferior vOT, including VWFA)</td>
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</table>

Test abbreviations: CFMT: Cambridge Face Memory Test (Brad Duchaine & Nakayama, 2000); WMFT: Warrington Recognition Memory Test (Warrington, 1984), BTFR: Benton Test of Face Recognition (Benton et al., 1983); CFPT: Cambridge Face Perception Test (Duchaine, Germine, & Nakayama, 2007).

Level of processing abbreviations: P: perception test; R: recognition test; I: identification test

Other abbreviations: PCA: Posterior Central Artery; VWFA: Visual Word Form Area; FFA: Fusiform Face Area; vOT: ventral occipito-temporal; mOT: medial occipito-temporal; WLE: word-length effect; AoA: age of acquisition

Unitalicized: when a study has included tasks that are well matched across categories (similar level of processing and similar experimental set-up).
<table>
<thead>
<tr>
<th>Paper</th>
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<td>Barton et al. (2010)</td>
<td>Reading: Perceptual Recognition Identification, Faces: Perceptual Recognition Identification</td>
<td>Word-sorting task: - 2 prosopagnosia patients (FFA not spared): sorting style: abnormal (Acc. and/or RTs); sorting content: no deficit (Acc. and RTs) - Alexic patient: sorting content: abnormal (Acc. and RTs); sorting computer style: no deficit (Acc. and RT); sorting handwriting style: no deficit: Acc., slightly elevated RT. - 1 prosopagnosia patient (right FFA spared): no deficit.</td>
<td>Dissociation (impaired face processing / preserved processing word content)</td>
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<td>Borkmann &amp; Plaut (2014)</td>
<td>Recognition Identification, Perception Recognition Identification</td>
<td>Prosopagnosics: - Severe face recognition deficits - Mild elevated RTs and WLEs on word reading and lexical decision tasks Alexics: - Severe reading deficits - Mild deficits on simultaneous face discrimination and simultaneous matching task</td>
<td>Association (impaired face processing / impaired word processing)</td>
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<tr>
<td>Bakch et al. (2006)</td>
<td>Identification Perception Recognition Identification, Recognition Identification</td>
<td>Face processing: - BITF (original): Normal accuracy, abnormal RT - BITF (time cut-off), WRMT, familiarity judgment, and famous face recognition: abnormal Reading: - 364 words/minute: very fast (99th percentile for 18.9 years of schooling)</td>
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<td>Guilford et al. (2006)</td>
<td>Recognition Identification Perception Recognition Identification</td>
<td>Pre-surgery: - Reading task: no deficit (Acc., RTs or WLEs), WRMT-faces: no deficit (Acc.) - Hemifield task: 10% errors. Post-surgery: - WRMT-faces: 0 errors - Word-reading and lexical decision: abnormal (RTs, Acc. and WLE on RT) - Hemifield task: 35% errors and large WLE on Acc - fMRI: word-specific activations disappeared post-surgery, no changes in face-specific activations</td>
<td>Dissociation (impaired word processing / preserved face processing)</td>
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<td>Gerlach et al. (2014)</td>
<td>Identification Recognition Identification</td>
<td>Abnormal face recognition in many patients with right lesions and also patients with left lesions - Abnormal reading in many patients with left lesions and in patients with right lesions</td>
<td>Association (impaired face processing in many left hemisphere patients, impaired reading in many right hemisphere patients)</td>
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<td>Hills et al. (2015)</td>
<td>Perception Recognition Identification Recognition Identification</td>
<td>Reading test: - Right lesion prosopagnosics: not abnormal (RT, Acc., or WLE) - Word-sorting task: - Content: no deficit - Handwriting or font style: abnormal performance for most patients (RT)</td>
<td>Dissociation (impaired face processing / preserved processing word content)</td>
</tr>
<tr>
<td>Authors</td>
<td>Year</td>
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<td>Martinaud et al. (2012)</td>
<td></td>
<td>Perception Identification Recognition</td>
<td>Word processing deficits seen in left lesion patients only. Face processing deficits seen in patients with right lesions, bilateral lesions and 1 patient with left lesion. 6 patients with selective deficit for one category. 1 with word-specific deficit and 1 with face-specific deficit: neither considered specific when using RSTD statistical criteria (Crawford &amp; Garthwaite, 2005). Non-significant dissociation: impaired face processing / preserved word processing; impaired word processing / preserved face processing.</td>
</tr>
<tr>
<td>Roberts et al. (2015)</td>
<td></td>
<td>Identification Perception Recognition</td>
<td>Patients as a group: - Naming famous faces: abnormal (RT and Acc.) - Famous face-to-name matching: abnormal (RT, not Acc.) Patients on an individual level: 9/19 patients abnormal naming famous faces and abnormal famous face-to-name matching. - Longer RTs on simultaneous face discrimination task associated with larger WLE. Association (impaired word processing / impaired face processing).</td>
</tr>
<tr>
<td>Robins et al. (2010)</td>
<td></td>
<td>Perception Recognition Identification Recognition</td>
<td>Word reading test: - Prosopagnosia group vs controls: no difference (Acc., RTs and WLE) - Prosopagnosics individually compared to controls: no elevated WLE. Card sorting test: - Prosopagnosia group vs controls: no difference for sorting according to content or according to style (Acc., RTs). - Prosopagnosics individually compared to controls: 1 subject abnormal for sorting word content (RT); 9 / 10 participants normal on all word processing measures. Dissociation (impaired face processing / preserved word processing).</td>
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<td>Smith-Spark &amp; Moser (2009)</td>
<td></td>
<td>Identification (non-words)</td>
<td>- Face naming task: no deficit (RT and Acc.); but smaller AoA effects compared to controls. Dissociation (impaired word processing / preserved face processing).</td>
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<td>Susilo et al. (2015)</td>
<td></td>
<td>Recognition Identification Recognition</td>
<td>Four prosopagnosia patients: no deficit (Acc. and RT) on all seven tasks when compared individually to controls. Dissociation (impaired face processing / preserved word processing).</td>
</tr>
<tr>
<td>Turkeltaub et al. (2014)</td>
<td></td>
<td>Identification Perception</td>
<td>Face similarity matching: no deficit (Acc.) - Reading words: abnormal (RTs and WLE). Dissociation (impaired word processing / preserved face processing).</td>
</tr>
</tbody>
</table>
TESTS OF WHOLE UPRIGHT FACE PROCESSING IN PROSOPAGNOSIA: A LITERATURE REVIEW

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Declarations of interest: none
Tests of Face Processing in Prosopagnosia

Highlights

- Many tests are used to assess whole upright face processing in prosopagnosia
- Whole upright face processing tests from recent literature are reviewed
- Tests varied greatly in experimental design and stage of face processing assessed
- Considerations related to test design are discussed
- A conceptual framework is proposed to guide test selection in future studies
Tests of Face Processing in Prosopagnosia

Abstract

Prosopagnosia refers to an acquired or developmental deficit in face recognition. This neuropsychological impairment has received increasing attention over the last decade, in particular because of an increased scientific interest in developmental prosopagnosia. Studies investigating prosopagnosia have used a variety of different clinical and experimental tests to assess face processing abilities. With such a large variety of assessment methods available, test selection can be challenging. Some previous works have aimed to provide an overview of tests used to diagnose prosopagnosia. However, no overview that is based on a structured review of the literature is available. We review the literature to identify tests that have been used to assess the processing of whole upright faces in acquired and developmental prosopagnosia over the last five years (2013-2017). We not only review tests that have been used for diagnostic purposes, but also tests that have been used for experimental purposes. Tests are categorised according to i) their experimental designs and, ii) the stage of face processing that they assess. On this basis, we discuss considerations regarding test designs for future studies. A visual illustration providing a structured overview of paradigms available for testing the processing of whole upright faces is provided. This visual illustration can be used to inform test selection when designing a study and to apply a structured approach to interpreting findings from the literature. The different approaches to assessment of face processing in prosopagnosia have been necessary and fruitful in generating data and hypotheses about the cause of face processing deficits. However, impairments at different levels of face processing have often been interpreted as reflecting a deficit in the recognition stage of face processing. Based on the data now available on prosopagnosia, we advocate for a more structured approach to assessment, which may facilitate a better understanding of the key deficits in prosopagnosia and of the level(s) of face processing that are impaired.

Keywords: acquired prosopagnosia, developmental prosopagnosia, assessment, review
1. Introduction

Prosopagnosia is a disorder characterized by an impairment in face identity recognition that can be more or less severe. People with prosopagnosia commonly complain about not being able to recognize famous people on TV and not being able to recognize friends and family. Some prosopagnosics even struggle to recognize themselves in a mirror. The term prosopagnosia was first coined by Bodamer in 1947 (Bodamer, 1947) to refer to: “the selective disruption of the perception of faces, one’s own face as well as those of others, which are seen but not recognized as faces belonging to a particular owner” (English translation from Ellis and Florence, 1990). While early research focused primarily on the deficit following brain injury: acquired prosopagnosia (e.g. De Renzi et al., 1991; Farah, 1991), a growing amount of work now focuses on developmental prosopagnosia (e.g. Susilo and Duchaine, 2013; Towler et al., 2016). In these cases, the disorder is not attributable to a known neurological injury, instead, the ability to recognise faces has not developed adequately in childhood (Duchaine and Nakayama, 2006a; McConachie, 1976). While acquired prosopagnosia is rare, approximately 2.5% of the population is thought to suffer from developmental prosopagnosia (Bowles et al., 2009; Kennerknecht et al., 2006a).

A large body of research has been produced on prosopagnosia and many tests have been developed over the years to diagnose prosopagnosia and to characterize face processing abilities in these individuals. Interestingly, there is no agreement regarding the diagnostic criteria for prosopagnosia and the tests that should be used to make the diagnosis (Barton and Corrow, 2016a, 2016b; Bate and Tree, 2017). The tests that have been used to assess face processing vary regarding the stimuli that they use and their experimental set-up, as well as regarding the aspects of face processing that they tap into. While some tests assess processes related to the visual encoding of faces, others test the ability to store and match representations of faces. There are also many tests
that focus on the more semantic aspects of face processing. It is not surprising that such diverse tests are used as the ability to recognise a face involves many different processes, and impairments of any of these processes may lead to prosopagnosia. Traditionally, a distinction has been made between apperceptive prosopagnosia, that is caused by a deficit of visual perceptual encoding of faces, and associative prosopagnosia that is caused by a deficit in accessing facial memories (De Renzi et al., 1991). Although the relevance of the distinction between an apperceptive and associative form is still debated, it is generally acknowledged that prosopagnosia does not refer to one single disorder, but instead a family of disorders with different functional impairments all leading to face processing problems (Barton and Corrow, 2016b, 2016c).

With so many tests available, selecting which tests to use to evaluate different aspects of face processing in prosopagnosia is challenging. There are articles available that aim to provide an overview of tests used to assess face identity processing in prosopagnosia (Barton and Corrow, 2016c, 2016a; S. L. Corrow et al., 2016; Dalrymple and Palermo, 2016) but they only focus on tests used for diagnostic purposes and are not based on a structured review of the literature. There are also articles discussing some of the important methodological aspects that must be taken into consideration when evaluating assessment methods. Ramon (2018) highlights three important aspects that should be considered during experimental design and interpretation of results: processes (e.g. levels of processing assessed), paradigms (e.g. simultaneous matching tasks versus old/new familiarity task) and procedures (e.g. differences in inter-item similarity or number of items included in a task). Here, we present a review of the literature, aiming to identify tests that have been used to assess either diagnostically or experimentally the processing of whole upright faces in prosopagnosia over the last five years. Tests are first categorised according to their experimental paradigms, and differences in experimental designs are described and discussed. They are then categorised according to Bruce & Young’s (1986) stages of face processing. A visual overview of
identified paradigms classified according to level of processing is presented. This visual illustration of available tests is designed to help guide test selection in future studies. Finally considerations related to experimental aspects of the assessments methods are discussed. While procedural aspects such as for example trial numbers, exposure duration and item similarity are important, these are not discussed in detail in this paper.

The use of the term face processing rather than face recognition here is intentional, as it is more broadly encompassing. When referring to face processing in this paper, we are only referring to aspects related to the processing of the identity of a face, spanning from the detection of a facial stimulus to the access of semantic information based on a facial stimulus, and not aspects related to for example emotion processing.

2. Method

We searched Web of Science for all articles in English featuring the term prosopagnosia in their title and PubMed for articles featuring the term prosopagnosia in their title or abstract. As the aim was to provide an overview of tests currently used in the literature, only articles that were published within the past 5 years (between 2013-2017) were included in the review. The search in Web of Science gave 102 hits and the search in PubMed gave 203 hits. Studies that did not include assessment of people with prosopagnosia, that did not include any measurements of face processing abilities, or did not provide details about how face processing was tested, were excluded. In all, 110 neuropsychological, experimental, and neuroimaging studies were included in the review (see supplementary material for full list). Behavioural tests that were used in the included papers for experimental or diagnostic purposes were identified, analysed and categorised. Only tests assessing the processing of the identity of whole upright faces were included. Tests and experiments focusing primarily on specific effects like the part-whole effect, the inversion effect, or the composite face effect were not included in the analysis as they reflect perceptual mechanisms that may not be
directly relatable to individual differences in face processing abilities (see Rezlescu et al., 2017 for a discussion of these effects). In the studies reviewed, questionnaires, semi-structured interviews and rating tools were often used to assess face processing difficulties. As these tools measure subjective complaints and are radically different in their set-up, they were not included in the main analysis of this review.

3. Results

In this section a detailed list of types of face processing tests is provided. Tests are categorized according to their experimental set-up, more specifically the types of facial stimuli used, the experimental design applied, and the type of response required. While some tests use familiar faces, others use novel faces as stimuli. This choice affects the type of experimental set-up that can be used and the type of response that can be demanded. First, tasks using novel faces are described, then tasks using faces familiar to the participants. Although they are not the main focus of the review, questionnaires, semi-structured interviews and rating tools are briefly reviewed and listed in a table. The different paradigms are illustrated in figure 1.

[Figure 1 about here]

3.1. Face detection

Only a few of the papers reviewed included face detection tests (figure 1: 1. Detection). Mooney faces-tests use two-tone black and white pictures of faces with no clear facial features. Participants are shown a mixture of images, some with a face and some without and they must determine whether a face is present or not (Jansari et al., 2015; Ulrich et al., 2017; originally presented in Mooney, 1957). In another type of face detection task, participants are shown 25 images at a time in 5x5 grids and they must determine whether a face is present or not. In these search tasks, distractors can be scrambled faces (figure 1, image 1A) or other categories of visual
stimuli (figure 1, image 1B) (Dalrymple and Duchaine, 2016; Martinaud et al., 2012; originally presented in Garrido et al., 2008).

3.2. Face categorization and face judgement

These tasks involve categorising or judging faces according to specific criteria (figure 1, 2. Categorisation and judgement). In some tests, faces are presented one at a time and participants must categorise according to a criterion such as gender (Bate et al., 2015; Esins et al., 2016; Pizzamiglio et al., 2017; originally presented in Thomas et al., 2008) (figure 1, image 2A). Other tests use two alternative forced choice (2AFC) paradigms (figure 1, image 2B) in which two faces are shown at a time and participants determine, for example, which face is the oldest or the most beautiful one (Bate et al., 2015; Pizzamiglio et al., 2017; originally presented in Thomas et al., 2008).

3.3. Simultaneous discrimination and matching

Many studies use tasks in which participants are shown several faces simultaneously that must be matched according to similarity. These tasks are referred to here as simultaneous discrimination and matching tasks (figure 1: 3. Simultaneous discrimination and matching). In some versions of the task, a target face is provided as a base of comparison, in others not (see appendix for test details). In same /different paradigms (often called simultaneous discrimination tasks in the literature, illustrated in figure 1, image 3Aa), participants are shown two faces and asked either to determine if the two faces are the same or different (Behrmann and Plaut, 2014; Burton et al., 2010; Kamminga et al., 2015; Kawagoe et al., 2017; Kumfor et al., 2016; Roberts et al., 2015; Shah et al., 2015c; Tanzer et al., 2016; Ulrich et al., 2017; White et al., 2017), or asked to determine how similar the two faces are on a scale from 1 to 7 (Esins et al., 2016). In odd one out paradigms, three or four faces are shown simultaneously and participants must determine which face is different from the others (figure 1, image 3Ab). In most cases two or three identical faces are
presented together with a morphed version of the same face identity, which is the odd one out (Liu et al., 2016; Pancaroglu et al., 2016). In one task three pictures of the same face identity taken from different views are presented with a different face identity that is also taken from a different view (Behrmann et al., 2016). In simultaneous matching paradigms, a target face identity is typically presented at the top of the screen along with two test faces below creating a two-alternative forced-choice (AFC) task (figure 1, image 3B). Participants must select which face or image is identical to the target (Behrmann and Plaut, 2014; Tanzer et al., 2016, 2013; Weiss et al., 2016) or most similar to the target face (Davies-Thompson et al., 2016; DeGutis et al., 2014). In variations of this paradigm, some use 3AFC (Bate et al., 2015, 2014, Dalrymple et al., 2017, 2014a, 2014b; Dalrymple and Duchaine, 2016; Ulrich et al., 2017), 4AFC (Mendez et al., 2015) or even 5AFC options instead (Albonico and Barton, 2017) (figure 1, images 3B and 3Ca).

Two of the most widely used tests of face processing are simultaneous face matching tasks with targets. In Benton’s Test of Facial Recognition (see appendix for full list of studies reviewed using this test), participants are presented with six test faces and must select the ones that match the identity of a target face (figure 1, image 3Cb.). In the first part all faces are presented from identical front views, in the second part, the target face is presented from front view but the test faces are presented from side views and in the third part, all faces are presented from front view but the lighting conditions are different for the test faces than the target face (test originally presented in Benton et al., 1994, see Appendix for full list of studies using the test). The Cambridge Face Perception test takes a slightly different approach. Participants are presented with a target face and 6 test faces that have been more or less morphed away from the target face. Subjects are required to sort the test faces so that they are ordered from the most to the least similar to the target (figure 1, image 3Cc, test originally presented in Duchaine et al., 2007, see Appendix for full list of studies using the test).
3.4. Delayed face discrimination and matching

Many tasks do not present the target and test items simultaneously. In *delayed matching/discrimination* and *old/new recognition memory* tasks, there is a time gap between the presentation of the target and the test items. *Delayed discrimination and matching tasks* are presented first. In these tasks, a trial usually involves first presenting a target face, then a mask and finally one or more test faces on a new screen (see appendix for test details) (figure 1: 4. Delayed discrimination and delayed matching). In *same/different* paradigms, a target face is followed by a single test face (figure 1, image 4A). The task involves determining whether the two faces (target and test face) are the same identity or not (Daini et al., 2014; De Heering and Maurer, 2014; DeGutis et al., 2014; Fisher et al., 2017; Meek et al., 2013; Rezlescu et al., 2014; Susilo et al., 2013). *Delayed alternative forced choice* paradigms also exist (figure 1, image 4Ba). Participants are presented with a target face, and then a series of test faces on a new screen. They must determine which of the test faces matches the identity of the target face. Delayed2AFC paradigms are commonly used (Busigny et al., 2014; Longmore and Tree, 2013). In one study, an additional option for response is that neither of the faces match the target (Kawagoe et al., 2017). 4AFC and 6AFC have also been used in delayed tasks (Biotti et al., 2017a; Shah et al., 2015a) (figure 1, image 4C). Sometimes, target identities are presented dynamically using video material (Longmore and Tree, 2013; Maguinness and Newell, 2015). Some delayed paradigms present more than one target face identities in order to measure working memory capacity. In one study, participants are presented with two or more target face identities presented sequentially and participants must then determine which of three test faces was one of the target face identities (DeGutis et al., 2014). In another study, four target face identities are shown simultaneously on the screen and then participants are presented with one face and must determine whether it was one of the target identities or not (Jackson et al., 2017).
3.5. Old/new face recognition

The term old/new face recognition task is used to refer to tasks with two parts. A learning phase in which a series of target faces are learnt and a test phase in which participants must identify targets amongst distractors (see appendix for test details) (figure 1: 5. Old/new recognition). The number of targets to be learnt as well as the exact delay between learning phase and test phase vary between experiments. In simple old/new face recognition tasks, participants are presented with a series of target faces one at a time in the learning phase. In the test phase, they are again presented with a series of target faces and novel faces one at a time and must determine whether the face they are seeing is from the series of identities learnt previously (figure 1, image 5A) (Canzano et al., 2016; Dalrymple et al., 2017, 2014b; Dalrymple and Duchaine, 2016; Esins et al., 2016; Finzi et al., 2016; Fisher et al., 2017; Rezlescu et al., 2014; Suárez-González et al., 2016; Susilo et al., 2015; Tabuas-Pereira et al., 2016). In a few studies, the faces of the learning phase are presented in a video (Eins et al., 2016; Longmore and Tree, 2013). In old/new recognition forced choice paradigms, the test phase involves presentation of two or more faces simultaneously, one from the learnt series, and one or more novel face(s) (figure 1, image 5B and 5C). Participants must select the face that they have seen before. The most famous test that is designed in this way is the Warrington recognition memory test (Warrington, 1984), which is used in many of the studies reviewed and which exists in many versions using different faces as stimuli (Albonico and Barton, 2017; Busigny et al., 2014; Corrow et al., 2016; Davies-Thompson et al., 2016; Hills et al., 2015; Liu et al., 2016, 2015; Longmore and Tree, 2013; Moroz et al., 2016; Pancaroglu et al., 2016; Rubino et al., 2016). The Cambridge Face Memory Test (CFMT; Duchaine and Nakayama, 2006b; see appendix for list of studies using the test) is the most widely used face processing test at present. The test combines a delayed matching (figure 1, image 4c.) and old/new recognition (figure 1, image 5c.) design. In the learning phase, participants must learn six target identities, one at a time.
For each face the following learning procedure is carried out. The target is presented sequentially from three different views (left 1/3 profile, a frontal view, and a right 1/3 profile). This is followed by immediate recognition, where the participants must find the target identity amongst two distractor faces. In total, there are three immediate recognition trials for each target identity. In this block, the target item is identical in learning section and in the immediate recognition. In the second block, all six target faces are presented simultaneously in frontal view for 20 seconds, and participants are instructed to memorize the faces. Then, participants must identify novel images of target faces that are presented alongside two distractors. In the third block, novel images with added visual noise are used (Duchaine and Nakayama, 2006b). The CFMT has become a key diagnostic tool for prosopagnosia, therefore, most studies in our review use this test. Many versions of this test exist. There are an Australian and Chinese version of the test (Burns et al., 2017b; Maguinness and Newell, 2015; McKone et al., 2012, 2011; Palermo et al., 2017; Rivolta et al., 2017). Two child versions have been made. The first uses a similar experimental set-up as the adult version but uses children faces as stimuli (Bennetts et al., 2017; Dalrymple et al., 2017, 2014b, 2014a; Dalrymple and Duchaine, 2016) in order to compensate for the own-age-bias (Hills and Lewis, 2011). The second uses adult faces as stimuli but uses a 2AFC set-up to lower the difficulty of the task (Croydon et al., 2014). A video version of the test has also been used (Palermo et al., 2017, 2011).

The paradigms described above primarily use novel faces as stimuli. In the following sections, tasks including familiar faces as stimuli are described.

3.6. Face familiarity

*Face familiarity* tests involve determining whether a face is familiar or not. No retrieval of semantic information related to the face is required (figure 1: 6. Face familiarity). Two experimental set-ups
are often used (see table 1 for details). In Yes/no paradigms, famous faces are intermixed with novel faces and shown one at a time (figure 1, image 6A). Participants determine if the face is famous or not (Albonico and Barton, 2017; Corrow et al., 2016; Mendez et al., 2015; Pancaroglu et al., 2016). In some studies, participants must name or provide other semantic information about the faces considered familiar, thereby combining familiarity and naming paradigms (Davies-Thompson et al., 2016; De Heering and Maurer, 2014; Hills et al., 2015; Liu et al., 2016; Moroz et al., 2016; Palermo et al., 2017; Rivolta et al., 2017). In one version of this test, faces are not presented sequentially one at a time, but are instead presented as a list on a sheet of paper in a questionnaire format. The participants must fill out whether the face is familiar or not and provide information about the celebrity (Liu and Behrmann, 2014; Tanzer et al., 2013; Weiss et al., 2016). Famous face pointing paradigms involve a different set-up. Four faces are shown simultaneously and participants are asked to point at, and in some cases also name, the face that is famous (Kamminga et al., 2015) (figure 1, image 6C).

Table 1: Face familiarity tasks

<table>
<thead>
<tr>
<th>References</th>
<th>Stimuli</th>
<th>Design</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albonico and Barton, 2017; J. C. Corrow et al., 2016</td>
<td>100 faces (mix of famous and novel)</td>
<td>Familiar: yes/no</td>
<td></td>
</tr>
<tr>
<td>Avidan et al., 2014; Avidan and Behrmann, 2008; Liu and Behrmann, 2014; Rosenthal et al., 2017; Tanzer et al., 2013; Weiss et al., 2016</td>
<td>56 famous</td>
<td>Familiar: yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Barton et al., 2001; Davies-Thompson et al., 2016; Fox et al., 2013; Hills et al., 2015; Liu et al., 2016; Moroz et al., 2016</td>
<td>? famous</td>
<td>Familiar: yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Bate et al., 2015</td>
<td>14 family/friends</td>
<td>Familiar: yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Bennetts et al., 2015</td>
<td>30 famous</td>
<td>Rate familiarity (5-point scale)</td>
<td>Naming</td>
</tr>
<tr>
<td>Bennetts et al., 2017</td>
<td>10 staff from school</td>
<td>Familiar: yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>De Heering and Maurer, 2014</td>
<td>30 famous</td>
<td>Familiar: yes/no</td>
<td>Naming (or other sem)</td>
</tr>
<tr>
<td>Grossi et al., 2014</td>
<td>50 famous</td>
<td>Familiar: yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Mendez et al., 2015</td>
<td>24 famous</td>
<td>Familiar: yes/no</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 novel</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Tests of Face Processing in Prosopagnosia

<table>
<thead>
<tr>
<th>Study</th>
<th>Famous</th>
<th>Novel</th>
<th>Familiar:</th>
<th>Naming</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuner and Schweinberger, 2000</td>
<td>32</td>
<td>32</td>
<td>yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Palermo et al., 2017, 2011, Rivolta et al., 2017, 2014</td>
<td>20</td>
<td>20</td>
<td>yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Pancaroglu et al., 2016</td>
<td>?</td>
<td>?</td>
<td>yes/no</td>
<td>Naming</td>
</tr>
<tr>
<td>Pizzamiglio et al., 2017</td>
<td>9</td>
<td>9</td>
<td>yes/no</td>
<td>2 parts: cropped and not cropped</td>
</tr>
</tbody>
</table>

? Information not provided in the specific paper

3.7. Name-to-face matching

*Name-to-face matching* tasks are an alternative way of assessing the ability to identify famous faces that do not require participants to generate their names (figure 1: 7. Name-to-face matching). In some studies, a name-to-face matching paradigm is used in which a number of faces are shown simultaneously on a screen together with a name (presented visually and/or verbally), and participants are asked to select the face that matches the name (Mendez et al., 2015; Olson et al., 2015; Roberts et al., 2015) (figure 1, image 7A). Distractors here can be a mixture of famous faces and novel faces. In one study, participants are shown the face of a celebrity (that they previously couldn’t recognise) together with a novel unknown face and are asked to indicate which is the face named by the examiner (Fox et al., 2013). The set-up can also be inversed. In this case, pictures of familiar faces are shown one at a time, and the participant is asked to indicate from a list names, which name matches each face (Ramon et al., 2016) (figure 1, image 7B).

3.8. Face naming

*Famous face naming* tasks are a standard component of neuropsychological assessment of dementia and have traditionally been used to assess semantic memory in that context (Albert et al., 1979; Lezak, 2012) (figure 1: 8. Naming familiar faces). In the context of prosopagnosia research, they are primarily used to assess face processing abilities and are often included when diagnosing the disorder (Barton and Corrow, 2016a). Typically, pictures of famous people are shown one at a time on a screen and participants are asked to name the person presented (figure 1, image 8). If they cannot provide the name, they are asked to provide other semantic information about the person.
There are many versions of famous face naming tests, primarily because famous faces must be selected according to the demographics of the participants (e.g. age and country) (see table 2 for details). This is to ensure that as many participants as possible have been exposed to as many of the famous people included as possible. The number of trials varies greatly in the different versions of the test. While most paradigms use unlimited exposure durations, some limit exposure (e.g. Ulrich et al., 2017).

Table 2: Famous and familiar (non-famous) face naming tasks

<table>
<thead>
<tr>
<th>References</th>
<th>Stimuli</th>
<th>Cropped</th>
<th>Sociocultural context</th>
<th>Exposure</th>
<th>Familiarity check (after)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bala et al., 2015</td>
<td>74 famous faces</td>
<td>yes</td>
<td>Poland</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Bate et al., 2014; Bennetts et al., 2015; Anna K. Bobak et al., 2017; Burns et al., 2017a, 2017b, 2014; Duchaine et al., 2007; Duchaine and Nakayama, 2005; Finzi et al., 2016; Fisher et al., 2016, 2017; Lohse et al., 2016; Longmore and Tree, 2013; Nemeth et al., 2014; Parketny et al., 2015; Song et al., 2015; Susilo et al., 2015; John Towler et al., 2016b, 2016a; Yovel and Duchaine, 2006</td>
<td>60 famous faces</td>
<td>yes</td>
<td>US and Canada</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Behrmann et al., 2016; Behrmann and Plaut, 2014</td>
<td>Famous faces</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Busigry et al., 2014</td>
<td>121 famous faces</td>
<td>no</td>
<td>US</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Cattaneo et al., 2016</td>
<td>42 famous faces</td>
<td>yes</td>
<td>Italy</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Corrivetti et al., 2017</td>
<td>Famous faces</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Everhart et al., 2015</td>
<td>12 recent presidents</td>
<td>?</td>
<td>US</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Fletcher et al., 2013</td>
<td>24 famous faces</td>
<td>?</td>
<td>UK</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Irish et al., 2017</td>
<td>Famous faces</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Liu et al., 2014</td>
<td>16 famous people</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Maguinness and Newell, 2015</td>
<td>40 famous people</td>
<td>yes</td>
<td>Ireland</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Malaspina et al., 2017</td>
<td>45 famous faces</td>
<td>yes</td>
<td>Italy</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Meek et al., 2013</td>
<td>Famous face</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
</tr>
<tr>
<td>Mendez et al., 2015</td>
<td>24 famous faces</td>
<td>yes</td>
<td>US</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>O'Brien, 2018</td>
<td>18 famous faces</td>
<td>?</td>
<td>US</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Pal et al., 2013</td>
<td>20 famous faces</td>
<td>?</td>
<td>India</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Ramon et al., 2016</td>
<td>Familiar pupils morphed from average face to specific face</td>
<td>yes</td>
<td>Pupils that the subject worked with</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Roberts et al., 2015</td>
<td>40 famous faces</td>
<td>no</td>
<td>UK</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Sawamura et al., 2014</td>
<td>16 familiar faces (naming and pointing)</td>
<td>?</td>
<td>Japan</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Shah et al., 2015b, 2015a</td>
<td>34 famous faces</td>
<td>yes</td>
<td>UK</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
<tr>
<td>Suárez-González et al., 2016</td>
<td>34 famous faces</td>
<td>yes</td>
<td>Spain</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Tabass-Pereira et al., 2016</td>
<td>Famous faces</td>
<td>?</td>
<td>Portugal</td>
<td>Unlimited</td>
<td>no</td>
</tr>
<tr>
<td>Ulrich et al., 2017</td>
<td>77 famous faces</td>
<td>no</td>
<td>UK</td>
<td>500ms</td>
<td>no</td>
</tr>
<tr>
<td>Zhang et al., 2015; Zhao et al., 2017</td>
<td>30 famous faces</td>
<td>no</td>
<td>China</td>
<td>Unlimited</td>
<td>yes</td>
</tr>
</tbody>
</table>

? Information not provided in the specific paper

In all the paradigms using famous faces, faces of individuals that are personally familiar to the participant can be used instead. In the papers reviewed, this has been done with familiarity and
naming tests (Bate et al., 2015; Bennetts et al., 2017; Pizzamiglio et al., 2017). In one study, a face-to-name matching paradigm was used in which a face from the subject’s network is shown and the participant chooses the associated name from a list of familiar names (Ramon et al., 2016).

3.9. Variations in experimental set-up

The simultaneous matching, delayed matching and old/new recognition paradigms described exist in many versions (see appendix for details). In some tests, the target and test faces in “same conditions” are identical (exactly same photo of the same face). The task therefore becomes an image matching rather than a face matching task. Indeed, participants can complete the task by comparing specific details on the images and performance does not necessarily reflect the participant’s ability to build full facial representations and compare them across variable input stimuli. Many paradigms therefore change size (e.g., Fisher et al., 2017), lighting (e.g., Bate et al., 2015), view-point or head position (Behrmann and Plaut, 2014; Duchaine and Nakayama, 2006b), or expressions (Maguinness and Newell, 2015) or use different cameras (e.g., Burton et al., 2010) between target faces and test faces, so that participants must build whole representations of the faces in order to complete the task (see figure 2 and appendix).

![Figure 2: Example of techniques used.](image)
While many tasks use naturalistic faces others use computer generated faces (e.g. Biotti et al., 2017a; Rezlescu et al., 2014). Computer generated faces do not mirror stimuli from the real world as closely as photos of real-life faces but they allow greater control of stimuli. Many research projects also use faces that have been morphed in different ways (see Appendix). The term morphed is used to refer to different things in different studies. In some cases it refers to “mixing” two faces together and adjusting the levels of similarity between two stimuli (e.g. Behrmann and Plaut, 2014; Busigny et al., 2014), in other cases, it refers to making adjustments or changes to specific aspects of the faces (changing configuration/position of features or changing the features themselves) (e.g. Esins et al., 2016; Roberts et al., 2015). Another variation has to do with whether faces are cropped or not. In order to avoid participants using non facial characteristics to solve tasks (alternative compensatory strategies), many studies remove hair in the stimuli either by using hats (e.g. Roberts et al., 2015)(figure 3 b.) or by cropping the face and thereby also removing information regarding the contour of the face (e.g. Busigny et al., 2014) (figure 3 c.).

Tests can also vary according to the type of measurements used. While some of the tests use reaction times (RT) as the dependent measure, others use accuracy. Accuracy is typically considered a less sensitive measure than reaction times (Behrmann and Geskin, 2018; Geskin and Behrmann, 2018), however, tests using accuracy as the primary outcome measure can also be highly sensitive (Starrfelt and Robotham, 2018). The Cambridge Face Memory Test (CFMT;
Duchaine & Nakayama, 2006) is an example of a test that has been shown to be sensitive to small variations in face recognition ability although scores are based on accuracy (Cho et al., 2015). Overall, the sensitivity of a test depends more on its design than on whether it uses Accuracy or RT (or both) as the primary outcome measure.

3.10. Questionnaires, semi-structured interviews and rating tools

One of the most common ways of evaluating whether a person has face processing deficits is to ask subjects if they experience difficulties. In the literature reviewed, subjective complaints were assessed using more or less structured interviews, questionnaires and rating tools (see table 3 for details). There are many self-report questionnaires available and most use a Likert scale. The questionnaire from the Faceblind.org website (e.g. DeGutis et al., 2014b), the 20-item prosopagnosia index (PI-20) (Biotti et al., 2017b, 2017a; Biotti and Cook, 2016; Gray et al., 2017; Rubino et al., 2016; Shah et al., 2015b, 2015c) and the Face Recognition Questionnaire (Esins et al., 2016; Johnen et al., 2014; Kennerknecht et al., 2006a, 2006b; Palermo et al., 2017; Verfaillie et al., 2014) were the most widely used questionnaires assessing face identity recognition in the studies reviewed. The Faces and Emotions Questionnaire focuses not only on face identity recognition but it also has a section on face emotion recognition and vocal emotion recognition (Freeman et al., 2015; Gerlach et al., 2017, 2016; Klargaard et al., 2016). Some studies use semi-structured interviews rather than multiple choice questions to identify face identity recognition problems (e.g. Malaspina et al., 2017; Rubino et al., 2016). One included study used a semi-structured interview to evaluate face identity problems and its social impact (Dalrymple et al., 2014a). In one study, the face recognition skills of children were rated by parents on a single item Likert scale (poor to excellent) (Bennetts et al., 2017). As questionnaires, semi-structured interviews and rating tools are not the main focus of this study, they will not be further discussed.
Table 3: Questionnaires, semi-structured interviews and rating tools.

<table>
<thead>
<tr>
<th>Name of test</th>
<th>References</th>
<th>Group of interest</th>
<th>Design</th>
<th>Content</th>
</tr>
</thead>
<tbody>
<tr>
<td>· Faces and emotions questionnaire</td>
<td>· Freeman et al., 2015; Gerlach et al., 2017, 2016; Klargaard et al., 2016</td>
<td>DP</td>
<td>Self-report</td>
<td>· 54 items · 4 choice (definitely agree to definitely disagree)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face identity recognition · Face emotion recognition · Voice emotion recognition</td>
</tr>
<tr>
<td>· The 20-item prosopagnosia index</td>
<td>· Biotti et al., 2017b, 2017a; Biotti and Cook, 2016; Gray et al., 2017; Rubino et al., 2016; Shah et al., 2015b, 2015c</td>
<td>DP</td>
<td>Self-report</td>
<td>· 20 items · Likert scale 1-5 (strongly agree to strongly disagree)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face identity recognition · Attractiveness · Emotion</td>
</tr>
<tr>
<td>· Face recognition questionnaire</td>
<td>· Esins et al., 2016; Johnen et al., 2014; Kennerknecht et al., 2006a, 2006b; Palermo et al., 2017; Verfaillie et al., 2014</td>
<td>DP</td>
<td>Self-report</td>
<td>· 15 items · Likert scale 1-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face recognition · Some items unrelated to face recognition</td>
</tr>
<tr>
<td>· Prosopagnosia questionnaire Barton Faceblind</td>
<td>· DeGutis et al., 2014</td>
<td>DP</td>
<td>Self-report</td>
<td>· ? items · Likert scale 1-5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face recognition</td>
</tr>
<tr>
<td>· Self-reported general face recognition and own-race face recognition</td>
<td>· Palermo et al., 2017</td>
<td>DP (AP)</td>
<td>Self-report</td>
<td>· 3 items · Likert scale 1-9</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face recognition ability · Recognition of own race faces</td>
</tr>
<tr>
<td>· Metacognition about face recognition</td>
<td>· Palermo et al., 2017</td>
<td>DP (AP)</td>
<td>Self-report</td>
<td>· 77 items · Likert scale 0-9 (not at all to absolutely)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face recognition memory</td>
</tr>
<tr>
<td>· Questionnaire about face and voice identification</td>
<td>· Liu et al., 2016, 2015</td>
<td>AP (DP)</td>
<td>Self-report</td>
<td>· 10 items · Likert scale 1-7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face identification · Voice identification</td>
</tr>
<tr>
<td>· Prosopagnostic Questionnaire</td>
<td>· De Heering and Maurer, 2014</td>
<td>DP (AP)</td>
<td>Self-report</td>
<td>· 10 items · Likert scale 1-7</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Face identity memory</td>
</tr>
<tr>
<td>· Parental report rating</td>
<td>· Bennetts et al., 2017</td>
<td>DP</td>
<td>Observer rating</td>
<td>· 1 general item · Likert scale 1-5 (poor to excellent)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>· Parent rating of child’s face identity recognition skills</td>
</tr>
<tr>
<td>SEMI-STRUCTURED INTERVIEW</td>
<td>· Semi-structured interview</td>
<td>DP</td>
<td>Open answers</td>
<td>· Face recognition</td>
</tr>
<tr>
<td></td>
<td>· Malaspina et al., 2017</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>· Rubino et al., 2016</td>
<td>DP</td>
<td>Open answers</td>
<td>· Reported life-long difficulty with face recognition</td>
</tr>
<tr>
<td></td>
<td>· Dalrymple et al., 2014a</td>
<td>Children</td>
<td>Open answers</td>
<td>· Questions about face recognition and its social impact</td>
</tr>
</tbody>
</table>

? Information not provided in the specific paper

Abbreviations: DP: developmental prosopagnosia; AP: acquired prosopagnosia
4. Tests according to level of processing

In the literature, the same test is sometimes used by different researchers to make conclusions at different levels of processing. Here, in order to stimulate a discussion regarding which aspects of face processing are assessed with which tests, tests identified in the review were categorised explicitly according to stages of processing in figure 1. We used Bruce and Young's (1986) model of face processing as it, despite its simplicity, remains one of the models most commonly used for characterising different stages of face processing.

According to Bruce and Young' (1986) face recognition model, successful face recognition requires a series of sequential processing stages from structural encoding of the stimulus to access to semantic information. The model includes a perceptual stage that involves structural encoding, a recognition stage that is related to determining familiarity and an identification stage that is related to the retrieval of biographical information (Bruce and Young, 1986; S. L. Corrow et al., 2016). In figure 1, paradigms are categorised according to these stages that can be selectively impaired in acquired prosopagnosia and possibly also developmental prosopagnosia (Susilo and Duchaine, 2013). Note that the visual overview is not dependent on these levels being sequential, although this was originally assumed by Bruce & Young. Although it has become increasingly clear that face processing is a highly interactive process, it can still be useful to characterize tests according to which level(s) of processing they aim to assess.

Finding a face in a visual scene is considered a critical prerequisite for the activation of face-specific processing (Garrido et al., 2008). *Face detection* is a necessary part of the early visual analysis and encoding of a face stimulus and has therefore been placed at the perceptual level (see figure 1). *Simultaneous discrimination and matching* tasks have also been placed at the perceptual level as they often can be performed without storing a cohesive representation of the whole stimuli (see figure 1).
According to Barton and Corrow (2016c, p. 136), "Recognition implies the matching of a currently viewed stimulus to a stored perceptual representation, affirming that one has encountered the stimulus before." Many of the paradigms described assess this level of face processing. The length of time between the initial building of a face representation and presentation of the stimulus to be recognised differs between paradigms. In delayed matching tasks, targets and test faces are presented within seconds of each other so representation can be held in working memory. In old/new recognition tasks, a series of faces must be encoded and stored during a learning phase and many minutes, hours or even days elapse before the faces are shown for recognition. Representations can therefore not just be held in working memory, instead, they must be stored in long term memory. For familiarity tests using familiar faces, many years can have elapsed since the participant last encountered the face to be recognised.

The term identification is used here to refer to the process of matching a representation to associated semantic/biographical information. For faces, it involves matching a representation of a face that is being perceived to information about the person, such as their name, occupation or nationality. Name-to-face matching tests fall in this category. Tests that require naming a face verbally can be placed on a different level (see figure 1) as they require verbal production, which can be disrupted following brain injury.

Interestingly, small adjustments to test paradigms can change the level of processing assessed. For example, by adding a change of head position, change of lighting or change of expression between target and test face in a simultaneous discrimination or matching task (section 3.2.6), one can transform a perception test (that can be completed by detecting changes between images) into a recognition test (that requires a view-independent representation of the face to be built in order to be completed).
5. Discussion

There are advantages and disadvantages associated with many of the differences in experimental design described. The degree of familiarity of the faces used varies considerably and these differences have important implications. While some use novel faces, many use faces that are more or less familiar to the participants such as famous people, family, friends or colleagues. Using familiar faces has the major advantage that it mirrors more closely the difficulties that prosopagnosics describe in daily life. Using faces that participants are personally familiar with has the added advantage of ensuring participants have high levels of exposure to the faces (Ramon and Gobbini, 2018). There are however also various disadvantages associated with using personally familiar faces and these are primarily practical. The first disadvantage is that images of personally familiar faces are difficult and time-consuming to collect. Indeed, separate stimulus material must be built for each participant. There are two ways of getting these types of images. One can ask the participants who is being tested to provide photographs of family and friends, but faces in these images will often include facial expressions and extra-facial features such as glasses and hair that can make processing easier. Alternatively, one can take neutral photographs of the personally familiar individuals, which can be logistically challenging. There are also ethical considerations related to asking family members and friends to participate, when the purpose is to acquire pictures that will be used to assess whether the participant has a syndrome. The second disadvantage of using personally familiar faces is that participants may try to figure out who might be included in the material. The result of the test might therefore be a better measure of their deductive abilities than their face processing abilities.

By using famous faces instead of personally familiar faces, the same stimuli can be used for all subjects. This has the advantage of being less time-consuming and also makes it easier to compare performance across subjects. The main drawback of using famous faces is, however, that
prior exposure depends on the participants’ interests, age, and sociocultural background. One can therefore not be certain that all participants are equally familiar with the different faces.

A common disadvantage of tests using familiar faces (famous faces or personally familiar faces) is that they intrinsically also assess semantic knowledge. Indeed, an abnormal performance does not necessarily reflect a face processing impairment. There are various ways of checking whether abnormal performance on tasks using familiar faces are caused by semantic deficits, face processing impairments or variability in prior knowledge. Many studies that use a famous face naming task or familiarity judgement tasks, subsequently assess verbally whether participants know the identities used in the tests. A face identification score can be calculated on the basis of faces that the participant has proven to be familiar with in the verbal test. Person familiarity can be assessed verbally using a verbal version of a familiarity judgement task. In this case, a list of inter-mixed famous and novel names is provided and participants must determine which of the names are familiar. Person identification can also be assessed verbally. The assessor provides names of famous people, and the participant is asked to provide information (e.g. their occupation, nationality, etc.) about each identity. Barton and Corrow (2016c) provide an in-depth review on multi-modal person recognition and identification that can provide inspiration for assessment.

The familiar faces paradigms that are most commonly used are naming tasks. They are easy to get hold of and provide a relatively simple way of acquiring data related to face processing. An important limitation of naming tasks is that, in contrast to matching, pointing or familiarity tasks, they require a verbal response. A poor performance on a naming task could therefore not only be caused by a face processing deficit but also by a language-related deficits. This is particularly relevant when studying prosopagnosia following acquired brain injury but may also be relevant when studying face processing in developmental disorders like dyslexia (e.g. Sigurdardottir et al., 2015).
Many of the challenges and limitations described above are overcome by using faces that are novel to the participants. Differences in prior knowledge and semantic deficits are less likely to confound results. Indeed, when using novel faces, participants start with equal (non-) exposure to the stimuli (S. L. Corrow et al., 2016). The downside of using novel faces is, however, that a learning phase is necessary prior to assessment of recognition or identification abilities.

Different consideration related to choices of stimulus type should be taken into account when testing participants with acquired and developmental prosopagnosia. Using famous faces as stimuli might generally be more appropriate for participants with acquired prosopagnosia as they can be expected to have had normal experience with face processing prior to their injury. This is not necessarily the case for subjects with developmental prosopagnosia. Because of their life-long difficulties in processing faces visually, their interest in movies and television may be reduced, and they might therefore have had less exposure to famous faces as matched controls (S. L. Corrow et al., 2016).

Additional considerations may be warranted when assessing participants with acquired prosopagnosia. Level of difficulty may need to be adjusted to cater for the more or less severe levels of fatigue that many of these participants suffer from. Also, as many have visual field deficits, using central presentations of single faces (e.g. same/different paradigms) may be more appropriate when measuring reaction times than paradigms presenting multiple stimuli simultaneously (2AFC) as less eye movements are required. Indeed, participants with hemianopia typically make more eye movements to perceive the same visual areas as participants with full visual fields. It is also worth considering whether the single stimuli should be presented in the preserved visual field rather than centrally, so that viewing condition for patients with hemianopia and controls with intact visual fields are more similar. And on a more general note, despite reaction time measures often being considered more sensitive (see section 3.2.6), accuracy measures may in some cases be more
appropriate when assessing participants with brain injury as elevated reaction times in this group may be caused by more general slowing.

As discussed above, there are many factors that can be taken into consideration when selecting tests for studies investigating face processing in prosopagnosia. The broad variety of approaches that have been used to measure face processing in prosopagnosia have contributed to a large body of findings about the characteristics of prosopagnosia and about the processes underlying face processing. The amount of tests available can, however, make test selection difficult when designing a study. Interpreting findings from the literature can be equally challenging. Often, no matter the level of processing that has been assessed, subjects are described as having a face recognition deficit. Even if the test included in the study assesses the perceptual stage or identification stage of faces processing. Indeed, an abnormal performance on a test at one level can be caused by a deficit at a lower level. If for example a patient has an abnormal performance on an identification task, it could be caused by deficits at various levels. It could be caused by a deficit in encoding facial stimuli, a deficit in building or storing face representations, a deficit in accessing semantic knowledge associated to the face or a deficit semantic knowledge. Additional testing can be required to make more specific conclusions about the level(s) of processing that is (are)affected.

A large amount of prosopagnosia research has focused on investigating whether it is possible to have a face-specific impairment, or whether impairments in face processing are consistently accompanied by impairments in other visual categories. Particular care may be necessary when interpreting results from these types of studies. Indeed, when investigating dissociations between face processing deficits and deficits in other visual categories, checking that the same level of processing has been assessed across categories is highly relevant (Barton, 2018; Robotham and Starrfelt, 2017). Recently, a paper was published reviewing studies evaluating object
processing in cases with developmental prosopagnosia between 1976 and 2016 (Geskin and Behrmann, 2018). The review concluded that 20% had preserved object processing and 80% had deficits with objects. It was concluded that there was stronger evidence for an association than dissociation between faces and objects. The review did not, however, ensure that similar levels of processing were assessed across categories in each study, limiting the relevance of the findings with regards to discussions of associations and dissociations (Barton, 2018). A categorisation principle similar to the one presented here could be applied to paradigms assessing object and word processing. Together with the visual illustration proposed, this may make it easier for future research projects to select tests that are comparable across visual categories.

The different approaches to assessment of face processing in prosopagnosia have been necessary and fruitful in generating data and hypotheses about the cause of face recognition deficits. Based on the data now available on prosopagnosia, we advocate for a more structured approach to assessment, which may lead towards a better understanding of the key deficit(s) in prosopagnosia and of the level(s) of face processing that are impaired. The visual illustration (figure 1) provides a structured overview of the face processing tests that are currently being used. It can be used to support a more systematic approach to test selection in prosopagnosia research. For example, if one is interested in investigating whether face perception or face recognition is the key processing stage affected in a patient with developmental prosopagnosia, figure 1 can be used to identify paradigms that are available for testing the perception and recognition stage respectively. Specific references for previously devised experiments can then be found in the appendix. Figure 1 may also serve as a reminder of the importance of describing what stage(s) of face processing is(are) in focus, when carrying out face processing research. It can also be used to guide a structured approach to interpreting findings from the literature. Results can be classified according to level of
processing assessed and experimental design used, ensuring comparisons of results across studies of face processing are made on the basis of tests assessing comparable processes.

We are not suggesting here that all studies on prosopagnosia must assess processing at all the levels specified in Bruce & Young’s model (Bruce and Young, 1986). Tests should of course be selected according to the purpose of assessment. While there currently is no formal diagnostic criteria for congenital or acquired prosopagnosia (Geskin and Behrmann, 2018), various attempts have been made at standardising the diagnostic process. For example, the diagnostic criteria suggested by Barton and Corrow (2016b) and Dalrymple and Palermo (2016) provide important attempts at standardising the diagnostic process for developmental prosopagnosia. In studies investigating the underlying mechanisms of prosopagnosia, a greater level of specificity when describing the level of processing assessed and affected may lead to improvements regarding the specificity of the diagnostic criteria for prosopagnosia and to greater insights into possible subgroups of the disorder.
Role of the funding source

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Tests of Face Processing in Prosopagnosia


## Appendix: Simultaneous, delayed and old/new recognition tasks

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<tr>
<th>Experimental set-up</th>
<th>Response format</th>
<th>Experiment name (references)</th>
<th>Stimulus presentation</th>
<th>Special characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>The Jane Faces task</td>
<td>2 faces, horizontal</td>
<td>Cropped (shower-cap)</td>
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<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Morphed: feature identity, feature spacing and contour spacing</td>
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<tr>
<td></td>
<td></td>
<td>Simultaneous face discrimination task: Facemorph</td>
<td>2 faces, horizontal</td>
<td>Morphed: 2 faces together more or less</td>
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<tr>
<td></td>
<td></td>
<td>(Behrmann and Plaut, 2014)</td>
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<td></td>
</tr>
<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Upright/inverted alertness</td>
<td>2 faces, horizontal</td>
<td>Cropped</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Tanzer et al., 2016)</td>
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<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Glasgow Face Matching test</td>
<td>2 faces, horizontal</td>
<td>Different cameras</td>
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<td></td>
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<td>(Burton et al., 2010; Shah et al., 2015c)</td>
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<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Discrimination of upright and inverted faces (Avidan et al., 2014; Rosenthal et al., 2017)</td>
<td>2 faces, horizontal</td>
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</tr>
<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Local heroes test</td>
<td>2 faces, horizontal</td>
<td>Different cameras</td>
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<tr>
<td></td>
<td></td>
<td>(White et al., 2017)</td>
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<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Face and house perception task</td>
<td>2 faces, horizontal</td>
<td>Cropped</td>
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<tr>
<td></td>
<td></td>
<td>(Kawagoe et al., 2017)</td>
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<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Face-Perception task from Facial Affect and Identity Discrimination Task</td>
<td>2 faces, horizontal (40 trials)</td>
<td>Other task included: emotion discrimination</td>
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<tr>
<td></td>
<td></td>
<td>(Kamminga et al., 2015; Kumfor et al., 2016; Miller et al., 2012)</td>
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<tr>
<td>Simultaneous</td>
<td>Same/diff</td>
<td>Face-Matching task from Facial Affect and Identity Discrimination task</td>
<td>2 faces, horizontal (42 trials)</td>
<td>Change in expression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Kamminga et al., 2015; Kumfor et al., 2016; Miller et al., 2012)</td>
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<tr>
<td>Simultaneous</td>
<td>Scale 1 to 7 same to different</td>
<td>Featural and Configural Sensitivity Test</td>
<td>2 faces, horizontal</td>
<td>Cropped</td>
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<tr>
<td></td>
<td></td>
<td>(Esins et al., 2016)</td>
<td></td>
<td>Computer generated Morphed: features or configuration</td>
</tr>
<tr>
<td>Simultaneous</td>
<td>3AFC (odd one out) 3AFC (odd one out)</td>
<td>Discrimination of feature position, shape and external contour</td>
<td>3 faces, horizontal (1 morphed).</td>
<td>Change in size Morphed: changes in configuration, feature shape, or external contour</td>
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<tr>
<td></td>
<td></td>
<td>(Malcolm et al., 2004; Pancaroglu et al., 2016)</td>
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<tr>
<td>Simultaneous</td>
<td>3AFC (odd one out) 3AFC (odd one out)</td>
<td>Test of the perception of the spatial relationships and features in faces</td>
<td>3 faces, horizontal</td>
<td>Morphed: eye brightness, interocular distance, mouth position</td>
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<tr>
<td></td>
<td></td>
<td>(Barton et al., 2002; Liu et al., 2016)</td>
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<tr>
<td>Simultaneous</td>
<td>4AFC (odd one out)</td>
<td>Oddity task: Faces, Scenes, high and low ambiguity familiar objects</td>
<td>4 faces (3 same identity, 1 different identity)</td>
<td>Change of view</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(Behrmann et al., 2016)</td>
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<tr>
<td>Simultaneous</td>
<td>2AFC</td>
<td>Simultaneous face matching</td>
<td>1 target face and 2 test faces below</td>
<td>Cropped Change of view</td>
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<tr>
<td></td>
<td></td>
<td>(Behrmann and Plaut, 2014; Tanzer et al., 2016, 2013)</td>
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<tr>
<td>Simultaneous</td>
<td>2AFC</td>
<td>Simultaneous face matching</td>
<td>1 target face two test faces below</td>
<td>Cropped</td>
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<tr>
<td></td>
<td></td>
<td>(Behrmann et al., 2005; Weiss et al., 2016)</td>
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<tr>
<td>Tests of Face Processing in Prosopagnosia</td>
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<tr>
<td><strong>Simultaneous 2AFC</strong></td>
<td>The Philadelphia face perception battery: similarity task – no change of viewpoint (DeGutis et al., 2014; Nemeth et al., 2014; Thomas et al., 2008; D’Gutis: cropped and without colour)</td>
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<tr>
<td><strong>Simultaneous 2AFC</strong></td>
<td>Matching facial age and facial identity (Olson et al., 2015)</td>
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<tr>
<td><strong>Simultaneous 2AFC</strong></td>
<td>Simultaneous face matching with morphed faces with or without change of view (Davies-Thompson et al., 2016)</td>
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<tr>
<td><strong>Simultaneous 2AFC</strong></td>
<td>Face matching task: peripheral/foveal (Van Belle et al., 2015)</td>
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<tr>
<td><strong>Simultaneous 5AFC</strong></td>
<td>Normal faces and also High contrast -high spatial frequency faces: Simultaneous matching (Albonico and Barton, 2017)</td>
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<tr>
<td><strong>Simultaneous 3AFC</strong></td>
<td>Viewpoint matching test: Simultaneous matching with change of viewpoint (Ulrich et al., 2017)</td>
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<tr>
<td><strong>Simultaneous 3AFC</strong></td>
<td>Face matching test (Bate et al., 2015, 2014)</td>
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<tr>
<td><strong>Simultaneous 4AFC</strong></td>
<td>Face configuration test (Mendez et al., 2015)</td>
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<tr>
<td><strong>Simultaneous 3AFC</strong></td>
<td>Dartmouth Face Perception Test for children (Dalrymple et al., 2017; Dalrymple, Fletcher, et al., 2014; Dalrymple, Garrido, et al., 2014; Dalrymple &amp; Duchaine, 2016)</td>
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<tr>
<td><strong>Simultaneous Order according to similarity</strong></td>
<td>Cambridge Face Perception Test (Albonico and Barton, 2017; Avidan et al., 2014; Bate et al., 2015, 2014; Bennett et al., 2015; Biotti et al., 2017b; Biotti and Cook, 2016; Anna K Bobak et al., 2017; Burns et al., 2017b, 2014; Dalrymple et al., 2014b; DeGutis et al., 2014; Duchaine et al., 2007; Finzi et al., 2016; Fisher et al., 2017, 2016; Gerlach et al., 2016; Gerlach and Krumborg, 2014; Johnen et al., 2014; Klargaard et al., 2016; Liu et al., 2015, 2014; Maguinness and Newell, 2015; Palermo et al., 2017; Pancaroglu et al., 2016; Panketny et al., 2015; Rezlescu et al., 2014; Rivolta et al., 2017, 2014; Rosenthal et al., 2017; Rubino et al., 2016; Shah et al., 2015a, 2015b; Suarez-González et al., 2016; Susilo et al., 2013; Tanzer et al., 2016, 2013, John Towler et al., 2016a, 2016b; Ulrich et al., 2017; Vung et al., 2016)</td>
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<tr>
<td><strong>Simultaneous Select from 6 faces</strong></td>
<td>Benton Facial Recognition Test (Benton &amp; Van Allen, 1968; Ennio De Renzi &amp; di Pellegrino, 1998; Benton et al. 1983) (Behrmann and Plaut, 2014; Buono et al., 2016; Buisigny et al., 2014; Canzano et al., 2016; Cattaneo et al., 2016; Daini et al., 2014; De Heering and Maurer, 2014; Everhart et al., 2015; Fox et al., 2013; Gomez et al., 2015; Grossi et al., 2014; Jansari et al., 2015; Liu-Shuang et al., 2016; Liu et al., 2016; Longmore and Tree, 2013; Lueschow et al., 2015; Maguinness and Newell, 2015; Malaspina et al., 2017, 2016; Meek et al., 2013; Mendez et al., 2015; Palermo et al., 2017; Pancaroglu et al., 2016; Tabass-Pereira et al., 2016; Verfaillie et al., 2014; Villa-Bonomo et al., 2013; Xu and Biederman, 2014; Yetkin-Ozden et al.)</td>
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<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Task Description</td>
<td>Delay Type</td>
<td>Notes</td>
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<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Face perception task</td>
<td>Shown face, then another, either same or different.</td>
<td>Cropped</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Sequential matching</td>
<td>Target 500 ms, mask 250 ms, test image 500 ms.</td>
<td>Computer-generated faces Change of view Other categories: bodies, objects</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Delayed Faces-Objects-Bodies Perception Task (FOBPT)</td>
<td>Target 500 ms, mask 500 ms, test image 500 ms Faces</td>
<td>Computer-generated faces Change of view +/- morphed from test face Other categories: bodies, objects</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Change detection task - morphed</td>
<td>Face, then new face</td>
<td>Morphed (feature, non-emotional expression, emotional expression)</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Queen Square Face Identity Test</td>
<td>two sequentially presented faces</td>
<td>Change in expression</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Delayed matching</td>
<td>1 face, then another face</td>
<td>Cropped Change in expression Change of size Other task: Same emotion yes/no</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>Sequential matching task of faces</td>
<td>1 face, then another face</td>
<td>Computer-generated faces Modified (eyes, nose, and mouth) Other categories: faceless bodies and headless bodies.</td>
</tr>
<tr>
<td>Delayed</td>
<td>Same/diff</td>
<td>The Monkey Jane Task: Included inverted trials (both S and target inverted.)</td>
<td>1 face, then another face</td>
<td>Morphed: feature/configuration Other category: Monkey faces</td>
</tr>
<tr>
<td>Delayed</td>
<td>2AFC</td>
<td>Face discrimination at the individual level</td>
<td>1 face (1 sec), delay (1 sec.), then 2 test faces (1 same, 1 new).</td>
<td>Cropped Other categories in test: birds, boats, cars, chairs</td>
</tr>
<tr>
<td>Delayed</td>
<td>2AFC</td>
<td>Matching</td>
<td>1 face, then 2 side (1 same, 1 new)</td>
<td>Cropped Change of view Other category: car</td>
</tr>
<tr>
<td>Delayed</td>
<td>2AFC</td>
<td>Delayed matching of faces</td>
<td>1 face, then 2 faces (1 same, 1 new). faces or cars.</td>
<td>Cropped Change of view Other category: car</td>
</tr>
<tr>
<td>Delayed</td>
<td>2AFC</td>
<td>Discrimination of similar items</td>
<td>1 face then 2 test faces (1 same, 1 new)</td>
<td>Cropped Morphed from 20-100% of dissimilarity Other category: car</td>
</tr>
<tr>
<td>Delayed</td>
<td>2AFC</td>
<td>Left face, right face or neither</td>
<td>1 face (3 sec), delay (3-5 sec) then 2 test faces (1 same, 1 new).</td>
<td>Cropped Other category: house Not cropped/cropped Change in expression Change of view</td>
</tr>
<tr>
<td>Delayed video</td>
<td>2AFC</td>
<td>Delayed matching: 2 parts</td>
<td>1 target face (video or 3 sequential pictures) then 2 cropped faces (1 same, 1 new)</td>
<td>Cropped (hat) Change of view</td>
</tr>
<tr>
<td>Delayed video</td>
<td>2AFC</td>
<td>Matching of facial identity of moving and static faces</td>
<td>1 target face (picture or video) then 2 test faces presented sequentially.</td>
<td>Cropped Other categories: hands, butterflies, chairs</td>
</tr>
<tr>
<td>Delayed</td>
<td>6AFC</td>
<td>Delayed matching</td>
<td>1 target face, mask (2 sec or 8 sec), then 6 test faces.</td>
<td>Cropped Computer-generated faces Change of view Other categories: cars and</td>
</tr>
<tr>
<td>Delayed</td>
<td>4AFC</td>
<td>Delayed matching with change of view</td>
<td>1 face then 4 faces</td>
<td>Cropped Computer-generated faces Change of view Other categories: cars and</td>
</tr>
</tbody>
</table>
| Delayed Working memory capacity | ?AFC | Kaufman Assessment Battery for Children (K-ABC)-faces  
(Kaufman and Kaufman, 1993) (Martinnaud et al., 2015). | 1 or 2 target faces then array of test faces (incl. Target). | torsos  
Change of view  
For children |
|---|---|---|---|---|
| How many faces in working memory | How many faces in working memory | TEMA subtest for memory faces  
(Daini et al., 2014)(Reynolds and Bigler, 1995) | Target faces to recognise from sets of test face with an increasing number of targets and distractors. | Computer-generated faces |
| How many faces in working memory | Face working memory test: how many faces? (with inversion)  
(DeGutis et al., 2014) | 2 target faces sequentially, 3 test faces. Which was one of the target faces? Then increase number of target and test faces | Croped 6 faces in all as stimuli |
| Yes/no | Face working memory load test  
(Jackson et al., 2017) | 4 test faces presented simultaneously (1-3 full faces and 1-3 scrambled faces) then 1 target face. Present initially yes/no | |
| Old/new | Simple | Old / new face recognition test  
(Duchaine et al., 2006; Finzi et al., 2016; Fisher et al., 2017, 2016; Parketny et al., 2015; Susilo et al., 2015; John Towler et al., 2016b, 2016a; Yang et al., 2016; Zhao et al., 2017) | Learning: 10 targets  
Test: 10 targets and 30 novel mixed  
Cropped Other categories vary: Houses, cars, horses |
| Old/new | Simple | Old / new face recognition test: child version  
(Dalrymple et al., 2017, 2014b; Dalrymple and Duchaine, 2016) | Learning: 10 targets  
(children faces)  
Test: 10 targets and 30 novel mixed (children faces)  
Cropped Children stimuli. For children  
Other categories: Flower |
| Old/new | Simple | Prospagnosia test  
(Sakurai et al., 2016) | Learning: 5 targets  
(frontal)  
Test: 15 test faces presented successively  
Part 2: 15 min later, test 3 sets of 5 faces including the 5 target faces.  
Change of view |
| Old/new | Simple | Subtest og Test of memory and learning  
(Reynolds and Bigler 1996) (Canzano et al., 2016) | Recognize of learnt faces previously learned in a canonical perspective |
| Old/new | Simple | Wechsler Memory Scale–Third Edition* (WMS-III) Faces  
(Suárez-González & Crutch, 2016; Tabuas-Pereira et al., 2016) | Learning: 24 target faces sequentially  
Test: 48 faces sequentially (24 targets and 24 distractors)  
Part 2 after 30 repeat test.  
Cropped Change in expression |
| Old/new | Simple | Surprise Recognition test  
(Esins et al., 2016) | Learning: describe emotion in face in video  
(16 videos)  
Test: presentation of targets and novel faces one at a time mixed (static images) |
| Old/new | Simple | Old/new test with dynamic Stimuli (videos) Facial Motion Advantage Test:  
(Disons et al., 2016) | Learning:18 target faces in video  
Test: target faces intermixed with new identities.  
Part 1: target and test faces identical  
Part 2: change hairstyle between target and test |
| Old/new | Simple | Recognising faces learnt from static images and in motion – also inverted session  
(Longmore and Tree, 2013) | Learning: 8 target faces (4 static, 4 moving/video) shown 3 times  
Test phase: videos or static images  
Change of view  
Change of hairstyle |
| Old/new | 2AFC | Warrington recognition memory test:  
(Davies-Thompson et al., 2016; Warrington, 1984) | Learning: 50 faces sequentially  
Test: 50 pairs sequentially |
### Tests of Face Processing in Prosopagnosia

<table>
<thead>
<tr>
<th>Old/new</th>
<th>Format</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>Old/new</td>
<td>3AFC</td>
<td>Cambridge Face Memory test*: 2 stages (Albonico and Barton, 2017; Avidan et al., 2014; Bala et al., 2015; Bate et al., 2015, 2014; Behrmann et al., 2016; Bennetts et al., 2015; Biotti et al., 2015a, 2017; Biotti and Cook, 2016; Anna K Bobak et al., 2017; Burns et al., 2014; Canzano et al., 2016; Cattaneo et al., 2016; C. C. Corrow et al., 2016; Corrow et al., 2018; Dalrymple et al., 2014; Davies-Thompson et al., 2016; DeGutis et al., 2014; Duchaine and Nakayama, 2006b; Esins et al., 2016, 2014; Finzi et al., 2016; Fisher et al., 2017, 2016, Gerlach et al., 2017, 2016; Gerlach and Krumborg, 2014; Gomez et al., 2015; Gray et al., 2017; Hills et al., 2015; Jansari et al., 2015; Johnen et al., 2014; Klargaard et al., 2016; Liu-Shuang et al., 2016; Liu et al., 2016, 2015; Liu and Behrmann, 2014; Lohse et al., 2016; Longmore and Tree, 2013; Luessow et al., 2015; Maguinness and Newell, 2015; Malaspina et al., 2017, 2016; Moroz et al., 2016; Nemeth et al., 2014; O’Brien, 2018; Palermo et al., 2017; Pancaroglu et al., 2016; Parketny et al., 2015; Pizzamiglio et al., 2017; Rezlescu et al., 2014; Rivolta et al., 2017, 2014; Rosenthal et al., 2017; Rubino et al., 2016; Shah et al., 2015a, 2015b; Song et al., 2015; Suárez-González et al., 2016; Susilo et al., 2015, 2013, Tanzer et al., 2016, 2013, John Towler et al., 2016b, 2016a; Towler et al., 2017; Ulrich et al., 2017; Weiss et al., 2016; Xu and Biederman, 2014; Yang et al., 2016) Learning: learn 6 target faces from different views Test: identify target faces from distractors Change of view Cropped</td>
</tr>
<tr>
<td>---------</td>
<td>---------</td>
<td>------------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Old/new</td>
<td>3AFC</td>
<td>Same set-up CFMT</td>
</tr>
<tr>
<td>Old/new</td>
<td>3AFC</td>
<td>Children’s faces, 6 targets to learn, and 3AFC in test phase</td>
</tr>
<tr>
<td>Old/new</td>
<td>2AFC</td>
<td>Uses adult faces, 5 targets, and a 2AFC format</td>
</tr>
<tr>
<td>Old/new</td>
<td>3AFC</td>
<td>CFMT set-up but study stage: 8 short films of people interacting. Test phase image of faces.</td>
</tr>
</tbody>
</table>

Abbreviations: Simultaneous: simultaneous discrimination/matching task; Delayed: delayed discrimination/matching task; Old/new: old/new recognition; AFC: alternative forced choice.
Figure 1 caption:

Figure 1: Visual overview of paradigms assessing whole upright face processing. Paradigms are categorised according to their experimental set-up and according to Bruce & Young’s (1986) stages of processing (perception, recognition and identification stages indicated by arrows in the left margin of the figure).
8. Naming familiar faces

7. Name-to-face matching

6. Face familiarity (familiar faces)

5. Old/new recognition

4. Delayed discrimination and delayed matching

3. Simultaneous discrimination and matching

2. Categorisation and judgement

1. Detection
Appendix C: Article 3
Similar incidences of face and word recognition deficits in patients with left and right posterior stroke

Ro Julia Robotham\textsuperscript{1}, Sheila Kerry\textsuperscript{2}, Grace Rice\textsuperscript{3}, Alex Leff\textsuperscript{2}, Matthew Lambon Ralph\textsuperscript{3} & Randi Starrfelt\textsuperscript{1}

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\textsuperscript{2}Institute of Cognitive Neuroscience, University College London, UK
\textsuperscript{3}MRC Cognition and Brain Sciences Unit, Cambridge University, UK

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\textbf{Acknowledgements:} We would like to thank all the patients and control participants who participated in this study.
Abstract

Face and word processing have for decades been thought to rely on cognitive processes that are highly lateralized, with face and word processing relying more heavily on the right and left hemisphere respectively. Much of this evidence has come from single case studies of patients with pure alexia, a selective reading deficit and patients with pure prosopagnosia, a selective face recognition deficit. As such studies typically involve the assessment of patients with rare symptoms, they constitute a non-representative sample of patients, and may have led to biased conclusions about the lateralisation of the visual processing of faces and words.

The aim of the current study was to investigate the lateralisation of face and word processing in a large sample of patients selected on the basis of lesion location rather than symptom profile. 58 patients with lesions in the areas supplied by the posterior cerebral artery and 31 controls were tested with the WOF, a novel paradigm assessing face, word and object recognition, as well as with the CFMT and a reading-out-loud task. Performance on the face tests and word tests were compared between the patients with unilateral left and unilateral right hemisphere lesions. The data was also examined to identify whether there were patients with patterns of dissociation between faces and words.

For most conditions of the WOF test and for the CFMT, there was no significant difference between mean performance between the left hemisphere and right hemisphere patient groups. At the individual level, the proportion of patients in each group with face recognition deficits and visual word processing deficits, respectively, did not differ significantly. In the reading-out-loud task, the left hemisphere group performed significantly worse than the right hemisphere group. Four patients fulfilled the criteria for a dissociation with impaired visual word processing and preserved face recognition.
It is concluded that face and word processing may be supported by processes that are more bilaterally distributed than previously thought and that word recognition may at least in part be supported by some processes that are not involved in face recognition.
1. Introduction

Face and word processing have for decades been thought to rely on cognitive processes that are relatively independent and highly lateralized, with face processing relying more heavily on the right hemisphere (RH) and word processing relying more heavily on the left hemisphere (LH). Findings from neuropsychological single case studies provided some of the earliest evidence of this (for a review see Farah, 1991). Over the years, there have been reports in the literature of patients with impaired visual face processing and preserved processing of other visual categories as well as reports of patients with impaired written word processing and preserved processing of other visual categories (see Farah, 2004 for a review). Taken together, pure alexia (a selective reading deficits) and pure prosopagnosia (a selective deficit in face recognition) have been considered as evidence of a double dissociation between the visual processing of faces and words and led researchers to conclude that face and word processing rely, at least in part, on independent cognitive processes. While most cases that have been described with pure prosopagnosia have lesions in the RH or bilateral lesions, most cases with pure alexia have LH lesions, suggesting that face and word processing are supported by processes that are strongly lateralized (Barton, 2008; Farah, 1991; Leff, Spitsyna, Plant, & Wise, 2006).

The extent of the independence and lateralization of face and word processing has been the focus of much discussion over the past decade. It has been suggested that many single case studies describing patients with seemingly selective deficits may have suffered from methodological limitations, and that all with “pure” prosopagnosia have word processing deficits and that all patients with “pure” alexia will always have reading deficits if assessed with sensitive enough measures (Behrmann & Plaut, 2013).

In a recent review of studies carrying out in-depth assessment of both face and word processing in participants with acquired prosopagnosia, developmental prosopagnosia, alexia or
dyslexia, we concluded, however, that there is “convincing evidence that reading can be preserved in acquired and developmental prosopagnosia and also evidence (though weaker) that face recognition can be preserved in acquired or developmental dyslexia” (Robotham and Starrfelt, 2017, p. 6). That face and word processing can be selectively affected following brain injury and in developmental disorders constitutes evidence that face and word processing are, at least in part, supported by independent processes. The debate regarding the extent to which the processes supporting face and word processing are independent, is far from settled.

Most neuropsychological studies that have contributed to the debate so far have been investigations of single cases or case series that have selected patients according to their symptom profiles. Typically, these studies involve the assessment of patients with very rare or highly specific symptoms, and therefore represent a very selective and non-representative sample of patients. It is not unlikely that findings from single case studies have led to biased conclusions about the lateralization of face and word processing (Gerlach, Marstrand, Starrfelt, & Gade, 2014).

In the current study, we took a different approach and investigated visual perceptual abilities in a group of patients selected based on their lesion localization rather than symptom profile. We assessed face, word and object processing abilities in a large group of patients with lesions in the areas supplied by the Posterior Cerebral Artery. We compared performance between the group of patients with unilateral LH lesions and unilateral RH lesions in the different visual categories. We also investigated whether face processing deficits were more common following RH lesions than LH lesions, and whether word reading deficits were more common following LH lesions than RH lesions. If indeed face and word processing are supported by highly overlapping and common networks, then we would expect similar incidences of face processing deficits and word processing deficits following LH and RH lesions respectively. If instead face and word processing are supported by processes that are independent and highly lateralized, then we should only expect face
processing deficits following unilateral RH or bilateral lesions, and only expect word reading deficits following unilateral LH or bilateral lesions. Another, more likely scenario, as would be predicted by Behrmann and Plaut's Many-to-Many hypothesis (2013), is that face processing deficits will be seen following lesions in either hemisphere, but that they will be more common and more severe following RH lesions, and that word reading deficits will be seen following lesions in either hemisphere, but will be more common following LH lesions.

To relate our findings to the single case literature, we also investigated whether any patients had patterns of dissociations between reading abilities and face recognition abilities.

2. Method

The data described in the present paper was collected in the context of the Back of the Brain project, a study investigating visual perceptual processes in a group of patients with lesions in the areas supplied by the posterior cerebral artery. At the time of the current study, 63 patients and 33 healthy control participants had been assessed with the same large battery of sensitive lower-level, intermediate and higher-level visual perceptual tests.

In this paper, only data from a sub-set of tests included in the Back of the Brain project are analysed and discussed. We present data from a novel paradigm comparing word, object and face recognition that we designed: the WOF test. As the WOF paradigm is novel, we also present data from a commonly used face recognition test, the Cambridge Face Memory Test (Duchaine and Nakayama, 2006), and a commonly used reading paradigm, a single word reading-out-loud task.
2.1. Patients

Patient recruitment and assessment was carried out at two research centres: The Institute of Cognitive Neuroscience, University College London and the Neuroscience and The Aphasia Research Unit, University of Manchester. Patients in Manchester were recruited from local hospitals and rehabilitations services and patients in London were recruited through Dr. Alexander Leff’s Hemianopia Clinic at the National Hospital for Neurology and Neurosurgery. Patient inclusion and exclusion criteria are described in Table 1. All patients provided informed written consent in accordance with the Declaration of Helsinki.

Table 1: Patient inclusion and exclusion criteria for Back of the Brain project

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 18 years of age</td>
<td>Suspected dementia</td>
</tr>
<tr>
<td>English as first language</td>
<td>Previous damage to the central nervous system</td>
</tr>
<tr>
<td>Stroke located in areas supplied by Posterior Cerebral Artery</td>
<td>History of moderate to severe traumatic brain injury other</td>
</tr>
<tr>
<td>Single embolic or hemorrhagic stroke (multiple lesions accepted if all located in</td>
<td>than stroke</td>
</tr>
<tr>
<td>the PCA)</td>
<td>Known drug or alcohol abuse</td>
</tr>
<tr>
<td>Minimum 9 months post-stroke</td>
<td>Known severe psychiatric disorder prior to stroke or after</td>
</tr>
<tr>
<td></td>
<td>stroke</td>
</tr>
<tr>
<td></td>
<td>Exclusion criteria for MRI scans</td>
</tr>
<tr>
<td></td>
<td>Cortical blindness</td>
</tr>
<tr>
<td></td>
<td>Known eye disorder prior to stroke</td>
</tr>
</tbody>
</table>

The analysis in the current study was based on data from 58 patients as data for 5 patients was missing for one or more of the tests included (tests omitted due to lack of time or patient fatigue). 5 patients had bilateral lesions, 32 patients had unilateral LH lesions and 21 patients had unilateral RH lesions. The median age for the whole patient group was 63 years (mean=61.7; SD=12.6; range: 28–87 years), median years of education was 16 (mean=14.2; SD=2.6; range: 8-19 years) and median number of months since stroke was 23 (mean=39.9; SD=51.6; range: 9-300 months) (see table 2 for patient background information). There was no significant difference in median age, years of education, or months since stroke between the unilateral left lesions and unilateral right lesions groups (see table 3).
Table 2: Patient background information

<table>
<thead>
<tr>
<th>Lesion site</th>
<th>Subject</th>
<th>Age</th>
<th>Years of education</th>
<th>Months since stroke</th>
<th>Visual field deficit</th>
<th>Handedness</th>
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<td>20</td>
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<td>12</td>
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<td>13</td>
<td>96</td>
<td>Left hemianopia</td>
<td>RH (100)</td>
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<td>14</td>
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<td>RH (100)</td>
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<td>Left</td>
<td>PL503</td>
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<td>RH (87,5)</td>
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<td>17</td>
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</tbody>
</table>

Table 3: Median (mean/standard deviations) for the control group and three patient groups, as well as number and frequency of patients in each group with scores below cut-off for each task. Comparisons of median performance and frequency of deficits between left and right hemisphere groups. RTs based on correct responses only.

<table>
<thead>
<tr>
<th></th>
<th>Control group (N=31)</th>
<th>LH group (N=32)</th>
<th>RH group (N=21)</th>
<th>Bilateral group (N=50)</th>
<th>Median score difference: LH vs. RH</th>
<th>Cut-off</th>
<th>Frequency of deficits in LH group</th>
<th>Frequency of deficits in RH group</th>
<th>Frequency of deficits in Bilateral</th>
<th>Difference in frequency: LH vs. RH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>70 (66.6/12)</td>
<td>64.5 (63.2/12)</td>
<td>62 (59.6/14)</td>
<td>65 (61.0/7)</td>
<td>$z = -0.956, p = .339$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Education</strong></td>
<td>16 (14.9/2)</td>
<td>13 (13.9/3)</td>
<td>16 (14.4/3)</td>
<td>17 (15.2/2)</td>
<td>$z = -0.836, p = .403$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Months since stroke</strong></td>
<td>21.5 (39/47)</td>
<td>23 (41/62)</td>
<td>36 (45/30)</td>
<td>$z = -0.392, p = .695$</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Delayed matching</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face (Acc.)</td>
<td>48</td>
<td>44 (43.8/3)</td>
<td>43 (39.7/7.4)</td>
<td>43 (40.5/6.6)</td>
<td>$z = -0.082, p = .935$</td>
<td>37.9</td>
<td>28% (9)</td>
<td>24% (5)</td>
<td>80% (4)</td>
<td>$\chi^2 = 0.121, p = .727$</td>
</tr>
<tr>
<td>Object (Acc.)</td>
<td>48</td>
<td>43 (42.2/3.3)</td>
<td>38.5 (38.7/6.1)</td>
<td>40 (38.8/5.7)</td>
<td>$z = -0.027, p = .978$</td>
<td>35.6</td>
<td>25% (8)</td>
<td>29% (6)</td>
<td>60% (3)</td>
<td>$\chi^2 = 0.083, p = .773$</td>
</tr>
<tr>
<td>Word (Acc.)</td>
<td>48</td>
<td>47 (46.7/1.3)</td>
<td>46 (43.2/6.1)</td>
<td>46 (44.6/3.9)</td>
<td>$z = -0.388, p = .698$</td>
<td>44.1</td>
<td>44% (14)</td>
<td>38% (8)</td>
<td>61% (3)</td>
<td>$\chi^2 = 0.167, p = .683$</td>
</tr>
<tr>
<td>Face (RT)</td>
<td>630 (693/230)</td>
<td>870.5 (955/439)</td>
<td>825 (890/275)</td>
<td>1145 (1034/292)</td>
<td>$z = -0.318, p = .750$</td>
<td>1152</td>
<td>19% (6)</td>
<td>19% (4)</td>
<td>40% (2)</td>
<td>$p = 1.0^b$</td>
</tr>
<tr>
<td>Object (RT)</td>
<td>722 (758/213)</td>
<td>875 (925/311)</td>
<td>849 (879/235)</td>
<td>1108 (1132/136)</td>
<td>$z = -0.518, p = .604$</td>
<td>1183</td>
<td>9% (3)</td>
<td>14% (3)</td>
<td>41% (2)</td>
<td>$p = .671^f$</td>
</tr>
<tr>
<td>Word (RT)</td>
<td>567 (537/145)</td>
<td>793.5 (914/416)</td>
<td>731 (757/240)</td>
<td>953 (983/247)</td>
<td>$z = -1.191, p = .234$</td>
<td>827</td>
<td>44% (14)</td>
<td>38% (8)</td>
<td>80% (4)</td>
<td>$\chi^2 = 0.167, p = .683$</td>
</tr>
<tr>
<td><strong>Surprise recognition</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Face (Acc.)</td>
<td>12</td>
<td>12 (11.4/1)</td>
<td>12 (10.8/2)</td>
<td>7 (6.8/1.1)</td>
<td>$z = -0.081, p = .936$</td>
<td>9.5</td>
<td>22% (7)</td>
<td>19% (4)</td>
<td>100% (5)</td>
<td>$p = 1.0^b$</td>
</tr>
<tr>
<td>Object (Acc.)</td>
<td>12</td>
<td>11 (10.3/1.3)</td>
<td>9 (8.8/1.8)</td>
<td>10 (9.4/2.2)</td>
<td>$z = -1.199, p = .231$</td>
<td>7.8</td>
<td>25% (8)</td>
<td>14% (3)</td>
<td>40% (2)</td>
<td>$p = .494^e$</td>
</tr>
<tr>
<td>Word (Acc.)</td>
<td>12</td>
<td>11 (11.1/1.2)</td>
<td>11 (10.3/2.3)</td>
<td>12 (11.0/0.4)</td>
<td>$z = -0.250, p = .803$</td>
<td>8.6</td>
<td>6% (2)</td>
<td>0% (0)</td>
<td>0% (0)</td>
<td>$p = .512^e$</td>
</tr>
<tr>
<td>Face (RT)</td>
<td>1593 (1877/786)</td>
<td>2379 (3044/1791)</td>
<td>2143 (2413/1194)</td>
<td>2781 (4419/2789)</td>
<td>$z = -1.009, p = .313$</td>
<td>3450</td>
<td>34% (11)</td>
<td>10% (2)</td>
<td>40% (2)</td>
<td>$\chi^2 = 4.230, p = .04^*$</td>
</tr>
<tr>
<td>Object (RT)</td>
<td>1986 (2182/868)</td>
<td>2554.5 (3226/2153)</td>
<td>2225 (2453/789)</td>
<td>3311 (3764/2309)</td>
<td>$z = -0.691, p = .490$</td>
<td>3919</td>
<td>25% (8)</td>
<td>10% (2)</td>
<td>20% (1)</td>
<td>$p = .282^e$</td>
</tr>
<tr>
<td>Word (RT)</td>
<td>1358 (1559/597)</td>
<td>2003.5 (2618/1479)</td>
<td>1690 (2157/1034)</td>
<td>2107 (2965/1999)</td>
<td>$z = -0.709, p = .478$</td>
<td>2754</td>
<td>34% (11)</td>
<td>14% (3)</td>
<td>40% (2)</td>
<td>$\chi^2 = 2.633, p = .105$</td>
</tr>
<tr>
<td><strong>Reading-out-loud</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acc.</td>
<td>75</td>
<td>75 (74.6/0.7)</td>
<td>73 (63.6/18.2)</td>
<td>74 (73.6/1.7)</td>
<td>$z = -2.223, p = .026^*$</td>
<td>73.2</td>
<td>56% (18)</td>
<td>43% (9)</td>
<td>60% (3)</td>
<td>$\chi^2 = .910, p = .340$</td>
</tr>
<tr>
<td>RT</td>
<td>591 (610/101)</td>
<td>1001 (1241/702)</td>
<td>722 (784/222)</td>
<td>1369 (1540/879)</td>
<td>$z = -2.592, p = .010^*$</td>
<td>811.7</td>
<td>63% (20)</td>
<td>33% (7)</td>
<td>80% (4)</td>
<td>$\chi^2 = .4316, p = .038^*$</td>
</tr>
</tbody>
</table>

| CFMT                       |                      |               |                |                        |                                 |        |                               |                                |                                 |                                  |
| Acc.                       | 72                   | 53 (51.5/11.4)| 41 (43.6/12.4) | 47 (44.4/9)            | $z = -0.573, p = .566$         | 34.5   | 22% (7)                      | 29% (6)                      | 60% (3)                         | $\chi^2 = 0.307, p = .579$      |

* $p < 0.05$; ** $p = 0.01$

* Median (mean/SD)

* Cut-off set at 2SD from the control mean, except for the CFMT where cut-off was set at 1.5SD from the mean

* Percent of patients in group with performance below cut-off (number of patients in group with performance below cut-off)

* Calculated using Pearson’s chi-square test. In cases in which expected frequencies were lower than 5 in any cell, Fisher’s exact test was used (†).
2.2. Control participants

Control participants were recruited and assessed at the University of Manchester. Inclusion and exclusion criteria for control participants are described in Table 4. In all, 33 control participants had been recruited and assessed in the Back of the Brain project at the time of the current study. Participants were recruited to match the patients as closely as possible regarding age and education at the group level. The analysis in the current study was based on data from 31 control participants as data for one participant was missing for one of the tests and one participant’s data had to be excluded from the analysis due to problems with data collection on one of the tests. The control group had a median age of 70 (Mean = 66.6 years; SD=11.6; range: 26–84 years) and was significantly older than the patient group when compared using the Mann-Whitney U test ($z = -2.414, p=.016$). The control group’s median years of education was 16 (Mean=14.9; SD=2.2; range: 11-17 years) and did not differ significantly from the patient group when compared using the Mann-Whitney U test ($z = -1.041, p=.298$).

Table 4: Control inclusion and exclusion criteria for Back of the Brain project

<table>
<thead>
<tr>
<th>Inclusion criteria</th>
<th>Exclusion criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>Over 18 years of age</td>
<td>Suspected dementia</td>
</tr>
<tr>
<td>English as first language</td>
<td>History of damage to the central nervous system</td>
</tr>
<tr>
<td></td>
<td>History of moderate to severe traumatic brain injury other than stroke</td>
</tr>
<tr>
<td></td>
<td>Known drug or alcohol abuse</td>
</tr>
<tr>
<td></td>
<td>Known severe psychiatric disorder (current or past)</td>
</tr>
<tr>
<td></td>
<td>Known eye disorder</td>
</tr>
<tr>
<td></td>
<td>Colour blindness</td>
</tr>
<tr>
<td></td>
<td>For controls that are scanned: normal exclusion criteria for MRI scans</td>
</tr>
<tr>
<td></td>
<td>Dyslexia</td>
</tr>
</tbody>
</table>
2.3. Experiments

2.3.1. The WOF test

The Word-Object-Face (WOF) test involves two parts: a delayed matching test and surprise recognition test. The delayed matching part assesses the ability of a participant to build a short-term representation of a stimulus and then match it with the same or a novel stimulus. The surprise recognition part, which follows immediately after, is an old/new recognition paradigm that assesses whether participants later can recognise stimuli that were used in the Delayed Matching part of the test. Words, objects and faces are assessed independently in each part. With its two separate parts, a distinction can be made between recognition problems that are caused by a deficit in storing a representation over longer time from deficits related to problems in creating a short-term representation of a stimulus and matching it with a currently viewed stimulus (Robotham & Starrfelt, in press). The test was run on laptop computers with screen resolution of 1366 x 768 (London: Dell latitude e6430 running on CORE i5 Windows 7 Professional; Manchester: Lenovo T560 running on Windows 7).

Part I: Delayed matching

Material

For each category, four groups of three visually similar stimuli were used (12 uncropped faces, 12 words, and 12 objects). All images were in black and white. The faces were selected from the Radboud Faces Database (Langner et al., 2010). All faces were presented from frontal view with neutral emotional expressions. Two clusters of three male faces were used and two clusters of three female faces were used. The three faces in a cluster had similar hairstyles and similar visual features (see figure 1). For the word stimuli, 4 clusters of three 4-letter words were used. Words in the same group only differed by one letter. In group 1, the first letter changes: hand, band, land; in group 2,
the second letter changes: bind, bond, bend; in group 3, the third letter changes: beat, belt, bent; and in group 4: the fourth letter changes: heal, heat, head. The task can therefore not be performed by focusing on a single letter position. Words were presented in lowercase writing in Aarial font. The object stimuli included four clusters of images representing four different object categories. There were 3 visually similar cars, 3 visually similar butterflies, 3 visually similar boots, and 3 visually similar flowers.

<table>
<thead>
<tr>
<th>A.</th>
<th>B.</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Stimuli" /></td>
<td><img src="image2" alt="Stimuli" /></td>
</tr>
</tbody>
</table>

Figure 1: A. Stimuli used for the delayed matching part of the *WOF* test presented in clusters of three. For different trials, the test stimulus is always a stimulus coming from the same cluster. B. Novel stimuli used for the surprise recognition part of the *WOF* test. Each novel stimuli is presented with the stimulus in the same position in A.
Procedure

The three categories were assessed in separate blocks in the following order: faces, words and objects. A practice session with four practice trials preceded each block. One trial consisted of a target stimulus followed by a test stimulus (see figure 2). In 50% of trials, the test stimulus was the same as the target stimulus, and in 50% of trials, the test stimulus was a different stimulus (coming from the same cluster). Participants were asked to determine whether the test and target stimuli were the same or different. Accuracy (Acc.) and Reaction Times (RT) were recorded. To avoid the task being a change detection task, test images presented were smaller (2/3) or bigger (4/3) than the target images. Each block (category) involved 48 trials. And each cluster of 3 stimuli was assessed through 12 trials (see table 5).

Figure 2: Trial outline for the delayed matching part of the WOF test.
Table 5: Stimulus presentation for trials used for to assess one cluster with e.g. stimulus A, B and C. 50% of same trials and 50% of different trials, test stimulus is smaller than target stimulus in 50% of trials and bigger in 50% of trials. Trials are presented randomly within a block.

<table>
<thead>
<tr>
<th>Trial nr. or a cluster</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
<th>11</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Target stimulus (medium size)</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>A</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td>C</td>
<td>C</td>
</tr>
<tr>
<td>Test stimulus (small or large)</td>
<td>A</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>B</td>
<td>B</td>
<td>C</td>
<td>A</td>
<td>C</td>
<td>C</td>
<td>A</td>
<td>B</td>
</tr>
</tbody>
</table>

Part II: Surprise recognition

Material

The 36 stimuli used in the Delayed Matching part of the test were re-used in this part of the test. 12 novel faces, 12 novel words, and 12 novel objects were also included. The novel stimuli were selected so that they pairwise closely matched the stimuli used in the Delayed Matching part of the test. Each new face was selected to look highly similar to a face used in the Delayed Matching part of the test. Each new word differed from the words previously used with 1 letter only. Each new object was selected to look highly similar to one of the objects previously used (see figure 1). Similarity between images was not formally parametrically controlled.

Procedure

The Surprise Recognition paradigm was run directly after the Delayed Matching paradigm. Categories were again presented in separate blocks and were presented in the same order as in the Delayed Matching paradigm: faces, words and objects. One trial consisted of a novel face and a target face being presented vertically on a screen. In 50% of trials the target was on top and 50% of trials the target was at the bottom of the screen. Participants were asked to determine which of the images they had seen before by pressing the ↑key or the ↓key. A trial ended when the participant
pressed a response key (see figure 4). Acc. and RTs were recorded. Each target face was presented once. There were therefore 12 trials in each block.

Figure 3: Trial outline for old/new recognition paradigm.

2.3.2. Reading-out-loud task

Participants were also assessed with a more commonly used reading task: a single word reading task in which participants were asked to read 3, 5, and 7-letter words out loud one at a time (task described in Starrfelt et al., 2009).

Material

25 3-letter words, 25 5-letter words, and 25 7-letter words were used in the experiment. Words were matched for frequency. Mean frequencies (SD in parentheses) from Kucera and Francis (1967) for 3, 5, and 7 letters words were 99 (85), 101 (95), and 100 (54), respectively. All words were selected from Osswald et al. (2002, Appendix A).
Procedure

Words were presented centrally on a computer screen in 50-point Courier New lower case (white letters on a black background), one at a time. Participants were asked to read the words out loud as quickly and accurately as possible. Reaction times were measured using a voice key attached to serial response box. The experimenter recorded errors. There was a 1 second interval between response and presentation of the next stimulus. Subjects were requested to read the words out loud as quickly and accurately as possible. The initiation of a verbal response terminated the presentation of the words and triggered the voice key. The maximum response time was set at 4000ms. A practice version with 10 trials was administered first. The reading-out-loud task was run on a desktop computer (Windows 7 Enterprise, 64-bit operating system, 24 Inch BenQ XL2430T screen with a resolution of 1920x1080).

2.3.3. Cambridge Face Memory Test

Participants were also tested with the Cambridge Face Memory Test (CFMT) that assesses face recognition and is commonly used to diagnose prosopagnosia (Duchaine and Nakayama, 2006). The test starts with a learning phase, in which participants must learn six target identities, one at a time. For each face the following learning procedure is carried out. The target is presented sequentially from three different views (left 1/3 profile, a frontal view, and a right 1/3 profile). This is followed by immediate recognition, where the participants must find the target identity amongst two distractor faces. In total, there are three immediate recognition trials for each target identity. In this first block, the target item is identical in learning section and in the immediate recognition. In the second block, all six target faces are presented simultaneously in frontal view for 20 seconds, and participants are instructed to memorize the faces. Then, participants must identify novel images of
target faces that are presented alongside two distractors. In the third block, novel images with added visual noise are used. This test was run on the same laptops used for the WOF experiment.

2.4. Data analysis

The data analysis performed in this study was similar to the data analysis performed in Gerlach et al. (2014). Data analysis was first done at the group level and then at the individual level. Accuracy scores and mean reaction times for correct trials were calculated for each patient for all tests (except for the CFMT, for which the outcome measure is accuracy only). Mean scores and median scores were then calculated for the four groups for all tests (controls, left unilateral lesion, right unilateral lesion, and bilateral lesion). As the primary focus of this paper concerns the respective contributions of the left and the right hemispheres to visual perception, mean scores of the LH patient group were compared to mean scores of the RH patient group on each test. The non-parametric Mann-Whitney procedure was used as the comparisons were based on small sample sizes (LH: N=32; RH: N=21) and the data for most conditions was not normally distributed.

Data was also examined at the individual level. The frequency of patients with unilateral left, unilateral right, and bilateral lesions, who performed below cut-off on each test, was calculated (cut-off set at 2 SD below control mean for all tests, except for CFMT where cut-off was set at 1.5 SD). The incidences of deficits between the LH group and RH group for the different conditions were then compared using Pearson’s chi-square test (in conditions in which the expected frequencies were lower than 5 in any cell, the Fisher’s exact test was used instead). As there can be immense variability in performance levels in individual stroke patients, comparisons of levels of incidence between groups was likely to be more informative than the comparisons of group means.
The data was also analysed to identify if any patients with unilateral (LH or RH) lesions showed dissociations between face recognition and reading. This was done in the following ways: 

1) Patients with an accuracy score below cut-off on the reading-out-loud task and with scores within the normal range in the CFMT (as well as in all face conditions of the WOF test) were identified. Patients with scores below cut-off on the CFMT and with accuracy scores within the normal range in the reading-out-loud task (as well as in all word conditions of the WOF test) were also identified.

2) Data from the patients identified in step one were analysed by the programme dissoscbsayes_ES_CP (Crawford, Garthwaite, & Ryan, 2011) to evaluate whether the difference in scores on the CFMT and the reading-out-loud test fulfilled Crawford and Garthwaite's (2007) criteria for a classical or strong dissociation (the programme uses a combined Bayesian/frequentist criteria for a dissociation).

3) Studies commonly compare performance on the CFMT and a reading-out-loud test, as done above. However, as the tests have different task demands (3 alternative forced-choice versus naming), dissociations are difficult to interpret. Therefore, for patients who were shown to fulfil criteria for a classical dissociation in step 2, an extra analysis was carried out to ensure that the dissociation wasn’t caused by differences in experimental design but instead related to category-specific deficits. For these patients, differences between accuracy scores on the face and word condition (with similar task demands) in the delayed matching part of the WOF experiment were analysed to see if any patients showed a classical dissociation between these conditions (Crawford & Garthwaite, 2007), when applying Bayesian criteria (Crawford et al., 2011).
3. Results

3.1. WOF test

Group mean and median performance (Acc. and RT) for the Delayed Matching and Surprise Recognition parts of the test are presented in Figure 5. For the Delayed Matching part of the test, mean performance (Acc. and RT) for the control group suggest that the object condition was the most difficult, followed by the face condition and then by the word condition. The object condition also yielded the worst mean acc. and RT for the Surprise Recognition part of the test. Mean accuracy was lower for the word condition than the face condition, whereas the opposite pattern was observed for mean RTs.

At the group level, performance for all three patient groups was lower (lower mean acc., higher mean RT) than controls across all conditions (figure 5). Accuracy and RT profiles for the unilateral LH and unilateral RH groups were similar to controls for both parts of the test. The bilateral patients had a slightly different profile at the group level, with a particularly low mean accuracy on the face condition in both parts of the test, and a particularly high RT on the face condition in the Surprise Recognition part of the test. Direct comparisons showed no significant differences in median performance between the LH and RH groups in any of the conditions of the Delayed Matching and Surprise Recognition test (see Table 3).
Figure 5: Group means for delayed matching Acc. (A.), delayed matching RT (B.), surprise recognition Acc. (C.) and surprise recognition RT (D.)
At the individual level, there was a high incidence of abnormal performance in the face conditions of the test (Table 3). Similar incidences of scores below cut-off were observed in the face conditions for patients with left and right hemisphere lesions (incidences of scores below cut-off varied between 19% and 28% in the Delayed Matching and Surprise Recognition parts of the test). While the frequency of patients with abnormally high RTs were similar between the LH and RH groups in the Delayed Matching part of the test, there were significantly more patients in the LH group with abnormally high RTs in the Surprise Recognition part of the test.

A high proportion of patients scored below cut-off in the word condition of the Delayed Matching part of the test, whereas the proportion of patients scoring below cut-off on the word condition of the Surprise Recognition part of the test was much lower. The frequency of patients with LH and RH lesions performing below cut-off in the word conditions of the test were highly similar (Delayed Matching frequency of abnormal word recognition acc.: 38% in RH and 44% in LH and frequency of abnormal RT: 38% in RH and 44% in LH; Surprise Recognition frequency of abnormal acc.: 0% in RH and 6% in LH and frequency of abnormal RT: 14% in RH and 34% in LH) and were not found to be significantly different.

There was no significant difference in incidence of performance below cut-off for the LH group and RH group in the object condition of the Delayed Matching and Surprise Recognition part of the test.

The bilateral group had a higher proportion of patients with deficits than the unilateral LH and RH groups across most conditions, and had a particularly high proportion of patients with abnormal scores in the face conditions of the experiment (80% of bilateral patients scored below cut-off in the Delayed Matching part of the test and 100% scored below cut-off in the Surprise Recognition part of the test).
3.2. Reading-out-loud task

Results for this experiment are also presented in table 3. We analysed overall accuracy as well as correct RTs. Word length effects (WLE) were not calculated as the WLE as a measure is not directly comparable to the Acc. and RT measures acquired for the other visual categories.

The bilateral patient group performed worst as a group, and patients with LH lesions performed significantly worse (Acc. and RT) as a group than patients with RH lesions. At the individual level, 60% of bilateral patients, 56% of patients with LH lesions and 43% of the RH patients had an accuracy below cut-off. The frequency of abnormal scores did not differ significantly between groups. There was, however, a significant difference in frequency of deficits in RTs between LH and RH patients on the reading-out-loud test (63% of LH patients vs. 33% of RH patients had abnormally high RTs).

3.3. Cambridge Face Memory Test

Performance of the control group on the CFMT in the current study (mean=51.5, SD=11.4) was similar to the performance of elderly participants in a large normative study (performance for 61 participants aged 50-81: mean=52, SD=11.2; Wilmer et al., 2012).

The bilateral patient group had the lowest mean accuracy score on the CFMT. There was no significant difference between the median score of the LH group and the RH group. For the CFMT, the cut-off for impaired performance was set at 1.5SD below control mean (34.5). Setting the cut-off at 2SD below control mean would have been problematic as it would have been close to chance level (CFMT is a three-alternative forced choice paradigm, so chance performance is at 33% correct – corresponding to an accuracy of 24). While deficits were most common in bilateral patients
Face and Word Recognition Deficits in Patients with Left and Right Posterior Stroke

(60%), a similar proportion of patients with unilateral LH (21.9%) and unilateral RH (28.6%) patients scored below cut-off on this task.

3.4. Dissociations between face recognition and written word processing

Six patients with lesions in the LH and five patients with RH lesions scored below cut-off (Acc.) on the *reading-out-loud task*, while performing within the normal range on the *CFMT* and in all face conditions of the *WOF* test (see appendix for individual patient data). Five of these LH patients and two of these RH patients fulfilled the criteria for a putative classical dissociation between the *CFMT* and the *Reading-out-loud* task (Crawford & Garthwaite, 2007) when applying Bayesian criteria (Crawford et al., 2011) (see Table 6). For these patients, an extra analysis we carried out to ensure that the dissociation between face and word processing was not caused by differences in experimental design between the *CFMT* (3 alternative forced-choice) and the *reading-out-loud task* (naming). Accuracy scores of the face and word condition in the delayed matching part of the *WOF* experiment were compared. Three of the LH patients and one of the RH patients also fulfilled the criteria for a putative classical dissociation between these conditions (Crawford & Garthwaite, 2007), when applying Bayesian criteria (Crawford et al., 2011) (see Table 6).

Two patients with RH lesions (no LH lesion patients) scored below cut-off on the *CFMT*, while performing within the normal range on the *reading-out-loud task* (Acc.) and in all word conditions of the *WOF* test. Neither of these RH patients fulfilled the criteria for a classical dissociation (Crawford & Garthwaite, 2007) when applying Bayesian criteria (Crawford et al., 2011) (see Table 7). It is notable, that their RTs were also within the normal range on the *reading-out-loud task*, providing additional evidence that their reading was unimpaired.
Table 6: Tests for dissociations for patients with abnormal score on reading-out-loud test but scores within control range on the CFMT using program: DissocsBayes_ES_CP.exe (Crawford & Garthwaite, 2007)

<table>
<thead>
<tr>
<th>Patient</th>
<th>CFMT</th>
<th>Reading (Acc.)</th>
<th>Z_{DCC}</th>
<th>95% CI</th>
<th>DM Faces (Acc.)</th>
<th>DM Words (Acc.)</th>
<th>Z_{DCC}</th>
<th>95% CI</th>
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<td></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>PL508</td>
<td>54</td>
<td>70</td>
<td>4.48**</td>
<td>3.1 to 5.9</td>
<td>45</td>
<td>46</td>
<td>0.9</td>
<td>0.5 to 1.4</td>
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<tr>
<td>PL531</td>
<td>48</td>
<td>29</td>
<td>42.71**</td>
<td>29.6 to 56.4</td>
<td>40</td>
<td>41</td>
<td>3.1**</td>
<td>1.9 to 4.3</td>
</tr>
<tr>
<td>PM002</td>
<td>41</td>
<td>35</td>
<td>36.7**</td>
<td>25.3 to 48.5</td>
<td>45</td>
<td>41</td>
<td>4.8**</td>
<td>3.3 to 6.2</td>
</tr>
<tr>
<td>PM004</td>
<td>42</td>
<td>24</td>
<td>47.1**</td>
<td>32.6 to 62.2</td>
<td>44</td>
<td>39</td>
<td>6.0**</td>
<td>4.1 to 7.8</td>
</tr>
<tr>
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<td>63</td>
<td>69</td>
<td>5.9**</td>
<td>4.2 to 7.7</td>
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<td>48</td>
<td>-0.3</td>
<td>-0.7 to 0.2</td>
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<tr>
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<td>73</td>
<td>1.9</td>
<td>1.3 to 2.6</td>
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<tr>
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<td>73</td>
<td>1.8</td>
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<tr>
<td>PL520</td>
<td>49</td>
<td>69</td>
<td>5.1**</td>
<td>3.4 to 6.8</td>
<td>47</td>
<td>44</td>
<td>3.1**</td>
<td>2.2 to 4.0</td>
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<tr>
<td>PL539</td>
<td>49</td>
<td>73</td>
<td>1.4</td>
<td>0.8 to 1.9</td>
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<td>0.3</td>
<td>-0.1 to 0.6</td>
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</tbody>
</table>

*p < 0.05; **p < 0.01 (Two-tailed). Correlation between control scores on CFMT and Reading-out-loud (Acc.) = -0.12, Correlation between control scores on DM faces (Acc.) and DM words (Acc.) = 0.5.

Table 7: Test for dissociations for patients with abnormal CFMT score but normal score on reading (3,5,7 words) using program: DissocsBayes_ES_CP.exe (Crawford & Garthwaite, 2007)

<table>
<thead>
<tr>
<th>Patient</th>
<th>CFMT</th>
<th>Reading (Acc.)</th>
<th>Z_{DCC}</th>
<th>95% CI</th>
</tr>
</thead>
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<td></td>
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<td></td>
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<tr>
<td>PL535</td>
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<td>75</td>
<td>-1.4</td>
<td>-1.9 to -0.9</td>
</tr>
<tr>
<td>PL525</td>
<td>33</td>
<td>75</td>
<td>-1.5</td>
<td>-2.0 to -0.9</td>
</tr>
</tbody>
</table>

*p < 0.05; **p < 0.01 (Two-tailed). Correlation between control performance CFMT and Reading-out-loud (Acc.) = -0.12

3.5. Summary of results

On the newly developed WOF task, there was no significant difference between median performance of the LH lesion group and the RH lesion group in any conditions. The LH and RH lesion groups performed on average worse than the control group but had a similar performance profile across conditions.

At the individual level of analysis, a substantial proportion of patients had abnormal performance (Acc. and RT) in the face condition of the Delayed Matching and Surprise Recognition
sections of the test. Abnormal performance (Acc. and RT) was also common in the word condition of the *Delayed Matching* section of the test, but was less common in the word condition of the *Surprise Recognition* part of the test.

Abnormal performance in the face conditions of the *Delayed Matching* and *Surprise Recognition* parts of the test were as common in the LH patient group as in the RH patient group. Similar results came from the *CFMT*, a commonly used test for assessing face recognition. 29% of RH patients scored below cut-off and so did 22% of LH patients.

The proportion of patients with LH and RH lesions with abnormal scores in the word conditions of the test were also highly similar. While abnormal RTs in the word conditions of the test were more common in the LH group than in the RH group, the difference in frequency was not found to be significant. Frequency of patients with abnormal accuracy scores was also similar between groups on a *reading-out-loud* test that is commonly used to assess reading abilities. However, significantly more patients with LH lesions had abnormal RTs on the *reading-out-loud* test than RH patients.

The bilateral group performed worse than the LH and RH groups on almost all measurements and there was a higher proportion of patients with bilateral lesions than with LH or RH lesions performing outside the expected range in almost all conditions.

4. Discussion

Single case studies from neuropsychology have contributed strongly to the idea that face and word processing rely on processes that are largely independent and highly lateralised. However, as such studies commonly base their investigations on patients with rare and unusual patterns of deficits, the conclusions drawn from these studies may be biased. An approach in which patients are selected according to lesion localisation rather than symptom profile may provide useful additional
information that could lead to a richer and more nuanced understanding of the processes underlying face and word processing.

In this study, a large group of patients were recruited based on lesion localisation (stroke in the region supplied by the Posterior Cerebral Artery). Patients and controls were assessed with the WOF test, a novel paradigm assessing face, object and word recognition abilities, as well as the Cambridge Face Memory Test and a single word reading-out-loud test. In all, 32 patients with unilateral LH lesions, 21 patients with unilateral RH lesions and 5 patients with bilateral lesions, as well as 31 control participants, were tested.

The WOF test enables the assessment of word, object and face recognition using the same experimental paradigm, thereby ensuring that differences in performance between the different visual categories are not caused by task-dependent factors. The test includes a delayed matching part and an old/new recognition part, which offers the additional advantage of enabling the distinction between problems that are caused by a deficit in storing a representation over longer time from problems in creating a short-term representation of a stimulus and matching it with a currently viewed stimulus. A core finding from the WOF test was that there were a significant number of LH patients with abnormal performance in the face conditions and a significant number of RH patients with abnormal performance in the word conditions of the experiment. Interestingly, the frequency of face recognition deficits was similar in the LH and RH patient groups, as was the frequency of word recognition deficits. These results provide evidence that face recognition and word recognition may be supported by processes that are more bilaterally distributed than what would be predicted based exclusively on the single case literature. The Cambridge Face Memory Test gave similar results, which suggests that the face recognition findings were not specific for our novel WOF paradigm.
While there was no significant difference in proportions of LH and RH patients with abnormal performance in the word conditions of the *WOF* task, there was a significant difference at the group level in the *reading-out-loud task*. A significantly higher proportion of patients with LH lesions than RH lesions showed abnormal RTs on the *reading-out-loud test* (no significant difference for Acc.). The discrepancy of results between the tasks could be due to task-related differences. While the WOF test assesses word recognition (match a stimulus with a previously stored representation), the *reading-out-loud* experiment assesses word identification (retrieval of stored knowledge related to a word and verbal mobilisation of the word) (Robotham & Starrfelt, in press).

The main limitation from the current study is that the patients included are not representative of all patients with PCA stroke. Due to the recruitment procedure adopted, severity of deficits and symptomatology will have influenced whether a participant was included in the *Back of the Brain* project. Therefore, incidences of deficits reported here should not be considered indicative of incidences of deficits in all patients with PCA stroke. However, as the same recruitment procedure was used for LH and RH patients, the comparisons made in the current study are likely to be informative, nevertheless.

There are a few examples in the literature of studies investigating face recognition and word recognition that have adopted lesion-based approaches similar to the approach used in the current study. Gerlach et al. (2014) investigated a wide range of visual perceptual abilities in 31 patients with stroke in the Posterior Cerebral Artery and reported, just like in the current study, that many patients with LH lesions also had face recognition deficits and that many patients with RH lesions also had reading deficits. The main limitation of that study is that the tests included crude clinical measures and that patients were tested within six weeks of the stroke. On the other hand, that such crude measures could reveal meaningful deficits in both reading and face recognition in both groups
of patients indeed suggests that they had true deficits with both categories. Martinaud et al. (2012) also tested 31 patients with posterior cerebral artery stroke and used more sensitive tests of face, object and word processing. At the group level, there were no interactions between lesion side and category except for one face processing task in which RH patients performed worse than LH patients. At the individual, abnormal accuracy on the word reading test was only observed in patients with LH lesions (3/15 patients with LH lesions and in 0/13 patients with RH lesions, see Supplementary table 3; Martinaud et al., 2012). These findings that stands in contrast to the findings from the current study, that showed that abnormal accuracy on the reading-out-loud test was also common in following RH lesions. Martinaud et al. (2012) also report abnormal face processing scores following LH lesions, but found, in contrast to our study, that these were more common following RH lesions (2/15 patients with LH lesions and 6/13 patients with RH lesions, see Supplementary table 2; Martinaud et al., 2012).

As mentioned in the introduction, findings from the single case literature provide evidence that visual word processing can be selectively impaired following brain injury and also evidence (though weaker) that visual face processing can be selectively impaired following brain injury (Robotham & Starrfelt, 2017), suggesting that face and word processing may at least in part be supported by independent processes. In our sample, we identified three patients with LH lesions and one patient with RH lesions who had impaired reading (reading-out-loud and word recognition) but preserved face recognition and who fulfilled the criteria for a classical dissociation, providing additional evidence that the visual processing of written words can be selectively impaired (preserved face recognition) following stroke and evidence that word processing may at least in part be supported by some independent processes. Interestingly, there is stronger evidence in the literature for dissociations going in the opposite direction (e.g. Hills et al., 2015, for a study
reporting preserved reading in acquired prosopagnosia and see Robotham and Starrfelt, 2017, for an overview of studies investigating dissociations between reading and face processing).

An interesting supplementary result from the current study is the large variation in the scores of controls on the CFMT. The cut-off based on the sample from this study was placed at 34.5 (1.5 SDs below the control mean), which is worryingly close to chance performance of 24 out of a max of 72 (three alternative forced-choice). The results presented here are similar to those presented in (Wilmer et al., 2012), suggesting that the finding of a large variability in performance in elderly controls, is not specific to our sample. These findings question the applicability of the CFMT for identifying face recognition deficits in elderly participants and warrants further attention.

Three scenarios were lined up in the introduction: 1) Similar incidences of face processing deficits and word processing deficits following LH and RH lesions respectively, providing evidence that face and word processing are supported by highly overlapping and common networks. 2) Face processing deficits are only observed following RH lesions or bilateral lesions and word reading deficits are only seen following LH or bilateral lesions, providing evidence that face and word processing are supported by processes that are fully independent and lateralized. 3) Face processing deficits are observed following lesions in either hemisphere but are more common and more severe following RH lesions, and word reading deficits are observed following lesions in either hemisphere but are more common following LH lesions, providing evidence that face and word processing are supported by processes that are largely distributed and overlapping, but that are somewhat lateralised.

This study that investigated profiles of impairment in a large group of patients based on their lesion localisation and gave the surprising results that LH and RH patients performed highly similarly as groups on face and word processing tasks. On most tests the incidences of deficits were
also highly similar between LH and RH patient groups. One test stood out: namely, the reading-out-
loud test involving verbal production, on which LH patients performed worse than RH patients. We
also found cases with impaired reading but preserved face recognition. Taken together, the findings
from this study do not match scenario 2, but instead point towards a combination of scenario 1 and
3. The findings suggest that face recognition and word recognition are supported by processes that
are highly overlapping and bilaterally distributed, but that word recognition is at least in part
supported by some processes that are not involved in face recognition.
References


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Appendix: Individual patient scores and mean RTs for the WOF test, the CFMT and the Reading-out-loud test and control mean (SD) for reference.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Lesion</th>
<th>WOF test⁴</th>
<th>Delayed matching</th>
<th>Surprise recognition</th>
<th>CFMT⁵</th>
<th>Reading (3.5, 7 words)⁶</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Acc.</td>
<td>Mean RT (correct)</td>
<td>Acc.</td>
<td>Mean RT (correct)</td>
<td>Acc.</td>
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<tr>
<td>Controls (N=31)</td>
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<tr>
<td>Lesion</td>
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<td>Objects</td>
<td>Words</td>
<td>Faces</td>
<td>Objects</td>
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<td>953*</td>
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</table>

*Scores below cut-off
Cut-off set at 1.5 SD from control mean
Cut-off set at 2 SD from control mean
A Danish Version Of The Oxford Cognitive Screen: A Stroke-Specific Screening Test Providing A Useful Alternative To Currently Used Tools

Short title: A Danish Version of The Oxford Cognitive Screen

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Abstract

Objective: Cognitive deficits are common following stroke and have negative consequences on quality of life, chances of returning to work and likelihood of developing depressive symptoms. It is important that cognitive deficits be identified in order to provide appropriate interventions and care, however, cognitive deficits can easily be overseen in a clinical context if they are not assessed directly. Dementia screening tools are often used to screen for cognitive deficits following stroke, despite their limitations in this context. The Montreal Cognitive Assessment (MoCA) is commonly used for this purpose in Denmark, however, there are no Danish norms available for the test. The aim of the current study was to collect reference material for a Danish version of the Oxford Cognitive Screen (OCS), a screening tool that is designed to identify clinically important cognitive deficits following stroke, and to evaluate cut-offs currently used in Denmark for the MoCA.

Method: A sample of healthy Danish participants aged 36-89 and with 4-22 years of education were assessed using the Danish version of the OCS and MoCA. Mean performance and 5th percentile cut-offs were calculated for OCS sub-tests and compared to other international normative studies. MoCA 5th percentile cut-offs were compared to the cut-off currently used in Denmark.

Results: Cut-offs and mean performance on the OCS subtests were similar to those provided by previous European OCS studies. Results on the MoCA suggest that the MoCA cut-off currently used in Denmark may be inappropriate.

Conclusion: The reference material presented here is an important prerequisite for using the Danish version of the OCS and the MoCA. Results from an international study report that the OCS is more sensitive than the MoCA for identifying cognitive deficits following stroke. A
validation study in a Danish stroke sample is still needed to evaluate the clinical use of the Danish version of the tool.

**Keywords**: Oxford Cognitive Screen; cognitive assessment; cognitive screening; stroke; Montreal Cognitive Assessment; norms
Introduction

In Denmark, approximately 15000 people suffer a stroke annually (Sundhedsstyrelsen, 2015). International incidence reports of cognitive deficits following stroke vary greatly in the literature. In a study assessing patients approximately two weeks after injury with a neuropsychological test battery, 91.5% of patients had a deficit in at least one cognitive domain (Jaillard, Naegele, Trabucco-Miguel, LeBas, & Hommel, 2009). At three months post-stroke, reported rates of post stroke dementia vary between studies from 6% to more than 30% (Pendlebury & Rothwell, 2009). Differences in methodological approaches, demographic and stroke characteristics are likely to contribute to the large variation in these estimates. Some of the most common cognitive deficits seen following stroke are neglect, aphasia, apraxia as well as impairments in executive functions, memory, attention and visual perception/construction (Jaillard et al., 2009; Leśniak, Bak, Czepiel, Seniów, & Czonkowska, 2008; Nys et al., 2007; Rasquin et al., 2004). These may not be picked up by commonly used cognitive screening tools, potentially contributing to lower incidence reports.

Cognitive deficits following stroke are known to have negative consequences on quality of life, chances of returning to work and likelihood of developing depressive symptoms (Hommel, Miguel, Naegele, Gonnet, & Jaillard, 2009; Nichols-Larsen, Clark, Zeringue, Greenspan, & Blanton, 2005; Nys et al., 2006; Pedersen, Jorgensen, Nakayama, Raaschou, & Olsen, 1996). The adverse effects on long-term functional outcome (Patel, Coshall, Rudd, & Wolfe, 2002; Tatemichi et al., 1994) lead to higher caregiver burden and higher societal costs. From a clinical point of view, identifying cognitive deficits is important in order to provide appropriate interventions and care. As cognitive deficits can be discrete and can easily be overseen in clinical contexts, screening can be useful.
There is no international gold standard for screening cognitive deficits following stroke. Assessment approaches vary from the use of very short screening tools, not originally designed for a stroke population, to the use of combinations of different neuropsychological tests of specific cognitive functions that are very time-consuming. Lengthy testing is rarely possible in the acute phase, as patients suffer from high levels of fatigue, and because of the financial costs it entails. Internationally, the short screening tools that are most widely used in stroke patients are the Mini Mental Status Examination (MMSE; Folstein et al., 1975) and the Montreal Cognitive Assessment (MoCA; Nasreddine et al., 2005). However, these tools are designed for dementia screening and not for assessment of cognitive deficits following stroke. The measures are designed to mirror cognitive profiles typically seen in dementia, and therefore focus highly on the assessment of memory, which is less prominent following stroke. In addition, they do not explicitly assess some of the core deficits that are more common after stroke such as neglect, apraxia and visual field deficits. Also, the evaluation of individual cognitive domains is not possible with the MMSE and the MoCA. Also, it has been reported, that symptoms such as aphasia and neglect, that are common following stroke, can contaminate performance throughout these tests (Pasi, Salvadori, Poggesi, Inzitari, & Pantoni, 2013).

According to the Danish Stroke Society (Dansk Selskab for Apopleksi), cognitive functions should be assessed at the first evaluation made by the occupational therapist or physiotherapist (Dansk Selskab for Apopleksi, 2013). Despite the limitations described above, MoCA is often used in this context. There is a recognised need for a screening tool that is specifically designed to identify clinically important cognitive deficits following stroke. The Oxford Cognitive Screen (OCS; Demeyere et al., 2015) was developed specifically for this purpose and may provide a useful alternative for obtaining more consistent screening
procedures of cognitive deficits following stroke in Denmark. The OCS was designed to maximise patient inclusion and can be used in the relatively acute phase after stroke (depending on severity, as early as same day, or as soon as the patient is able to interact for the duration of the test). It enables assessment of cognitive functions commonly affected by stroke and as administration time is only 15-20 minutes, it can be completed by patients suffering from severe fatigue. In contrast to screening tools like the MMSE or MoCA, the OCS is based on neuropsychological principles and thereby evaluates post-stroke cognition at the level of cognitive domains (Attention and Executive function, Language, Memory, Number processing, and Praxis). The tool can be used at bedside and requires the use of only one hand (patient with hemiparesis can thus participate). It also provides a “visual snapshot” (Figure 1) of the cognitive profile, that can be used to facilitate communication of results with health care professionals, the patient and caregivers. These considerations and features make the OCS an attractive tool for cognitive screening of stroke patients in the acute phase (Demeyere et al., 2016, 2015). In the original British validation study, evidence of content validity was provided and the test was shown to have a high level of specificity (Demeyere et al., 2015). An Italian study has shown that the OCS is more sensitive to cognitive deficits than the MMSE (Mancuso et al., 2018). Normative data are available for the original English version (Demeyere et al., 2015), a Cantonese version (Kong et al., 2016), an Italian version (Mancuso et al., 2016), and a Russian version (Shendyapina et al, in press). The test is currently being translated into various other languages.

[Figure 1 about here]

The main aim of the current study was to collect reference material for the Danish version of the Oxford Cognitive Screen. Additionally, the study aimed to evaluate the appropriateness of cut-offs currently used in Denmark for the MoCA, a test that is commonly
used to screen for cognitive deficits following stroke in Denmark. The OCS was translated to Danish and a group of healthy Danish participants were assessed with the tool. Participants were also assessed with the MoCA. Cut-offs were calculated for both tests. On the basis of the results we argue that the OCS is likely to provide a useful alternative when screening for cognitive deficits following stroke in a Danish context.

**Method**

**Materials**

The OCS includes the following material: A manual, a stimulus book, a scoring sheet and stimulus material. It consists of in all 10 sub-tests that enable assessment of five cognitive domains: Attention and Executive Function, Language, Memory, Number processing, and Praxis. Non-verbal stimuli are used when possible in order to minimize the influence of aphasia on tasks that are not designed to assess language. Patients with aphasia are also given the option to respond in writing, or by pointing at multiple-choice answers. In tasks that are not intended to assess neglect, stimuli are presented centrally along the vertical midline of the stimulus booklet. This reduces the influence of neglect on performance in tasks that are not aimed at assessing neglect. The ten sub-tests are described in detail in table 1.

[Table 1 about here]

[Figure 2 about here]

**Participants**

Ethical approval was given by the Local Ethics Committee at the Department of Psychology at the University of Copenhagen. The Department of Psychology at the University of
Copenhagen and the Neurological department at Aalborg University Hospital participated in recruitment and data collection. A wide range of recruitment strategies were applied to ensure a broad range of level of education and age of participants. Participants were recruited by advertising, by staff announcements, and by contacting hospital and university volunteers. Exclusion criteria included previous or ongoing neurological disorder, visual field deficit revealed during assessment, and not having Danish as first language. Written informed consent was obtained from the participants before the study. A gift card worth 150 Danish Kroner was given to each participant as compensation. 93 participants enrolled for the study between September 2017 and April 2018. Two participants were excluded. One participant was excluded because of possible cognitive decline (clinical signs of cognitive decline as well as a z score of -5.5 on the MoCA when adjusted for age, education and sex (Borland et al., 2017)). One participant was excluded because the assessor was informed, post-assessment, that he/she had epilepsy (despite stating prior to testing that he/she had no neurological disorders). The final dataset included 91 participants between 36 and 87 years of age and with 4 to 23 years of education (see table 2).

**[Table 2 about here]**

**Procedure**

**Translation Process**

The translation from English to Danish was carried out following the translation licence agreements with Oxford University Innovations, and specifically following the best practice guidelines provided in “Translation and Linguistic Validation Process” provided by Associate Professor Nele Demeyere, one of the developers of OCS. First, the British version was analysed to pinpoint possible items needing cultural adaptation/reconciliation. Only one task
required cultural adaptation: the sentence reading task. A Danish sentence was developed that fulfilled all the necessary requirements in agreement with Associate Professor Nele Demeyere. The translation to Danish was made independently by two Danish neuropsychologists. The Danish neuropsychologists together with the project manager then agreed on a merged Danish version. This version was then translated back to English by a third neuropsychologist (Danish speaking with English as first language). The back-translation was reviewed by the project manager together with the original OCS developers, and minor adjustments were made after agreement with the UK developers. The test was piloted on five Danish stroke patients, which lead to the reading sentence being adjusted. The translated version is available for use through Oxford University Innovations, who hold the copyright. The licences are free for use in publicly funded clinical practice and research. Please see links to licence request pages on www.ocs-test.org.

Assessment

Participants were assessed with the Danish version of the OCS (OCS-Dansk) followed by a Danish version (translation by Kirsten Abelskov) of the 7.0 version of the MoCA (Nasreddine et al., 2005) in the same session.

Results

Oxford Cognitive Screen

Data on the OCS was collected from 91 participants, however, due to assessor omissions, only 89 participants performed the praxis sub-test. Mean scores for the whole sample (n=91), as well as for the different age and education groups are presented in table 3. As age and low education have previously been shown to be associated with lower scores on subtests of OCS (Mancuso et al., 2016), the influence of age and education on OCS scores in our sample was
assessed using Pearson’s correlation (one-tailed tests). Age correlated significantly with the following scores: Reading scores (Acc.) ($r (89) = -0.210, p < .05$), Broken Hearts scores (RT) ($r (89) = 0.504, p < .01$), Praxis scores (Acc.) ($r (87) = -0.226, p < .05$), Recognition scores (Acc.) ($r (89) = -0.191, p < .05$), as well as Triangle scores (Acc.) ($r (89) = -0.192, p < .05$) and Alternating scores (Acc.) ($r (89) = 0.316, p < .01$) of the executive test. Correlations followed the expected direction for these subtests, with exception of the alternating accuracy scores of the executive test, for which performance improved with age. Higher education was associated with better Circle scores (Acc.) ($r (89) = 0.191, p < .05$) and Alternating scores (Acc.) ($r (89) = 0.187, p < .05$), but surprisingly, with worse Reading scores (Acc.) ($r (89) = -0.184, p < .05$).

For most subtests, raw scores did not follow normal distributions and scores had a very narrow range. Cut-offs for impairment were therefore determined using direct percentile conversions (Excel 2010 simple percentile function). Cut-offs were set at the 5th percentile (and 95th percentile for broken hearts subtest and executive task) and are provided in table 4.

**Discussion: OCS Results**

Mean performance of the Danish group were compared to those provided in the Italian (Mancuso et al., 2016) and the British (Demeyere et al., 2015) validation studies, both of which were based on larger samples (see table 5). The means from the Danish sample are highly similar to those provided in the larger studies. Cut-offs are also, with some exceptions, found to be similar across studies (see table 6). When comparing Danish cut-offs to those provided in the Italian study (with the largest sample), small differences were observed for the
Naming and the Praxis sub-tests, and a more substantial difference was observed for the Hearts cancellation test (accuracy as well as spatial and object asymmetry measures). As the sample used in the Italian study (N=489) is much larger than the sample in the current study (N=91), and as we do not expect cultural differences between Italy and Denmark to affect performances on this task, taking the Italian cut-offs into consideration when evaluating scores on this test is recommended. Indeed, for the Broken Hearts test, there may be a risk of under-diagnosing deficits when using the Danish cut-off for accuracy and a risk of over-diagnosing deficits when using the cut-offs (left and right) for spatial neglect. More generally, the high levels of similarity between the normative data provided in the current study and normative data based on other populations may be related to the highly non-verbal design of the test.

[Table 5 about here]

[Table 6 about here]

In the large Italian study, scores were also shown to correlate with age and years of education on most of the subtests (Mancuso et al., 2016). For these subtests, they provided cut-offs for the different age and education groups. Despite these variables correlating with scores on many tests, there were only three tests for which the true cut-off values differed depending on age and education: Naming (cut-off of <3 or <4), Broken Hearts- correct (cut-off varies between <44 and <48) and Recognition (cut-off of <3 or <4) (Mancuso et al., 2016). As described in the results section, scores also correlated significantly with age and/or education on some subtasks in the Danish sample. However, due to the modest size of the sample assessed and the uncertainties that this entails, separate cut-offs are not provided for
the different age and education groups. By using the general cut-offs provided, there may be a small risk on some tests of over-diagnosing cognitive deficits in participants who are elderly and/or have limited education. A Danish study with a larger sample is warranted in order to investigate whether different cut-offs are needed for different age and education groups.

**Montreal Cognitive Assessment**

The MoCA results are based on 88 participants, as data points are missing for three participants (assessment errors). The mean score was 26.22 (SD=2.44) and the 5th percentile (Excel 2010 simple percentile function) corresponded to 22.35. The minimum score was 19, the maximum was 30, and the median score was 26.5. Scores correlated significantly (Pearson’s correlation, one-tailed) with age (r(86) = -.214, p < .05) and education (r(86) = .218, p < .05).

**Discussion: MoCA Results**

There is currently no normative material available for the Danish version of the MoCA. Many health care professionals in Denmark therefore use the cut-off of 25/26 (1 point added to score if education ≤11) provided in the original Canadian validation study (Nasreddine et al., 2005). By applying the original Canadian cut-off of 25/26 (currently used in Denmark) to scores in the current study, 31 of the 88 healthy participants (35.2%) would have been considered to have pathological performance. This suggests that this cut-off may be inappropriate in a Danish context. A recent review found that when using a cut-off of 25/26, the MoCA has a poor specificity (over 40% of healthy controls scoring below 26 are false positives)(Davis et al., 2015). More recent studies, presenting normative data for translations of the MoCA, have shown that scores are strongly associated with age, years of education, and gender, and that cut-offs are generally lower than 25/26. A recent Swedish normative
A Danish Version of The Oxford Cognitive Screen

study of a large population-Based cohort (N=860) (Borland et al., 2017), showed that cut-offs (placed at -1.5 SD) varied between ≤21 and ≤25, depending on participants’ age, education, and gender. In a Spanish study (N=563), 5th percentile cut-offs varied between ≤18 and ≤25 (Pereiro et al., 2017). The differences between cut-offs provided in these different studies suggest that there could be problems related to using norms cross-culturally and, therefore, local norms should be used for MoCA.

In the current study, a 5th percentile cut-off is provided for MoCA based on the whole sample. However, normative data for MoCA from other countries based on larger samples have shown the importance of providing age and education based norms. Due to the modest sample size, we were unable to provide age and education based norms for the Danish MoCA. A larger study is needed in Denmark in order to provide strong normative data for clinical use. Nevertheless, findings of the present study suggest that the cut-off scores currently used in Denmark (25/26) are likely to be too strict, and may falsely classify a significant number of patients as cognitively impaired.

**Overall Discussion**

Many people are affected directly by stroke every year in Denmark, and incidence of cognitive deficits is high in this group. Cognitive deficits can have severe negative consequences on functional outcome and are associated with high societal costs. Many cognitive symptoms are subtle and can easily be overlooked in hospital settings; guidelines therefore recommend systematic screening of cognitive functions in this population. Many health care professionals use short dementia screening tools such as the MoCA or the MMSE to screen for cognitive deficits in stroke. In Denmark, the MoCA is commonly used. These dementia screening tools suffer from various limitations when used in a stroke population:
they put high demands on verbal abilities, do not enable evaluation of individual cognitive
domains, and do not assess some of the cognitive symptoms which are common in stroke,
such as neglect, apraxia and visual field deficits. In Denmark, there is thus a need for a
screening tool that is specifically designed to screen for cognitive deficits following stroke.

In this study, we investigated whether the Oxford Cognitive Screen could be useful in
this context. Administration time is 15 minutes, it can be used at the bedside, enables
assessment of individual cognitive domains, and reduces contamination of language deficits
and neglect to tasks evaluating other cognitive domains. The OCS has also been shown to be
more sensitive than dementia screening tools to cognitive deficits following stroke (Demeyere
et al., 2016; Mancuso et al., 2018). A British study compared the OCS’s and the MoCA’s
abilities to detect cognitive impairments in acute stroke (N=200) (Demeyere et al., 2016). The
OCS was shown to be more inclusive for patients with aphasia and neglect, less dominated by
left hemisphere impairments and generally more sensitive than the MoCA (87% vs 78%
sensitivity). A recent Italian study compared instead the OCS to the MMSE (n=325). While
approximately a third of patients performed under the cut-off (<22) on the MMSE, 91.6%
were impaired on at least one OCS domain, indicating higher sensitivity of the OCS. 100% of
participants who were impaired on MMSE showed abnormal performance on the OCS
(Mancuso et al., 2018).

The main aim of the current study was to provide Danish reference data for the OCS.
The study also aimed to evaluate to the appropriateness of the MoCA cut-offs currently used
in Denmark. Indeed, the MoCA is commonly used to screen for cognitive deficits in stroke
patients in Denmark, despite there not being local Danish norms available. A group of healthy
Danish participants were assessed with a Danish version of the OCS and the MoCA, and
results were compared to results from international studies.
Mean scores of the Danish sample on the OCS were similar to those provided by larger British (Demeyere et al., 2015) and Italian studies (Mancuso et al., 2016). The 5\textsuperscript{th} percentile cut-offs were also similar to those provided in the large Italian study, increasing our confidence that despite the modest size of the sample in the current study, the Danish data presented here can be used in a clinical context. Our findings must however be interpreted cautiously as the study suffers from various limitations. Results showed that scores on some subtests correlated with age and/or years of education. Separate cut-offs should be calculated for the different age and education groups. However, such analyses were not carried out, as the modest sample size would have yielded too much uncertainty in the results. There is therefore a risk that for some subtests, cut-offs are too strict for participants in the older range and/or with lower education. A study collecting data on a larger sample of controls is needed to provide stronger and more detailed norms that are adjusted for age and education. It is worth noting, however, that despite age and education correlating with scores on many subtests, it is likely that, like in the Italian study, the true cut-off would only need to be adjusted according to age and education for very few sub-tests. Another limitation of the current study is that only healthy controls were assessed. Although validation studies for the original version of the test (Demeyere et al., 2015) and for a Cantonese version (Kong et al., 2016) have proven content validity for the OCS, a validation study comparing performances on the OCS to commonly used neuropsychological tests in a Danish stroke sample would provide additional information on the clinical value of the Danish version of the test.

Despite the limitations described above, we argue that the Danish version of the OCS is likely to provide a useful alternative to dementia screening tools currently used, when screening for cognitive deficits following stroke in Denmark. International studies have shown that the OCS is more sensitive than the MMSE and MoCA when screening for
cognitive deficits following stroke. A validation study in stroke patients is needed to
determine the clinical use of the tool in a Danish context. Results from the current study
suggest also that a lack of Danish age and education based norms for the MoCA, represent a
general problem related to using the MoCA in a Danish context, both for dementia patients
and other patient groups. Indeed, results suggest that the MoCA cut-off currently used in
Denmark is likely to be inappropriate. On a final note, it is worth stressing that the OCS is a
screening tool and does not enable the identification of discrete cognitive deficits. Discrete
cognitive deficits cannot be fully ruled out on the basis of a performance that is within the
normal range on the OCS. Neuropsychological assessment is still necessary for identifying
discrete deficits and for providing more detailed descriptions of cognitive impairments. We
argue however, that the OCS as a screening tool is useful for identifying patients in need of
further evaluation and care for their post stroke cognitive deficits.

**Ethical approval:** Ethical approval was waived by the Regional Ethics Committee (VEK) of
Greater Copenhagen because the project was not considered to fall under the regulations of a
health research project (Protocol number: H-17012594). The research protocol was approved
by the Institutional Ethical Review Board of the Department of Psychology, University of
Copenhagen (Approval number: IP-IERB / 26082017).

**Contributors:** R.J. Robotham was project manager for the research project. The study was
designed in collaboration with N. Demeyere. Data collection was shared between R.
Robotham and J. Riis. R. Robotham carried out data analysis and wrote the first draft of the
paper. The manuscript was finished in close collaboration between the three authors.
References


In press:

Table 1: Description of OCS sub-tests.

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<th>Task name</th>
<th>Domain</th>
<th>Description</th>
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</thead>
<tbody>
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<td>Picture naming</td>
<td>Language (expressive)</td>
<td>Participants are asked to name four pictures, one at a time (1 point/correct response).</td>
</tr>
<tr>
<td>Semantics</td>
<td>Language (receptive)</td>
<td>Participants are presented with four pictures simultaneously on one page and asked to point, one at a time, to pictures belonging to different categories (1 point/correct response).</td>
</tr>
<tr>
<td>Sentence reading</td>
<td>Language (expressive)</td>
<td>Participants are asked to read a 15-word sentence presented in four rows centrally on a page. The sentence includes four irregular words and four “high-neighbourhood” words (words for which the start or end is shared with many other words), enabling screening for both surface dyslexia and neglect dyslexia (1 point/word that is read correctly).</td>
</tr>
<tr>
<td>Orientation</td>
<td>Memory (orientation)</td>
<td>Participants are asked open-ended questions about what city they are in and what time of day, month and year it is. If a participant is unable to respond due to language problems, multiple choice options are presented (1 point/correct response after use of multiple choice).</td>
</tr>
<tr>
<td>Recall and recognition</td>
<td>Memory (episodic)</td>
<td>The verbal episodic memory sub-test first involves the participants recalling the sentence from the reading sub-test. If a participant is unable to recall the sentence, a multiple choice task is presented to test if participants can recognise four target words. The recollection score represents the number of items correctly recalled before multiple choice (max four). The recognition score represents the recollection score plus points for additional items recognised with multiple choice (max 4). In the third part, participants are asked four questions about tasks completed earlier on (1 point/correct response).</td>
</tr>
<tr>
<td>Number writing</td>
<td>Number processing</td>
<td>Participants are asked to write down multi-digit numbers to dictation (1 point/correct response).</td>
</tr>
<tr>
<td>Calculation</td>
<td>Number processing</td>
<td>Participants are required to solve four mental arithmetic questions. If a participant is unable to respond due to language problems, multiple choice options are presented in writing (1 point/correct response).</td>
</tr>
<tr>
<td>Broken hearts test</td>
<td>Attention (visual attention)</td>
<td>Participants are presented with complete and incomplete hearts on a horizontal A4 page, and are asked to cross out all the complete hearts. The incomplete hearts have a gap in the right or left side (see figure 2). A total correct score is provided with amount of full hearts correctly crossed out. A space asymmetry score is provided by subtracting the number of full hearts omitted on the left side of the page from the number of full hearts omitted on the left side of the page (positive score indicates left spatial neglect, negative score indicates right spatial neglect). An object asymmetry score is also calculated by subtracting the number of hearts with right gap that have been erroneously crossed out from the number of hearts with left gap that have been erroneously crossed out (positive score indicates left object-based neglect, negative score indicates right object-based neglect).</td>
</tr>
<tr>
<td>Trails task</td>
<td>Attention (executive function)</td>
<td>This is a trail test involves two simple tasks and one complex. In the two simple tasks, participants are required to connect circles amongst triangle distractors and then triangles amongst circle distractors. Items must be connected from the largest to the smallest. One point is given for each correct line. In the complex task, participants are asked to connect items by alternating between circles and triangles, whilst going from the largest to the smallest items. An executive score is calculated by subtracting the score on the alternating task from the scores on both simple tasks.</td>
</tr>
<tr>
<td>Test Type</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>---------------------------</td>
<td>---------------------------------------------------------------------------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Imitating meaningless</td>
<td>Participants are required to copy two meaningless sequences of two hand gestures, and two hand positions made by the examiner (max. 3 points per gesture or hand position).</td>
<td></td>
</tr>
<tr>
<td>Praxis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visual field</td>
<td>A simple confrontation test is used to assess the four quadrants of the visual field. The assessor holds his/her hands up in the upper quadrants and moves the fingers of one and then the other hand. The participant is required to point to the hand that is moving. The same procedure is followed for the lower quadrants. A point is given for correct response in each quadrant.</td>
<td></td>
</tr>
<tr>
<td>Visual perception</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 2: Number of participants in sample according to age and years of education

<table>
<thead>
<tr>
<th>Education Range (median)</th>
<th>36-65 (58)</th>
<th>65-75 (70)</th>
<th>75-89 (80)</th>
<th>Total: 36-89 (68)</th>
</tr>
</thead>
<tbody>
<tr>
<td>4-12 (10)</td>
<td>6</td>
<td>14</td>
<td>5</td>
<td>25</td>
</tr>
<tr>
<td>12-16 (14.5)</td>
<td>16</td>
<td>17</td>
<td>10</td>
<td>43</td>
</tr>
<tr>
<td>16-22 (18)</td>
<td>12</td>
<td>7</td>
<td>4</td>
<td>23</td>
</tr>
<tr>
<td>Total: 4-22 (14)</td>
<td>34</td>
<td>38</td>
<td>19</td>
<td>91</td>
</tr>
</tbody>
</table>
Table 3: Mean scores according to age and years of education on OCS subtests

<table>
<thead>
<tr>
<th>Task</th>
<th>Max</th>
<th>Overall</th>
<th>Age</th>
<th>Education</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>&lt;65</td>
<td>65-75</td>
<td>&gt;75</td>
</tr>
<tr>
<td>Naming</td>
<td>4</td>
<td>3.73</td>
<td>3.82</td>
<td>3.55</td>
</tr>
<tr>
<td>Semantics</td>
<td>3</td>
<td>3.00</td>
<td>3.00</td>
<td>3.00</td>
</tr>
<tr>
<td>Orientation</td>
<td>4</td>
<td>4.00</td>
<td>4.00</td>
<td>4.00</td>
</tr>
<tr>
<td>Visual field</td>
<td>4</td>
<td>4.00</td>
<td>4.00</td>
<td>4.00</td>
</tr>
<tr>
<td>Reading &lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>15</td>
<td>14.97</td>
<td>15.00</td>
<td>14.97</td>
</tr>
<tr>
<td>Writing</td>
<td>3</td>
<td>3.00</td>
<td>3.00</td>
<td>3.00</td>
</tr>
<tr>
<td>Calculation</td>
<td>4</td>
<td>3.90</td>
<td>3.85</td>
<td>3.95</td>
</tr>
<tr>
<td>Broken hearts</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Correctly crossed out)</td>
<td>50</td>
<td>47.02</td>
<td>46.82</td>
<td>47.08</td>
</tr>
<tr>
<td>Broken hearts (RT) &lt;sup&gt;1&lt;/sup&gt;</td>
<td>180</td>
<td>103.56</td>
<td>88.78</td>
<td>103.37</td>
</tr>
<tr>
<td>Spatial asymmetry</td>
<td>0</td>
<td>0.08</td>
<td>0.00</td>
<td>0.08</td>
</tr>
<tr>
<td>Object asymmetry</td>
<td>0</td>
<td>0.04</td>
<td>-0.12</td>
<td>0.37</td>
</tr>
<tr>
<td>Praxis &lt;sup&gt;1&lt;/sup&gt;</td>
<td>12</td>
<td>10.75</td>
<td>11.21</td>
<td>10.53</td>
</tr>
<tr>
<td>Recollection</td>
<td>4</td>
<td>2.65</td>
<td>2.65</td>
<td>2.71</td>
</tr>
<tr>
<td>Recognition &lt;sup&gt;1&lt;/sup&gt;</td>
<td>4</td>
<td>3.87</td>
<td>3.97</td>
<td>3.82</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>4</td>
<td>3.95</td>
<td>3.94</td>
<td>3.97</td>
</tr>
<tr>
<td>Circles (Acc.) &lt;sup&gt;2&lt;/sup&gt;</td>
<td>6</td>
<td>5.95</td>
<td>6.00</td>
<td>5.95</td>
</tr>
<tr>
<td>Triangles (Acc.) &lt;sup&gt;1&lt;/sup&gt;</td>
<td>6</td>
<td>5.91</td>
<td>5.91</td>
<td>5.97</td>
</tr>
<tr>
<td>Alternating (Acc.) &lt;sup&gt;1,2&lt;/sup&gt;</td>
<td>13</td>
<td>12.51</td>
<td>12.62</td>
<td>12.42</td>
</tr>
<tr>
<td>Executive Score</td>
<td>-1</td>
<td>-0.65</td>
<td>-0.71</td>
<td>-0.50</td>
</tr>
</tbody>
</table>

<sup>1</sup>Scores correlated significantly with age (Pearsons, one-tailed).
<sup>2</sup>Scores correlated significantly with years of education (Pearsons, one-tailed).
Table 4: Cut-offs for impairment on OCS based on the whole sample (5th percentile and 95th percentile)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>Min</th>
<th>Max</th>
<th>Median</th>
<th>Mean</th>
<th>SD</th>
<th>5th Centile</th>
<th>95th</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naming</td>
<td>91</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>3.73</td>
<td>0.52</td>
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<td></td>
</tr>
<tr>
<td>Semantics</td>
<td>91</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3.00</td>
<td>0.00</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Orientation</td>
<td>91</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4.00</td>
<td>0.00</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Visual field</td>
<td>91</td>
<td>4</td>
<td>4</td>
<td>4</td>
<td>4.00</td>
<td>0.00</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Reading</td>
<td>91</td>
<td>14</td>
<td>15</td>
<td>15</td>
<td>14.97</td>
<td>0.18</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Writing</td>
<td>91</td>
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<td>3</td>
<td>3</td>
<td>3.00</td>
<td>0.00</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Calculation</td>
<td>91</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3.90</td>
<td>0.30</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Broken hearts</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Correctly crossed out)</td>
<td>91</td>
<td>29</td>
<td>50</td>
<td>48</td>
<td>47.02</td>
<td>3.84</td>
<td>39.5</td>
<td></td>
</tr>
<tr>
<td>Broken hearts (RT)</td>
<td>91</td>
<td>35</td>
<td>180</td>
<td>101</td>
<td>103.56</td>
<td>29.83</td>
<td>63</td>
<td></td>
</tr>
<tr>
<td>Spatial asymmetry</td>
<td>91</td>
<td>-3</td>
<td>3</td>
<td>0</td>
<td>0.08</td>
<td>1.33</td>
<td>-2</td>
<td>2</td>
</tr>
<tr>
<td>Object asymmetry</td>
<td>91</td>
<td>-2</td>
<td>1</td>
<td>0</td>
<td>0.04</td>
<td>0.39</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Praxis</td>
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<td>11</td>
<td>10.75</td>
<td>1.42</td>
<td>8</td>
<td></td>
</tr>
<tr>
<td>Recollection</td>
<td>91</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>2.65</td>
<td>1.07</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Recognition</td>
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<td>4</td>
<td>4</td>
<td>3.87</td>
<td>0.40</td>
<td>3</td>
<td></td>
</tr>
<tr>
<td>Episodic memory</td>
<td>91</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>3.95</td>
<td>0.23</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>Circles (Acc.)</td>
<td>91</td>
<td>4</td>
<td>6</td>
<td>6</td>
<td>5.95</td>
<td>0.27</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Triangles (Acc.)</td>
<td>91</td>
<td>5</td>
<td>6</td>
<td>6</td>
<td>5.91</td>
<td>0.28</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>Alternating (Acc.)</td>
<td>91</td>
<td>2</td>
<td>13</td>
<td>13</td>
<td>12.51</td>
<td>1.46</td>
<td>11</td>
<td></td>
</tr>
<tr>
<td>Executive score</td>
<td>91</td>
<td>-3</td>
<td>9</td>
<td>-1</td>
<td>-0.65</td>
<td>1.42</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
### Table 5: Mean scores compared across studies (Demeyere et al., 2015; Mancuso et al., 2016)

<table>
<thead>
<tr>
<th></th>
<th>Danish</th>
<th>Italian</th>
<th>British</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(N=89-91)</td>
<td>(N=489)</td>
<td>(N=140)</td>
</tr>
<tr>
<td>Naming</td>
<td>3.73</td>
<td>3.6</td>
<td>3.82</td>
</tr>
<tr>
<td>Semantics</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Orientation</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Visual field</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Reading</td>
<td>14.97</td>
<td>14.8</td>
<td>14.85</td>
</tr>
<tr>
<td>Writing</td>
<td>3</td>
<td>3</td>
<td>2.93</td>
</tr>
<tr>
<td>Calculation</td>
<td>3.9</td>
<td>3.8</td>
<td>3.9</td>
</tr>
<tr>
<td>Broken hearts (Correctly crossed out)</td>
<td>47.02</td>
<td>47.1</td>
<td>47.31</td>
</tr>
<tr>
<td>Spatial asymmetry</td>
<td>0.08</td>
<td>-0.1</td>
<td>-0.11</td>
</tr>
<tr>
<td>Object asymmetry</td>
<td>0.04</td>
<td>0</td>
<td>0.01</td>
</tr>
<tr>
<td>Praxis</td>
<td>10.75</td>
<td>11.4</td>
<td>10.84</td>
</tr>
<tr>
<td>Recollection</td>
<td>2.65</td>
<td>-</td>
<td>2.52</td>
</tr>
<tr>
<td>Recognition</td>
<td>3.87</td>
<td>3.4</td>
<td>3.72</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>3.95</td>
<td>3.9</td>
<td>3.83</td>
</tr>
<tr>
<td>Alternating (Acc.)</td>
<td>12.51</td>
<td>11.9</td>
<td>10.4</td>
</tr>
<tr>
<td>Executive Score</td>
<td>-0.65</td>
<td>-0.4</td>
<td>1.36</td>
</tr>
</tbody>
</table>

Participants in the British sample had a mean age of 65 (range: 36 to 88) and their mean length of education was 13.9 (Demeyere et al., 2015). The age of the participants in the Italian study ranged from 18 to 89 (Mancuso et al., 2016).
Table 6: Cut-offs compared across studies: 5th percentile (95th percentile) (Demeyere et al., 2015; Mancuso et al., 2016)

<table>
<thead>
<tr>
<th></th>
<th>Danish (n=89-91)</th>
<th>Italian (n=489)</th>
<th>British (n=140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Naming</td>
<td>3</td>
<td>2.9 to 3.7*</td>
<td>3</td>
</tr>
<tr>
<td>Semantics</td>
<td>3</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Orientation</td>
<td>4</td>
<td>3.9 to 4</td>
<td>4</td>
</tr>
<tr>
<td>Visual field</td>
<td>4</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Reading</td>
<td>15</td>
<td>14.1 to 15</td>
<td>14*</td>
</tr>
<tr>
<td>Writing</td>
<td>3</td>
<td>2.8 to 3</td>
<td>3</td>
</tr>
<tr>
<td>Calculation</td>
<td>3</td>
<td>3.3 to 3.8</td>
<td>3</td>
</tr>
<tr>
<td>Broken hearts</td>
<td>39.5</td>
<td>43.4 to 47.4*</td>
<td>42*</td>
</tr>
<tr>
<td>(Correctly crossed out)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Spatial asymmetry</td>
<td>-2 (2)</td>
<td>-3* (3)*</td>
<td>-2 (3)*</td>
</tr>
<tr>
<td>Object asymmetry</td>
<td>0 (1)</td>
<td>-2* (2)*</td>
<td>0 (0)*</td>
</tr>
<tr>
<td>Praxis</td>
<td>8</td>
<td>9*</td>
<td>8</td>
</tr>
<tr>
<td>Recollection</td>
<td>1</td>
<td>-</td>
<td>0*</td>
</tr>
<tr>
<td>Recognition</td>
<td>3</td>
<td>2.4 to 3.4</td>
<td>3</td>
</tr>
<tr>
<td>Episodic memory</td>
<td>3.5</td>
<td>3.4 to 3.8</td>
<td>3</td>
</tr>
<tr>
<td>Alternating (Acc.)</td>
<td>11</td>
<td>10.5 to 11</td>
<td>7</td>
</tr>
<tr>
<td>Executive score</td>
<td>(1)</td>
<td>(3)</td>
<td>(4)</td>
</tr>
</tbody>
</table>

*Cut-offs from international studies that differ from the Danish cut-offs.
In the Italian study, cut-offs were adjusted according to age and/or education for the sub-tests in which these variables influenced scores. For these sub-tests ranges of cut-offs are provided.
Figure 1: Visual snapshot
Figure 2: Broken Hearts Test
Appendix E: BOB- Supplementary Material
1. Developing the test battery
The behavioural test battery was designed to test the hypotheses of the Back of the Brain project (described in Chapter 1, Section 3 of the dissertation). The test battery had the following constraints determined by the project protocol and budget:
   A. Maximum 9 hours completion time for a typical patient with brain injury.
   B. Maximum three sessions distributed over three days for completion.
Creating the test battery involved the following steps:
Step 1: Identify lower-level, intermediate and high-level functions that are relevant for BoB

A literature search was carried out to identify functions that could be relevant to assess (Figure 1).

Figure 1: Functions that could be relevant to assess in the BoB project – “dream scenario”.
Step 2: Search literature to identify tests and create a “dream scenario” test battery.

Tests that fulfilled as many as possible of the following criteria were prioritised: in English, short (to limit fatigue), validated and/or previously used in research, central/vertical presentation of stimuli (to limit the effects of hemianopia on performance) and tests assessing non-visual functions must be as visually simple as possible. This leads us to a “Dream scenario” test battery (see Figure 2).

Figure 2: Overview of tests that should be included in BoB - "dream scenario" (tests that were excluded later in the process in Bold)
Step 3: Prioritise functions to assess and “kill your darlings” to create a “final version” of the test battery.

All tests for the dream scenario were acquired and/or created for the project. After piloting, selected test were shortened or removed to fit the time constraints. Only the tests/experiments considered most important were included in the final test battery (Figure 3).

Figure 3: BoB test battery - Final version
2. Behavioural test battery

Tests were either carried out using paper-and-pencil, Laptop computers with screen a resolution of 1366 x 768 (London: Dell latitude e6430 running on CORE i5 Windows 7 Professional; Manchester: Lenovo T560 running on Windows 7), or desktop computers with a screen resolution of 1920x1080 (Windows 7 Enterprise, 64-bit operating system, 24 Inch BenQ XL2430T screen).

2.1. Background information

2.1.1. Edinburgh Handedness Inventory - Short Form

Reason for inclusion: Cerebral lateralisation is known to be linked to handedness.

About the tool: The Edinburgh Handedness inventory (Oldfield, 1971) is the most commonly used handedness questionnaire (Fazio, Coenen, & Denney, 2012). The original questionnaire includes 10 items. In the BoB project we use a shorter 4-item version, which was developed based on confirmatory factor analysis that was shown to have good reliability, factor score determinacy, and correlation with scores on the 10-item inventory (Veale, 2014).

2.1.2. Geriatric Depression Scale - 15 (GDS-15)

Reason for inclusion: Depression and anxiety are known to be common amongst stroke survivors and are known to affect performance on cognitive tests (Barker-Collo, 2007; Hackett, Yapa, Parag, & Anderson, 2005; Townend et al., 2007). According to a meta-analysis of high quality observational studies, it was estimated that 33% of patients experience depression following stroke (Hackett et al., 2005).

About the tool: The Geriatric Depression Scale (GDS) is a self-report measure that was designed for depression screening in older adults (Yesavage et al., 1983). One of the main advantages of the tool is that questions are answered with simple yes/no options. It originally included 30 items, but a shorter 15 item version, the GDS-15, was shown to have similar test properties as the longer version (Sheikh & Yesavage, 1986). As most subjects in the BoB project are in the older age range, the GDS was chosen as a depression screening tool. To limit assessment time, the shorter version of the tool was chosen.

2.1.3. Oxford Cognitive Screen

Reason for inclusion: Stroke can lead to a wide range of cognitive deficits. Screening of cognitive deficits is carried out to determine whether participants have substantial cognitive deficits (in other domains than visual perception), in order to enable interpretation of poor performances on the experimental tasks included in BoB. Amongst others, memory, language, executive deficits, and neglect could potentially affect performance on many of the experiments. Although OCS is not a dementia screening tool, it should also enable identification of participants with severe cognitive deficits, who may have dementia.

About the tool: The Oxford Cognitive Screen is a cognitive screening tool specifically designed for Stroke patients (Demeyere, Riddoch, Slavkova, Bickerton, & Humphreys, 2015). It covers the main cognitive domains that are commonly affected by stroke: Language, Attention, Memory, Praxis, and Number processing. OCS sub-tests: Picture naming; Semantics/picture pointing; Orientation; Visual field; Sentence reading; Number processing (writing and mental arithmetic); Broken hearts (neglect); Meaningless gesture imitation (praxis); Memory (recall & recognition); Trail tasks (executive functions)

2.1.4. Digit span: forwards and backwards

Reason for inclusion: Working memory is not assessed in the Oxford cognitive screen. Many of the experiments included in the BoB put substantial demands on working memory. Digit span is a fast and efficient way of assessing working memory. Few patients in the project are expected to have aphasic deficits, so verbal assessment of working memory is appropriate.

About the test: Digit span (forwards and backwards) from the Wechsler Adult Intelligence Scale III was chosen as it enables quick assessment of working memory and has detailed norm data available.
2.1.5. Basic motor response: up-down

**Reason for inclusion:** Stroke can lead to general cognitive slowing (Benton, 1986). A very basic visual task was included to provide a baseline lower level visual reaction time measurement, that can enable interpretation of reaction time data acquired in more complex experimental tests.

**About the test:** This experimental task was developed specifically for measuring basic reaction times for the BoB project. Many of the reaction time tasks included in BoB project are 2AFC tasks. We therefore designed a simple visual 2AFC task in which participants must determine whether a stimulus is presented at the top or bottom of the screen (Figure 4). The stimulus they must respond to is a narrow black rectangle that extends from one side of the screen to the other. The stimuli was chosen to ensure that patients with hemianopia and various forms for agnosia can complete the task. There are four practice trials and 20 test trials.

![Figure 4: Trial display for the Basic motor response test.](image)

2.1.6. Adult Reading Questionnaire

**Reason for inclusion:** Some of the central hypotheses of the BoB project involve relations between pre-stroke reading experience/proficiency and severity of post-stroke aphasia and prosopagnosia. Therefore, an assessment tool for reading abilities prior to stroke was included. In addition, identification of patients with dyslexic reading is important when interpreting data from reading tests.

**About the test:** While there are many questionnaires designed to identify dyslexia in children, there are only a limited number of questionnaires designed to assess reading difficulties in adults. The Adult Reading Questionnaire (Leffly & Pennington, 2000) includes questions about experience with reading during childhood and reading ability in adulthood (reading speed and mistakes, reading habits, as well as memory for verbal information). Other tools, such as the Adult Dyslexia Checklist (Smythe and Everatt, 2001), the revised Adult Dyslexia Checklist (Vinegrad, 1994) and the Adult Reading Questionnaire (Snowling, Dawes, Nash, & Hulme, 2012) do not include questions about reading during childhood and only focus on current reading abilities.

2.2. Low-level and intermediate visual perception

2.2.1. Computerised Visual Field Test

**Reason for inclusion:** Visual field defects are common following posterior cerebral artery stroke and can impact performance on many visual perceptual tasks (Zihl, 2011).

**About the test:** The computer Visual Field Screening Test (c-VFT) was developed at the Department of Psychology at University of Copenhagen. Commonly used perimetry tests are time consuming and can be difficult to run on patients with mobility limitations. The c-VFT can be run on a laptop computer and therefore be carried out at bedside and only takes approximately five minutes to administer. The test probes 48 points within a radius of 10 degrees of visual angle (dva) around a central fixation cross. The points are equally sized dark circles presented against a light grey background. The stimuli probe at 1, 2, 5, and 10 degrees of visual angle. The test includes assessment of points along the horizontal and vertical meridians.
(see Figures 5 and 6). Integrity of visual field along the horizontal meridian is particularly relevant for reading. The c-VFT has been validated against the Esterman test and the Humphrey Visual Field Analyzer (HFA), central 10-2 that are perimetry tests commonly used in clinical settings (Nordfang, M., Uhre, V., Robotham R., Kerry, S., and Christensen, J.L., & Starrfelt, R., paper ready for submission).

Figure 5: Illustration of location of probes.
2.2.2 Freiburg Visual Acuity Test And Contrast Test (FrACT) – automatic

A. FrACT: Landolt C Acuity Test

*Reason for inclusion:* Low visual acuity can affect performance on many visual tasks. Although our participants can use glasses during experiments we want to know the status of their visual acuity when using glasses/lenses. Stroke patients are often in the older age range and can be expected to have acuity problems. The FrACT Landolt C visual acuity test was chosen for the BoB project as, in contrast to Log MAR charts in which all stimuli are presented simultaneously on a chart, stimuli are presented one at a time in the centre of the screen. This is useful for patients with visual field deficits or who are visually disorientated. Another advantage of FrACT is that Landolt Cs are used as stimuli rather than letters. The test is therefore better suited for patients with some forms of reading deficits than tests using letters from the alphabet.

*About the test:* The FrACT presents Landolt Cs one at a time on a computer screen with varying sizes to assess visual acuity. It uses an adaptive staircase procedure to measure acuity threshold (Bach, 2006, 1996). For more information about the test: https://michaelbach.de/fract.

B. FrACT: Contrast Sensitivity Test

*Reason for inclusion:* It has been hypothesised that the visual processing of faces and words could rely differentially on low or high contrast information, and that differences in abilities to process low or high contrast visual information may explain why patients are more impaired in one category than the other.

*About the test:* The FrACT contrast sensitivity test presents a Landolt C target one at a time on a computer screen (Buhren, Terzi, Bach, Wesemann, & Kohnen, 2006). The target has variable contrast levels (0.1% to 99.9%) and is presented in four different orientations. An adaptive staircase procedure is used to measure contrast threshold. For more information about the test: https://michaelbach.de/fract.

2.2.3 The Farnsworth D-15 test of colour perception

*Reason for inclusion:* The test was included to identify congenital colour blindness as well as acquired achromatopsia. Assessment of colour perception was included as it is possible that a deficit in colour perception affects the ability to recognise some types of complex stimuli more than others. It has been shown...
that achromatopsia can co-occur with prosopagnosia, however, little is known about the relationship between the two deficits (Bouvier & Engel, 2006).

About the test: The test is a modification of the Farnsworth-Munsell 100 Hue test (Farnsworth, 1943). The 15 cap version is intended for screening purposes (Linksz, 1966). The test contains 15 caps with different colours. One cap, the “pilot” cap, is fixed to the left of the tray. The other caps are presented to the participant in mixed order. Participants are asked to “select the cap which is the closest possible match to the pilot cap”. The chosen cap is placed to the right of the pilot cap. The participant must then “choose the closest colour match to the cap that was just chosen”. This procedure is repeated until all caps have been placed in a row. Different result patterns indicate different forms of colour vision defects.

2.2.4. L-POST
Reason for inclusion: Difficulties in processing complex visual stimuli can potentially in some cases be caused by deficits in mid-level visual perceptual processing. By assessing mid-level visual perception, we can investigate whether some types of mid-level perceptual deficits affect the processing of some visual categories more than others.

About the test: The Leuven Perceptual Organization Screening Test (L-POST) is a screening tool designed to assess deficits in mid-level vision (Torfs, Vancleef, Lafosse, Wagemans, & de-Wit, 2014; Vancleef et al., 2015). It includes 15 subtests assessing a wide range of mid-level processes, such as figure-ground segmentation, local and global processing, shape perception, and the ability to use a range of grouping cues including common fate, co-linearity, proximity, and closure. It is designed for clinical and research use. In the original internet-based version of the test, performance is determined on the basis of accuracy alone. We created a version of the test in OpenSesame (an open source program for making experiments) to collect both accuracy and reaction time measurements. Sub-tests: Fine shape discrimination; Shape ratio discrimination (Efron); RFP contour integration; Figure–ground segmentation; Embedded figure detection; RFP texture segmentation; Kinetic object segmentation; Dot counting; Global motion detection.

2.3. High-level visual processing

2.3.1. WOF: Words, Objects and Faces Test
Reason for inclusion: This test uses the same paradigm to assess face, word and object recognition, leading to easier comparison across categories.

About the test: The test was developed specifically for the BoB project and involves two parts: a sequential matching part and an old/new recognition test. The sequential matching part is designed to assess the ability of a participant to build a short-term representation of a stimulus and then match it with the same or a novel stimulus. It enables direct comparison across the categories: faces, words and objects. The old/new recognition part involves participants being presented with two stimuli and deciding which of the two they have seen during the sequential matching part of the test. It assesses the ability to store representations in more long-term memory and enables comparison across categories. The test is described in detail in Article 3, Appendix C.

2.3.2. Word reading: lexical decision
Reason for inclusion: Comparable task across categories: Decision famous/non-famous face, Decision word/non-word (lexical decision), Decision object/non-object. All three tasks involve determining whether one has seen a given stimulus before or not.

About the test: The lexical decision task involves determining whether a stimulus is a word or a non-word. It is commonly used to assess reading abilities (e.g. Johnston and Barry, 2006; Kast et al., 2010; Susilo et al., 2015)

2.3.3. Object decision test
Reason for inclusion: This roughly parallels the lexical decision and famous or not decision tasks, giving us the possibility for cross category comparisons of performance. This test involves determining whether an image is depicting an object or a non-object. This test, along with picture naming and categorisation, allows
Supplementary Material: BoB Behavioural Test Battery

us to check the integrity of the ventral stream (for object recognition) at several levels of processing. Object decision is a perceptually demanding object recognition task and yet some patients with pure alexia perform within the normal range on this test (even with regards to category effects).

About the test: Images are presented one at a time and participants are required to respond whether it depicts an object that exists or not. The test has been used in many publications (Christian Gerlach, 2009; Starrfelt, Habekost, & Gerlach, 2010).

2.3.4. Famous face familiarity: yes/no

Reason for inclusion: The test assesses the ability to recognise a face as familiar. Participants must match the perceived face to a representation stored in long term memory. Participants are shown one face at a time and must determine if it is a famous face or a novel face. This receptive semantic task is a measure of semantic processing without the need for a verbal (naming) output. It is comparable to the Object Decision and lexical decision tasks but uses famous faces instead.

About the test: Face familiarity tests have often and for many years been used to assess face recognition abilities (Barton, Cherkasova, & O’Connor, 2001).

2.3.5. Cambridge Face Memory Test

Reason for inclusion: The most widely used test in literature for assessing face recognition abilities and for diagnosing acquired and developmental prosopagnosia.

About the test: The test involves learning a set of new faces and then recognising them amongst distractors (Duchaine & Nakayama, 2006).

2.3.6. Cambridge House Memory Test

Reason for inclusion: The most widely used test in literature for assessing prosopagnosia is the Cambridge face memory test. Here we non-face control task for this testing house recognition to see if a patient’s deficit is face-specific or not.

About the test: The test has the same experimental set-up as the Cambridge face memory test but involves learning a set of new houses and then recognising them amongst distractors (Martinaud et al., 2012).

2.3.7. Faces questionnaire

Reason for inclusion: It is important that patients with prosopagnosia be identified. One of the common core criteria used to diagnose prosopagnosia is that the patient has "Complaints of impaired face recognition in daily life". Another reason for including a face recognition questionnaire is to check whether there is a correlation between self-reporting of face recognition difficulties and performance on face processing tasks.

About the test: 10 questions were selected from the Face Identity Recognition part of the Faces and Emotions questionnaire (Freeman, Palermo, & Brock, 2015), which is designed to evaluate congenital prosopagnosia. Questions were adjusted to be appropriate for people with acquired brain injury. To ensure that problems are indeed related to brain injury, an extra question was added; “My ability to recognise faces has got worse since my stroke/head injury?”.

2.3.8. Word reading (3, 5, 7 letter words)

Reason for inclusion: A core characteristic of pure alexia is the word length effect, which this experiment measure. Subjects with hemianopia also typically show a word length effect (although more modest).

About the test: The test has been used in many investigations of pure alexia. The design used in the BoB project was highly similar to the design used in Starrfelt et al. (2009).

2.3.9. Word reading: lexical variables

Reason for inclusion: The test is included to evaluate whether participants have reading deficits and what type. Are difficulties general or more pronounced for non-words or exception words than regular words.

About the test: Participants are presented with words one at a time on the screen and must read the words out loud. The test includes 20 non-words, and 84 real words of which 42 are regular and 42 are exception words (used in Behrmann & Plaut, 2014).
2.3.10. Naming single letters, digits and 3-letter words

**Reason for inclusion:** The reasons for inclusion are twofold. To evaluate participants’ letter/digit/word naming abilities and to familiarise the participants with the stimuli for the TVA single item experiment.

**About the test:** This test is a version of Experiment 2a in Habekost, Petersen, Behrmann, & Starrfelt (2014) which includes single letters and words. A digit condition was added. Participants are asked to name 30 single letters, 30 single digits, and 30 three letter words in different blocks. RTs and accuracy is measured.

2.3.11. TVA: single items (digits, letters, and words)

**Reason for inclusion:** This experiment measures the visual component of letter, word, and digit recognition without being affected by motor components of the response. This is to be compared with the naming task described above, and may indicate if a deficit arises in visual recognition or naming.

**About the test:** This test is a version of Experiment 2b in Habekost, Petersen, Behrmann, & Starrfelt (2014) which includes single letters and words, and measures the word superiority effect. A digit condition was added to enable analysis of the relationship between letter and digit recognition. The test is a psychophysical experiment presenting stimuli (letters, words and digits in separate blocks) at varying, short exposure durations (20, 30, 50, 80 and 100 msec, 10 trials per exposure duration per stimulus type). The dependent measure is overall accuracy across exposure durations, which can be compared between stimulus types. In addition, TVA-based analyses (see Starrfelt, Gerlach, Habekost, & Leff, 2013) Starrfelt et al., 2013, Experiment 2 for such analyses of similar data) can be carried out on these data, allowing for estimation of perceptual threshold and processing speed for digits, letters, and words respectively.

2.3.12. NEALE (text reading)

**Reason for inclusion:** To obtain a measure of word reading comprehension and sentence reading.

**About the test:** Participants are asked to read two passages of 26 words and 56 words, followed by four and eight comprehension questions, respectively. This is a standardised test that produces a measure of words read per minute and participants’ ability to comprehend what they are reading. The Neale (Neale, 1999) was used in a recent study involving participants with Central Alexia (Woodhead et al., 2018).

2.3.13. Picture (object) naming

**Reason for inclusion:** One of the ways we can compare visual recognition across categories directly is by comparing naming of objects, words and famous faces (RT and accuracy). OBS: A limitation of this is that the difficulty level differs between categories as well as the level of specificity (faces at the individual level, whereas objects at the category level).

**About the test:** The test has been used in previous studies (Roberts et al., 2012). Patients have to name 45 black and white line drawings of objects. The stimuli consist of 30 living items (animals, insects) and 15 non-living items (musical instruments, vehicles, tools). Within the living items there is a manipulation of “homomorphy” (Tranel, Logan, Frank, & Damasio, 1997); the amount to which an items contour is shared with other exemplars within that category (15 living items had high homomorphy and 15 living items had low homomorphy). For example, most common animals including cats and dogs have high homomorphy because most have four legs, pointy ears and a tail. Whereas, more unusual animals including giraffes, elephants, peacocks have low homomorphy because the degree of overlap between them and other exemplars is minimal. Previous studies have shown that this cohort of patients produce a category effects during naming, in other words performance is worse when naming living items compared to non-living items. The manipulation of homomorphy was included to test the hypothesis that any such category effects are due to low-level perceptual effects caused by the high homomorphy overlap in living items compared to non-living items (which tend to be more unique in their contour). Both accuracy and reaction times were recorded for this test.

2.3.14. Object Categorisation (natural/manmade)

**Reason for inclusion:** This receptive semantic task is a measure of visual recognition and visual-semantic processing without the need for a verbal (naming) output. Category effects (natural vs manmade) can also be looked at as there are living/non-living category distinctions built into the test. Visual superordinate categorisation is a fairly simple task, and response times in this test may be used as baseline RTs in
comparison to other tests using pictorial stimuli. The same stimuli are also used in the more difficult Object Decision Task (2.3.3.), and results from the two experiments may be compared to evaluate differential effects of category and/or visual similarity on performance.

About the test: This test is a short version of the object categorisation tasks used by e.g. Gerlach (2001) and Gerlach, Klørgaard, Petersen and Starrfelt (2017). Stimuli are 36 Snoglass and Vanderwart line drawings, 18 representing natural objects and 18 representing man-made objects. Images are presented one at a time and participants are required to respond whether it depicts an natural or a manmade object.

2.3.15. Naming famous faces

Reason for inclusion: One of the ways we can compare visual recognition across categories directly is by comparing naming of objects, words and famous faces (RT and accuracy). OBS: A limitation of this is that the difficulty level differs between categories as well as the level of specificity (faces at the individual level, whereas objects at the category level).

About the test: This test was used in a previous case-series investigation of PCA stroke cases (Roberts et al., 2015). Participants are presented with a picture of a famous face and asked to provide their name. If they are unable to provide their name, recognition of the person is tested (e.g., provision of why the person is famous, what they do, where they live etc.). The main measure for this test was accuracy, reaction time data was not scored due to the duration of responses. Responses were scored according to whether the correct name was provided or whether there was correct semantic information provided.

2.4. ASSOCIATED FUNCTIONS

2.4.1. Writing to dictation

Reason for inclusion: To test if a reading deficit observed in PA may also exist in a mild form in spelling. Only low predictability was included, as the original test was 80 items and we needed a harder, shorter version.

About the test: The impact of semantic memory impairment on spelling: Evidence from semantic dementia (Graham, Patterson, & Hodges, 2000). Low frequency, low predictability words have lower semantic veracity and are predicted to be harder to spell than those of higher frequency.

2.4.2. Surprise Handwriting Test

Reason for inclusion: To assess whether participants can read something that they have written and recognise their own handwriting. Early case studies of Pure Alexia describe participants as unable to read something they have written a short time previously (Collignon, 1972; Dejerine, 1892). Also, while reading is generally considered to be supported by processes that are left lateralised, some studies suggest that the processing of handwriting may be right lateralised and may occur together with face processing deficits (Barton et al., 2010; Hills, Pancaroglu, Duchaine, & Barton, 2015).

About the test: This test was devised for the purposes of the current study. On the first day of testing participants were asked to write a simple sentence taken from a level 1 passage in the Neale (Neale, 1999). Handwritten samples of the remaining sentences within this Neale passage were obtained. The participants’ writing was scanned into the computer and inserted as the second sentence within the Neale passage. The participants were presented with a level 1 passage from the Neale to read in four different handwritings, one of which was their own. Three measures were obtained; i) the time taken to read the passage, ii) whether the participant spontaneously recognised the handwriting as their own, and iii) whether they were able to identify the handwriting as their own upon forced choice.

2.4.3. Wayfinding Questionnaire: post-injury

Reason for inclusion: While the literature suggests that many patients with acquired prosopagnosia also have wayfinding problems, little is known about this relationship. The wayfinding questionnaire is designed to identify wayfinding problems after stroke. We have adjusted it into a pre- and post-injury version. 5 questions plus “Since my stroke/head injury it is more difficult for me to find my way and orientate myself”.

2.4.4. Synonym Judgement Task

Reason for inclusion: This test along with picture naming and WPM is one of the standard tests of semantic memory. This test can be used to explore even mild semantic memory problems (impaired accuracy on the hardest, lower frequency items).

About the test: The experiment has been used in many previous studies, including with other patient groups (Jefferies, Patterson, Jones, & Lambon Ralph, 2009), and healthy participants (Binney, Embleton, Jefferies, Parker, & Ralph, 2010). For each trial a target word is presented, alongside three choices. Participants are instructed to pick which of the choice items is associated with the target item. Stimulus presentation was adjusted so words are presented vertically rather than horizontally. Stimuli were presented visually and as spoken words, to avoid biasing against patients who struggled to read. The experimenter read each word out loud and pointed to each word on the screen (for this reason reaction times were not collected on this task). Stimuli vary both by imageability (high vs. low) and frequency (high, medium, low).

2.5. Tests that were excluded from battery due to time constraints

- Wechsler Abbreviated Scale of Intelligence: Vocabulary test
- BORB: Shape recognition and crowding
- Comprehensive Aphasia Test: writing
- Camel and Cactus
- Crowding – Quest
- TVA: Whole report
- Auditory Semantic tasks
- Warrington Recognition Test for Word and Faces
- Famous face-to-name matching
- Word-to-picture matching
### 2.6. Order of tests:

<table>
<thead>
<tr>
<th>Order</th>
<th>Test</th>
<th>Notes (e.g., testing conditions, equipment, response type)</th>
<th>Completion time (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Session 1</td>
<td>Background questionnaire (if not already completed)</td>
<td>Paper-and-pencil</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Handedness: Edinburgh short-form, 5 item (if not already completed)</td>
<td>Paper-and-pencil</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Depression: GDS-15</td>
<td>Laptop. Experimenter or patient responds on keyboard.</td>
<td>10</td>
</tr>
<tr>
<td>Session 1</td>
<td>Cognitive screening: Oxford Cognitive Screen</td>
<td>Paper-and-pencil</td>
<td>15</td>
</tr>
<tr>
<td>Session 1</td>
<td>Digit span forwards, backwards WAIS IV</td>
<td>Paper-and-pencil</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Basic motor response speed</td>
<td>Laptop. Subject responds SR box</td>
<td>3</td>
</tr>
<tr>
<td>Session 1</td>
<td>Face recognition and questionnaire (post-injury)</td>
<td>Laptop. Response sheet. Experimenter or patient responds on keyboard.</td>
<td>10</td>
</tr>
<tr>
<td>Session 1</td>
<td>WOF test (Words, objects and faces)</td>
<td>Laptop. Subject responds on SR box</td>
<td>25</td>
</tr>
<tr>
<td>Session 1</td>
<td>The Wayfinding Questionnaire (post-injury)</td>
<td>Laptop. Response sheet. Experimenter or patient responds on keyboard.</td>
<td>5</td>
</tr>
<tr>
<td>Session 1</td>
<td>Adult reading history questionnaire</td>
<td>Laptop. Experimenter or patient responds on keyboard.</td>
<td>10</td>
</tr>
<tr>
<td>Session 1</td>
<td>Writing CAT</td>
<td>Testing booklet. Response sheet for participant. Stopwatch</td>
<td></td>
</tr>
<tr>
<td>Session 1</td>
<td>Famous Face Familiarity: yes/no decision task</td>
<td>Laptop. Participant responds on SR box</td>
<td>10</td>
</tr>
<tr>
<td>Session 1</td>
<td>Object decision (object vs non-object)</td>
<td>Laptop. Participant responds on SR box</td>
<td>8</td>
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<tr>
<td>Session 1</td>
<td>Synonym</td>
<td>Laptop.</td>
<td>15</td>
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<tr>
<td>Session 2</td>
<td>Visual field testing</td>
<td>Desktop computer. Subject responds on keyboard.</td>
<td>5</td>
</tr>
<tr>
<td>Session 2</td>
<td>FrACT: Visual acuity</td>
<td>Desktop computer. Low light. Researcher responds on keyboard.</td>
<td>5</td>
</tr>
<tr>
<td>Session 2</td>
<td>FrACT: Contrast sensitivity</td>
<td>Desktop computer. Low light. Researcher responds on keyboard.</td>
<td>2</td>
</tr>
<tr>
<td>Session 2</td>
<td>Word reading, RT- voice-key: 3,5,7 letter words</td>
<td>Desktop. Low light. Dictaphone. Experimenter responds on response box.</td>
<td>10</td>
</tr>
<tr>
<td>Session 2</td>
<td>Picture naming</td>
<td>Desktop. Low light. Dictaphone. Experimenter responds on response box.</td>
<td>15</td>
</tr>
<tr>
<td>Session 2</td>
<td>Famous face naming</td>
<td>Desktop. Low light. Dictaphone. Experimenter responds on response box.</td>
<td>10</td>
</tr>
<tr>
<td>Session 2</td>
<td>Word reading, RT- voice-key: regular, irregular and non-words</td>
<td>Desktop. Low light. Dictaphone. Experimenter responds on response box.</td>
<td>15</td>
</tr>
</tbody>
</table>
### 3. Imaging protocol

The following scans are performed on all patients and on half of the controls (N=25):

- T1-weighted structural scan
- B0 Field Map
- Dual-echo EPI fMRI sequence
- Diffusion weighted imaging (b0 + 43 directions)

T1-weighted structural MRI scans are collected in order to characterise the patients’ brain lesions. The B0 Field Map scan is used to help improve the signal acquired from the functional localiser scan. Functional localiser scans are carried out to localise face and word selective regions in the brain. A custom dual-echo fMRI sequence is used for this purpose. Participants lie in the scanner and see pictures of unfamiliar faces, words, scrambled faces, and checkerboards, and are instructed to press a button when they see either a red dot or red letter (the main purpose of the task is to keep people awake) (Harris, Rice, Young, & Andrews, 2016). A dual-echo EPI sequence is used as opposed to a more traditional single-echo EPI sequence to get a better signal-to-noise ratio in the brain areas which are susceptible to signal distortion/noise, such as the anterior temporal lobes (where some of our patients have lesions) and the orbitofrontal cortices. This sequence has been used to great effect in both healthy participant samples and patient groups (Halai, Welbourne, Embleton, & Parkes, 2014). Finally, Diffusion Tensor Imaging is used to assess the integrity of white matter connections. The images are used to identify evidence of long-range “disconnections” caused by the PCA-strokes. More specifically, data from the localiser will be used to evaluate which brain regions are physically connected to the FFA and VWFA, and how these connections are disrupted by stroke. Imaging is not part of this PhD project and will therefore not be discussed further.
References


Supplementary Material: BoB Behavioural Test Battery


Non-published material:

Appendix F: Poster 1

Background

Face and words recognition has traditionally been thought to rely on highly specialised and relatively independent cognitive processes. Strong evidence for this has come from single case studies of patients with:

- pure prosopagnosia: a selective face recognition deficit
- pure alexia: a selective word recognition deficit

Recent theories, such as the many-to-many hypothesis (Behrmann & Plaut, 2013), suggest instead that the cognitive and cerebral processes underlying visual recognition are more distributed and interactive. While single case studies are well suited to investigate dissociations between deficits, larger groups of patients are needed to investigate associations predicted by a distributed model.

Aim of the study

The study aims to shed new light on the processes and cerebral architecture underlying visual recognition of faces and words. Some of the core research questions:

- Do face and word processing rely on processes that are largely independent or highly distributed and shared?
- What is the relationship between deficits in object, word or face processing and lower-level and intermediate visual perceptual deficits?
- Is there a relationship between premorbid reading skills and prosopagnosia following stroke?
- How do visual field defects affect higher-level visual perception?
- How are visual recognition and semantics related?
- Can reading be spared after a lesion in the left fusiform gyrus and can face recognition be spared after a lesion in the right fusiform gyrus?

Methods

70-100 patients
(stroke in posterior cerebral artery)

50 healthy controls
(matched as group for age and education)

Behavioural tests

All patients are assessed (>9 months post-stroke) a large battery of sensitive behavioural tests (see figure 1 for overview of functions assessed). Assessment of each patient carried out over 3 days (within maximum 3 weeks).

Imaging

- Structural T1 scan
- Functional localiser: faces and scrambled faces, words and checkerboards
- Diffusion tensor imaging (DTI) scan

What’s novel?

- Participants selected according to lesion localization, not according to symptoms → Expecting novel patterns of lesions and symptoms
- All participants assessed with the same wide range of functions with sensitive tests → Enabling direct comparison across subjects, which is often not possible across single case studies.
- Tests of face, word and object processing: Same level of processing tested across stimulus type.
- Large group of PCA patients included.

Status

- 25 patients tested (right lesions n = 6; left lesions n = 16; bilateral lesions n = 3)
- 3 control participants tested

International collaboration

Study design

University of Copenhagen
- Prof. Randi Starrfelt
- Ph.d. student: Julia Ro J. Robotham

University College London
- Prof. Alex Leff
- Postdoc: Sheila Kerry

University of Manchester
- Prof. Matt Lambon-Ralph
- Postdoc: Grace Rice

Back of the Brain Project

Introducing the Back of the Brain Project

Say hello to BoB

Ro J. Robotham1, Sheila Kerry2, Grace Rice3, Alex Leff2, Matt Lambon-Ralph3 & Randi Starrfelt1

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2Institute of Cognitive Neuroscience, University College London
3The Neuroscience and Aphasia Research Unit (NARU), University of Manchester

Figure 1: Behavioural test battery
Appendix G: Poster 2

Assessing Visual Perception: Towards a Systematic Approach

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Background
Visual perceptual deficits are common in neurological disorders:
- seen in around 30% of patients with acquired brain injury.
- also common in neurodegenerative disorders.
Can have significant negative effects on:
- activities of daily living, mental health and quality of life.
- general rehabilitation.
- performance on all neuropsychological tests using visual stimuli.
Visual perception should be assessed following brain injury. The literature does not provide a simple overview of tests available.

Aim
Create a framework that facilitates structured and systematic assessment of visual perceptual functions.

Method
- Visual perceptual tests and test batteries are identified in the literature.
- Tests and batteries are categorised according to their visual sub-processes.
- A simple visual framework is developed.

Conclusion
Assessment should also be carried out in the absence of visual perceptual complaints (insight often limited). Existing test batteries suffer from limitations:
- lack of norms
- too time-consuming
- only selected aspects of visual perception assessed
- include tests of functions that are theoretically relevant but that have limited clinical value
By combining individual sub-tests from different batteries, in-depth assessment is possible, but:
There is a need for a test battery enabling structured assessment of clinically relevant aspects of visual perception.
Appendix H: Poster 3

Comparing word and face recognition:
an insoluble conundrum

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Background
The relationship between face recognition and visual word recognition/reading has received increasing attention lately. One of the core research questions is: do face and word processing rely on processes that are:

- largely independent?
- or highly distributed and shared?

Studies using experimental, neuropsychological, and neuroimaging methods in both healthy and clinical groups have tried to answer this question. Conclusions are typically made based on comparisons between performances on tests of face and word processing. A test of object processing is often also included; as a control. Ideally, for comparisons to be made across categories, the tests should:

1. have similar task demands.
2. measure the same level(s) of processing.

Filling both criteria is more challenging than one may expect.

A simple framework
We propose a simple framework for broadly classifying tests according to the level of processing required: perceptual level, recognition level, and identification level (Figure 1 and Table 1). This can help ensure that tests of different stimuli assess similar levels of processing, enabling conclusions about the extent to which face and word processing rely on common mechanisms.

Figure 1: Framework for classifying tests of face, word and object recognition

<table>
<thead>
<tr>
<th>Level</th>
<th>Description</th>
<th>Typical Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Perceptual</td>
<td>Requires building but not storing a visual representation</td>
<td>Face perception, word perception</td>
</tr>
<tr>
<td>Recognition</td>
<td>Requires building and storing a short or long-term visual representation</td>
<td>Simultaneous face discrimination, delayed matching task</td>
</tr>
<tr>
<td>Identification</td>
<td>Requires access to stored semantic information about the stimulus</td>
<td>Single word reading (SWR), WLE</td>
</tr>
</tbody>
</table>

Table 1: Three levels of processing

Strategies that have been used
Having analyzed many studies comparing performances across categories, there are three commonly used strategies to select test paradigms:

- **Strategy 1**
  - Compare performance on typical tests of face processing to performance on typical tests of word processing (Figure 2).

- **Strategy 2**
  - Test the stimulus categories in the same experimental setup to ensure similar task demands (figure 3).

- **Strategy 3**
  - Compare typical effects found in normal participants or clinical groups with the different categories of stimuli (e.g., the face inversion effect and the word length effect) (Figure 4).

The strategies currently used are not satisfactory
When analyzing the three strategies described using the proposed framework, it becomes apparent that none of these strategies ensure that the same level of processing is being assessed across categories.

- **Strategy 1**: Commonly used reading tests are typically more semantic whereas the level of processing in typically used face recognition tests varies more.

- **Strategy 2**: Using the same experimental set-up, does not ensure that the same level of processing is being assessed. The semantic system is often highly involved in the word condition, but not in the other conditions.

- **Strategy 3**: Tasks used to assess face inversion effect and the word length effect are radically different, thereby making direct comparisons problematic.

Theoretical implication
To date, no test of face and word processing has been designed where the same experimental set-up has been used (ensuring similar task demands), while ensuring the same level(s) of processing are assessed. By analyzing the experimental paradigms used so far, it becomes apparent that differences in characteristics (visual and semantic) between faces and words as visual entities, make the problem of designing comparable tests seemingly impossible.

Recommendations
- Choose typical effects found in normal participants or clinical groups with the different categories of stimuli (e.g., the face inversion effect and the word length effect) (Figure 4).
- Choosing a test that requires similar task demands across categories, while ensuring the same level(s) of processing are assessed.

References
Behrmann & Plaut (2014), Cortex, 1102-1118.

Patient KH
Patient KH is a 65-year-old pure alexic stroke patient, who has participated in extensive testing in our lab (see poster 53. 4055). Depending on the test paradigm, he shows different patterns of deficits (Figure 4, 5 and 6, Table 3). Had the patient been assessed using the delayed matching task only (similar task demands across categories), he would have been considered to have preserved reading but impaired face recognition.

Table 3: KH overview of tests

<table>
<thead>
<tr>
<th>Task</th>
<th>Word processing</th>
<th>Face processing</th>
</tr>
</thead>
<tbody>
<tr>
<td>Single word reading (SWR)</td>
<td>*P &lt; 0.05, and **P &lt; 0.01. Crawford &amp; Howell's t-test</td>
<td>*P &lt; 0.05. Crawford &amp; Howell's t-test</td>
</tr>
<tr>
<td>Face inversion effect</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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Appendix I: Poster 4

Danish Reference Material for the Oxford Cognitive Screen: a stroke specific screening tool

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Background

• Every year, approximately 15,000 people have a stroke in Denmark.
• Cognitive deficits following stroke are common and have negative consequences on quality of life, return to work and likelihood of developing depressive symptoms.
• Important to identify cognitive deficits for appropriate interventions and care.
• Often MoCA used in Denmark, but:
  • Highly verbal
  • No assessment of individual cognitive domains
  • Some common stroke symptoms not assessed
  • Due to modest size of sample, cut-offs according to age and education not calculated.

Aim

Investigate whether the Oxford Cognitive Screen could provide a useful alternative to the MoCA, when screening for cognitive deficits following stroke in a Danish context.

Methods

Participants: healthy controls (N=91) (table 1)

• Danish as first language
• No neurological disorder
• No visual field deficit

Materials

• Montreal Cognitive Assessment (MoCA)
  • Dementia screening tool (Nasreddine et al., 2005), version 7.0 (Danish translation by Kirsten Abelskov)

• Oxford Cognitive Screen (OCS) – Dansk (figure 1)
  • Domain-specific cognitive screening tool
  • Symptoms common in stroke are assessed
  • Stroke-specific, aphasia / neglect friendly
  • 15-20 minutes completion time
  • Bedside assessment possible
  • Free
  • Cognitive profile for easy communication

Results

• OCS: Averages and cut-offs similar to Italian (N=489) and British (N=140) studies (table 2).
• MoCA: mean 26,22 (SD=2,44), 5th percentile 22,35.

Limitations

• Due to modest size of sample, cut-offs according to age and education not calculated.
• For some tasks: risk of over-diagnosing patients with low education and/or elevated age and underdiagnosing patients with high education and/or young age.
• The OCS is a screening tool and cannot identify all discrete deficits. It cannot replace a neuropsychological assessment.

Conclusions

• Results on OCS similar to international studies, increasing confidence of our results despite small sample.
• Results on MoCA suggest there are problems with cut-off of 25/26 currently used in Denmark.
• The OCS is useful for identifying patients in need of further evaluation and care.
• The OCS is a stroke specific screening tool for cognitive deficits that outperforms typically used screening tools developed for other patient populations.

It is free and takes 15-20 minutes to complete.

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