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Running Head: REHABILITATION OF FACE RECOGNITION IMPAIRMENTS

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Abstract

While much research has investigated the neural and cognitive characteristics of face recognition impairments (prosopagnosia), much less work has examined their rehabilitation. In this paper, we present a critical analysis of the studies that have attempted to improve face-processing skills in acquired and developmental prosopagnosia, and place them in the context of the wider neurorehabilitation literature. First, we examine whether neuroplasticity within the typical face-processing system varies across the lifespan, in order to examine whether timing of intervention may be crucial. Second, we examine reports of interventions in acquired prosopagnosia, where training in compensatory strategies has had some success. Third, we examine reports of interventions in developmental prosopagnosia, where compensatory training in children and remedial training in adults have both been successful. However, the gains are somewhat limited – compensatory strategies have resulted in laboured recognition techniques and limited generalisation to untrained faces, and remedial techniques require longer periods of training and result in limited maintenance of gains. Critically, intervention suitability and outcome in both forms of the condition likely depends on a complex interaction of factors, including prosopagnosia severity, the precise functional locus of the impairment, and individual differences such as age. Finally, we discuss future directions in the rehabilitation of prosopagnosia, and the possibility of boosting the effects of cognitive training programmes by simultaneous administration of oxytocin or non-invasive brain stimulation. We conclude that future work using more systematic methods and larger participant groups is clearly required, and in the case of developmental prosopagnosia, there is an urgent need to develop early detection and remediation tools for children, in order to optimise intervention outcome.

Keywords: Face recognition; prosopagnosia; neurorehabilitation; cognitive training; face processing.

The rehabilitation of face recognition impairments: A critical review and future directions

1. Introduction

Prosopagnosia is a cognitive condition characterised by a relatively selective deficit in face recognition. Traditionally the disorder has been described in a small number of individuals who acquire face recognition difficulties following neurological injury or illness, typically affecting occipitotemporal regions (de Renzi et al., 1994; Gainotti and Marra, 2011). Although acquired prosopagnosia (AP) in its purest form is a rare condition (Gloning et al., 1967; Zihl and von Cramon, 1986), many more individuals with brain damage are believed to experience moderate-to-severe face-processing deficits alongside other cognitive impairments (Hécaen and Angelergues, 1962; Valentine et al., 2006). Further, as many as 2.9% (Bowles et al., 2009) of the population may experience developmental prosopagnosia (DP) – an apparently parallel form of the disorder that occurs in the absence of neurological injury or lower-level visual deficits (e.g. Bate and Cook, 2012; Duchaine and Nakayama, 2005). While some people cope relatively well with prosopagnosia, it can have a devastating effect on an individual's everyday social and occupational functioning (Yardley et al., 2008). Hence, exploration of the remediation of prosopagnosia is an urgent clinical issue that, unfortunately, has received little attention to date. It is important to note that rehabilitation is not necessary in all cases of prosopagnosia –some people with DP cope relatively well, and many devise their own strategies to recognise the people around them (e.g., Fine, 2012). However, Yardley et al. (2008) note that the majority of their participants reported negative psychosocial experiences related to DP, particularly at a younger age. As such, investigations into the effectiveness of remediation techniques – especially those used in children – are important both on a theoretical and a practical level.

The few studies that have attempted to remedy face-processing deficits in individuals with AP or DP are summarised in Table 1. In the current paper, we present a critical review of substantive published attempts to rehabilitate AP and DP, examining both the design of each training programme and the research participants themselves, in an attempt to place the findings in the context of the wider neurorehabilitation literature. It has been argued that the main aim of neuropsychological rehabilitation is to reduce the impact of impairments on everyday living, whether through restoration of function or the adoption of coping strategies (Wilson, 2003). In the context of face recognition, rehabilitation may therefore encourage an individual to develop compensatory strategies that aid person recognition, or attempt to restore – or, in the case of DP, to develop – normal face-processing mechanisms via more extensive visuo-cognitive training (referred to as "remedial training" in this paper). Although the neurorehabilitation literature is vast, it has seldom been applied to disorders of face-processing. As such, current research offers little guidance as to which approach (compensatory or remedial) may be more effective in prosopagnosia, or the factors that may influence the effectiveness of each method. Therefore, the main aim of this review is to provide guidance on this issue.

< Insert Table 1 >

First, we address the question of whether the typical face-processing system retains neuroplasticity throughout the lifespan – in other words, is there evidence that the face-processing system might be able to learn or improve face-specific processing mechanisms at any point in time, or should prosopagnosia interventions focus primarily on critical periods of development or the development of compensatory strategies? Second, we examine

intervention studies in AP and DP, with a specific focus on factors that may affect success, including the nature of the disorder, the type of intervention, and individual differences between participants. Finally, we discuss future directions in the rehabilitation of prosopagnosia.

2. Does the typical face-processing system remain plastic throughout the lifespan?

The term "neuroplasticity" typically refers to a neural system's capacity to learn new skills or improve existing capabilities, either during normal development or after neurological damage (e.g. Huttenlocher, 2002). Traditionally, there have been two main theories on neuroplasticity (Thomas, 2003). The first proposes that an innate blueprint specialises cognitive systems for a particular function, which emerges during critical periods within development. This perspective suggests that once the relevant neural structures have been specialized for their purpose, any damage can only be overcome by the adoption of compensatory behavioural strategies. In face-processing, this might take the form of recognising people based on individual facial features, or using additional semantic cues during face encoding. In contrast, the other viewpoint proposes that the brain retains plasticity throughout the lifespan, and hidden reserves may aid the acquisition of new skills or compensate for damage – providing that appropriate intervention techniques are used. Drawing on the available neurorehabilitation literature, Thomas (2003) concludes that the brain's structures are not irreversibly determined by an innate plan, but plasticity is nevertheless limited. Further, these limits may fluctuate throughout development, and are not necessarily consistent across different neural systems. Therefore, before examining neuroplasticity in the context of prosopagnosia, it follows that neuroplasticity within the typical face-processing system should be examined. That is, is it theoretically possibly that face recognition skills can be improved at any point in the lifespan, or does research using neurotypical participants indicate that any plasticity in the neural face-processing system is short-lived following birth?

A dominant theory of the development of face-processing posits that crude brain circuits become specialized for face recognition in response to early visual experience with faces (the 'perceptual narrowing' hypothesis: Nelson, 2001). Evidence supporting this theory comes from findings that very young infants can discriminate between monkey and other-race faces, whereas older infants and adults no longer have this ability (e.g. Kelly et al., 2007; Pascalis et al., 2002). Although these findings suggest some plasticity in the face-processing system in the first few months of life, Nelson suggests that early specialization of neural tissue for face-processing may lead to a lack of plasticity in later years.

Behavioural studies tracking the development of face recognition skills also suggest that specialised face processing systems emerge early in life. In a review of developmental studies conducted to date, Crookes and McKone (2009) conclude that adult-like face-processing strategies are obtained by early childhood in qualitative if not quantitative terms, suggesting a window for plasticity only within the first years of life. For example, one key marker of mature face-processing skills is the ability to process faces on a holistic basis, taking into account the overall configuration of facial features and the spacing between them (Maurer et al., 2002). As Crookes and McKone note, evidence of holistic processing has been observed in children as young as 3 or 4 years using classical paradigms such as the face inversion effect (Sangrigoli and De Schonen, 2004), the composite effect (De Heering et al., 2007; Macchi Cassia et al., 2009a), the part-whole effect for upright but not inverted faces (Pellicano and Rhodes, 2003), and tests that assess sensitivity to spacing between facial features (McKone and Boyer, 2006; Pellicano et al., 2006). A second marker of adult-like face-processing skills is the "inner-feature advantage" whereby adults are more proficient at

recognizing familiar faces from the inner compared to the outer features (Ellis et al., 1979; Young et al., 1985) - a preference that has also been observed in children as young as 5 years of age (Wilson et al., 2007). Further, Pozzulo and Lindsay (1998) reported a meta-analysis that summarized findings from eye-witness studies that used children as participants. In agreement with the above studies, the authors noted that children as young as five years of age display adult-like performance in their ability to identify perpetrators from target-present (but not target-absent) line-ups. These studies therefore indicate that, despite evidence indicating a large increase in face recognition ability throughout childhood (presumably due to the need for more generalized mechanisms to develop), there is no qualitative change in face perception beyond 4-5 years of age. In fact, given increasing evidence that even infants are capable of holistic processing (Bhatt et al., 2005; Cohen and Cashon, 2001; Hayden et al., 2007) it is possible that face-processing skills are fully-developed at a very early age, implying a limit on plasticity beyond early childhood. This idea is supported by studies of adolescents and adults who were born with dense cataracts – despite the fact that the cataracts were removed before 7 months of age, participants show abnormal face-processing skills (Le Grand et al., 2001, 2004) but normal object discrimination (Robbins et al., 2010), indicating that early visual input is particularly important for the development of face-processing mechanisms.

While early visual input may be necessary for the initial development of face-processing mechanisms, it remains possible that these mechanisms can be refined or altered later in life. Despite evidence of early commitment to face-specific regions, neuroimaging studies suggest that the cortical face-processing system (Haxby et al., 2000; Gobbini and Haxby, 2007) continues to develop well into adolescence. For instance, Passarotti et al. (2003) found more diverse activation in the fusiform region for children as opposed to adults. Similarly, Gathers et al. (2004) reported that activation in the fusiform gyrus is not greater for faces compared with objects until 10 years of age, although they did note such activation more posteriorly in the inferior occipital region. Other studies suggest that both activation of the core face-processing system and connectivity between the different neural areas changes between the ages of 7 and 11 years (Cohen Kadosh et al., 2011, 2013). Event-related potential (ERP) components also continue to mature through late childhood into early adolescence: Taylor et al. (2004) reported that face inversion did not influence the face-specific N170 response until 8-11 years of age. While these findings raise the possibility that plasticity may remain in the face-processing system at least until adolescence, de Schonen et al. (2005) warn that plasticity during typical brain development is most likely due to modification of synaptic organization, rather than redistribution of face-processing mechanisms to other cortical regions. Hence, these findings do not imply that other neural areas can simply take over face-processing following brain damage.

There are also several lines of evidence that support the idea that the face-processing system may retain some plasticity even in adulthood. For instance, Germine et al. (2010) tested over 60 000 participants aged from pre-adolescence to middle-age on their ability to learn new faces. In three experiments, Germine and colleagues found that face learning ability improves up until the age of 30, although the recognition of inverted faces and name recognition peak at a much earlier age. Other evidence supporting plasticity in the adult face-processing system comes from studies of the other-race effect, or the finding that we are better at recognizing faces from our own race than those from other races (e.g. Malpass and Kravitz, 1969). Critically, one of the explanations for this effect is based on the presumption that the phenomenon reflects the lack of experience the viewer has had with faces from the other race (Hancock and Rhodes, 2008; Meissner and Brigham, 2001). Although the effect has been

observed in infants as young as three months of age (e.g. Kelly et al., 2005, 2007; Sangrigoli and de Schonen, 2004), evidence suggests it remains plastic and reversible even in adulthood. Specifically, Hancock and Rhodes (2008) found a reduced other-race effect, accompanied by increased holistic processing, for participants who reported higher levels of contact with another race (see also Meissner & Brigham, 2001; Rhodes et al., 2009; Sangrigoli et al., 2005; and de Heering & Rossion, 2008; Kuefner et al., 2008; Macchi Cassia et al., 2009b, for similar studies of the "own-age bias"). More interestingly, though, training can improve recognition of other-race faces. Tanaka and Pierce (2009) trained Caucasian students to discriminate between African-American and Hispanic faces, and reported an improvement in the recognition of novel stimuli of the same race, along with changes to the N250 ERP component to the other-race faces (see also Elliott et al., 1973; McKone et al., 2007). Notably, McKone et al. (2007) showed normal levels of holistic processing for trained cross-race faces, indicating that training can have an effect on the manner in which faces are processed, not just the accuracy with which they are identified.

In sum, behavioural and neural investigations using typical participants suggest that the face-processing system may retain some plasticity throughout childhood and into adulthood. This raises the possibility that it may be possible to rehabilitate face recognition deficits, at least in some circumstances.

3. Neurorehabilitation of acquired prosopagnosia

Anderson et al. (2001) outline two potential means of recovery following brain injury: the spontaneous healing of damaged tissue may lead to reactivation of pre-existing neural pathways, or anatomical reorganization may allow different neural areas to take over the behavioural function of the damaged area. Given evidence that the face-processing system retains some plasticity in adulthood, remediation of face-processing skills following neurological injury may be possible. However, as with any other acquired deficit, it is likely that a number of general constraints will influence the success of intervention. These might include the age at which the lesion was acquired, the severity of the lesion, and the precise functional implications of the lesion. These factors may dictate the type of intervention that is suitable for the individual, and whether it should focus on compensatory rather than remedial training.

3.1. Timing of injury

There is a general view that the developing brain has greater plasticity than the adult brain: Huttenlocher (2002) concludes that, across the neurorehabilitation literature, neuroplasticity in adults has generally been found to be lower than in children. Further, in early development there are higher levels of some genes and proteins that are required for neuronal growth, synaptogenesis and the proliferation of dendritic spines, and these levels significantly reduce with aging (Huttenlocher and Dabholkar, 1997). It therefore follows that compensatory reorganization and transfer of function is more likely after early brain injury (e.g. Elbert et al., 2001).

If plasticity in the developing face-processing system is greater in childhood than in adulthood, one would predict that spontaneous recovery might occur in children to a greater extent than in adults. There have been some instances of recovery of prosopagnosia in adults in the absence of any formal attempts at rehabilitation (e.g. Lang et al., 2006; Malone et al., 1982), but this is by no means consistent: many other cases have found no evidence of improvement or recovery over time (e.g. Sparr et al., 1991; Ogden, 1993; Spillman et al., 2000). However, work examining the effects of peri- or prenatal injuries on the development

of face recognition skills suggests that the infant system may be more plastic following damage than the adult system. For instance, Mancini et al. (1994) found that perinatal unilateral lesions only had mild effects on later face-processing abilities in children ranging in age from 5 to 14 years. In fact, less than half of the children were impaired at face- or object-processing, and face-processing deficits were no more common than object-processing deficits following a right hemisphere lesion.

Although these studies suggest some level of neural reorganisation is possible following early damage (see also Ballantyne and Trauner, 1999), it is important to note that age of injury does not have a straightforward relationship with plasticity in the face-processing system. de Schonen and colleagues (2005) reported a similar study with a group of 5- to 17-year-olds who acquired unilateral posterior lesions involving the temporal cortex during the pre-, peri- or postnatal period. In general, deficits in low-level configural processing were related to face-processing deficits in patients with a lesion acquired before or at birth, when visual experience starts. These findings converge with other work in the neurorehabilitation literature indicating that there may be a U-shaped effect of damage, with prenatal injury leading to the poorest outcome (i.e., with no evidence of transfer of function from the damaged site to intact tissue: Anderson et al., 2001); greater plasticity in early childhood leading to cortical reorganization and greater sparing of function; and more limited plasticity in late adolescence and adulthood. In a similar vein, advanced age at the time of injury may result in less complete recovery compared to younger persons with comparable injuries (Katz and Alexander, 1994). However, the mechanisms of this phenomenon are not known, and it may simply be that increasing age leads to a reduced capacity for compensation or reduced cognitive reserve (Lye and Shores, 2000) – in other words, a more general cognitive decline due to ageing may make it more difficult to relearn old skills or acquire new compensatory strategies.

Another factor that should be taken into account when considering age of injury is the extent of the lesion. Paediatric research has indicated that children with generalized cerebral insult can exhibit both slower recovery and poorer outcome than do adults who suffer similar insults, possibly because attention, memory and learning skills have not been fully developed (Hessen et al., 2007). Without these capacities, the child does not have the tools to efficiently acquire new abilities and cannot progress along the normal pathway of cognitive development.

In sum, evidence from lesion studies suggests that early neurological damage may be more amenable to rehabilitation, but this is modulated by complex interactions with the exact timing and extent of the damage. Currently it is difficult to relate this directly to the prosopagnosia rehabilitation literature, as there is only one study that has attempted to remedy AP in childhood. Ellis and Young (1988) studied an 8-year-old child (KD) who acquired prosopagnosia after anaesthetic complications damaged the lateral third and fourth ventricles at three years of age (see Table 1). The authors suggest that a persistent left-sided motor weakness implied a right hemisphere lesion, whereas initial loss of vision following the incident suggested bilateral occipital damage. She also had object agnosia, and the underlying deficit seemed to be an inability to construct adequate representations of visual stimuli. The researchers designed a remedial training programme that required KD to complete four tasks over a period of 18 months, including (1) simultaneous matching of photographs of familiar and unfamiliar faces, (2) paired discriminations of computer-generated schematic faces, (3) paired discriminations of digitized images of real faces and (4) the learning of face-name associations. Unfortunately, none of the programmes brought about

an improvement in KD's face-processing skills. It is unclear why this programme failed to work, although it is likely that the extensive bilateral damage may have prevented any gains (see section 3.2). Notably, this is the only study to date that has attempted to remedy AP acquired as a child, *and* the only study to attempt rehabilitation of a child with AP. As such, it is difficult to assess whether the lack of improvements following this intervention relate to the timing of the injury (3 years of age) or the timing of the intervention (8 years of age), or to comment on the cognitive characteristics/skills that may impact the success of the intervention (e.g., co-occurring object agnosia).

While age of injury may be an important determinant of the success of rehabilitation in AP, the timing of the intervention relative to the injury could also be an important consideration when planning interventions. For example, evidence from the stroke literature suggests that the speed of intervention following the cerebral incident may be fundamental for success. Some studies propose that there are parallels between plasticity mechanisms in the developing nervous system and those occurring in the adult brain immediately following stroke, but that this plasticity diminishes quickly (Biernaskie et al., 2004; Brown et al., 2009; Carmichael et al., 2005). This indicates that the brain may be most receptive to interventions immediately after a stroke, and suggests that early intervention could be crucial in these cases. However, it is currently unknown whether this temporarily increased plasticity extends to (a) the face-processing system, and (b) prosopagnosia acquired from insults other than stroke; it is also unclear whether it interacts with the age of the patient or other factors such as lesion location or severity.

3.2. Lesion size and location

Many causes of the lesions that bring about AP have been reported, including stroke, carbon monoxide poisoning, temporal lobectomy, encephalitis, neoplasm and head trauma. Further, recent reports have described cases of AP alongside degenerative conditions such as frontotemporal lobar degeneration (Josephs, 2007) and posterior cortical atrophy (McMonangle et al., 2006; Sugimoto et al., 2012), and after temporal lobe atrophy (Chan et al., 2009; Joubert et al., 2003). With such a wide range of preceding causes, attempts to rehabilitate AP must take into account the extent and location of neurological damage, and in particular how different patterns of damage may be associated with different deficits. For example, some recent detailed analyses indicate that the primary site of damage in most cases is to posterior regions of the brain (e.g. Arnott et al., 2008). However, damage to more anterior regions has been reported to bring about "prosopamnesia", a condition in which patients retain the ability to recognize faces that they knew before the neurological accident, but cannot create stable representations of new faces in memory (e.g. Crane and Milner, 2002). As no attempts have been made to rehabilitate prosopamnesia, it is unknown whether one type of impairment is more amenable to intervention.

Lateralisation of the lesion is another potentially important consideration. It was traditionally thought that AP results from unilateral damage to the right hemisphere, particularly the right occipitotemporal area. In line with this hypothesis, de Renzi et al. (1994) reported unilateral occipitotemporal lesions in three cases of AP, and cited 27 previously reported cases that presented with similar damage. However, some reports suggest the disorder can also result from unilateral left hemisphere lesions (Barton, 2008; Mattson et al., 2000), although de Renzi et al. (1987) suggested that prosopagnosia resulting from left hemisphere lesions can result in a more variable pattern of symptoms, and Gainotti and Marra (2011) suggest that AP cases involving left and right hemisphere lesions present with different patterns of functional

impairment. This suggests that right and left hemisphere cases may warrant different methods of intervention (see section 3.3).

AP has also been reported in the context of bilateral damage (e.g. Barton et al., 2002; Boutsen and Humphreys, 2002; Damasio et al., 1982). Some authors have suggested that unilateral lesions bring about more selective impairments in face-processing, whereas bilateral lesions cause more extensive disruption (Boeri and Salmaggi, 1994; Warrington and James, 1967). This latter suggestion seems logical, given that, when only one hemisphere is affected, it is plausible that neural areas in the undamaged hemisphere might compensate for lost abilities at least to some degree; whereas no such compensation can occur in individuals with damage to both sides of the brain. Indeed, in the more general neurorehabilitation literature, functional plasticity is generally not observed in cases of bilateral damage, and greater damage tends to lead to worse outcomes. Broadly speaking, plasticity is most associated with focal lesions where true recovery with relatively little compensation is possible, presumably because some of the tissue that is crucial for function is unaffected by the lesion (Moon et al., 2009). While large focal lesions may also be associated with good recovery, this tends to only occur when damage is unilateral.

When looking at instances of spontaneous recovery from AP, there is some indication that this occurred following unilateral (Glowic and Violon, 1981; Lang et al., 2006) rather than bilateral (Sparr et al., 1991; Ogden, 1993) damage. When it comes to formal interventions (summarized in Table 1) two of the three AP studies that have reported some success involve patients with unilateral damage (i.e. Polster and Rapscak, 1996; Francis et al., 2002); the other study reporting improvement involved a patient with bilateral damage that did not consistently affect the same areas of the brain (Powell et al., 2008). The two interventions that failed to show improvement (Ellis and Young, 1988; De Haan et al., 1991b) both involved patients with apparently more extensive bilateral damage.

3.3. Identifying the functional impairment

Initial cognitive assessments are required to inform the design of an intervention programme, although previous attempts at cognitive neuropsychological rehabilitation have often failed to follow this principle (Hillis, 1993; Wilson and Patterson, 1990). Fortunately, we have a relatively sophisticated understanding of the cognitive and neural underpinnings of the face-processing system, and dominant models of face recognition have traditionally been used to interpret cases of prosopagnosia and to guide intervention strategy. Traditionally, the face-processing system has been viewed as a sequential and hierarchical multi-process system, where impairment can occur at a variety of stages (Bruce and Young, 1986: see Figure 1). Specifically, an initial stage of early visual analysis is followed by "structural encoding", where view-centred representations (used to perceive changeable aspects of the face, such as emotional expression) are transformed into viewpoint-independent representations (used to perceive unchangeable aspects of the face – most notably identity). The face recognition units (FRUs) compare all stored representations of familiar faces to an incoming percept. If a match is achieved, access to semantic information is provided by the relevant person identity node (PIN), culminating in retrieval of the person's name. Although these processes are widely distributed across many neural systems that work in concert to process faces, specialized anatomical structures have been identified that largely map onto the functional stages proposed in the cognitive model (Haxby et al., 2000: see Figure 1).

< *Insert Figure 1* >

The modular model permits disruption either to specific sub-processes, or to the connections between different units. The sequential nature of the model assumes that processing cannot be continued (at least at an overt level) past a damaged stage. Thus, prosopagnosia may result from three loci of damage within the framework: first, an AP may be unable to construct an adequate percept of a face, which would affect all later stages of processing (i.e., they would be unable to recognize a face as familiar or identify it; e.g., patient HJA: Humphreys and Riddoch, 1987; patient BM: Sergent and Villemure, 1989); second, an AP may be able to achieve a normal face percept but cannot access stored face memories (the FRUs) – in this case, they would be unable to ascertain familiarity or identity (e.g., patient LH: Etcoff et al., 1991; patient NR: De Haan et al., 1992); or third, an AP may be able to perceive faces and make familiarity judgments, but fail to access person-specific information or PINs – in this case, they would achieve a normal face percept and a sense of familiarity with a face, but identification (i.e., access to any semantic information about the person) would remain poor (e.g., patient ME: De Haan et al., 1991a).

In the majority of cases reported in the literature, patients with AP retain the ability to recognise people on the basis of other, non-face cues (e.g., body, voice). In some cases, however, impairments in face recognition are a subset of a more general person recognition problem – this is often associated with damage to the right anterior temporal lobe (Gainotti, 2013). In other words, these cases represent a subtly different type of disorder – one of semantic memory. Various interpretations of the exact nature of semantic disorders of this type exist, including impaired overt access to an output from semantics (Hanley et al., 1989), inability to use a 'common access point' to gain semantic information (De Haan et al., 1991a), actual loss of person-based semantic knowledge (Evans et al., 1995; Laws et al., 1995), and damage to a specialised semantic store that contains information about singular objects (Ellis et al., 1989).

It therefore follows that an initial assessment should identify the functional locus of the impairment – be it perceptual, mnemonic, or a more general semantic memory problem – and training should be tailored to that weakness. Several cases in the AP rehabilitation literature demonstrate the importance of tailoring training programmes to the locus of the deficit. Most strikingly, Francis et al. (2002) created a number of therapy tasks tailored to patient NE, who had deficits at both structural and semantic levels, and/or deficits in the access links between structural and semantic knowledge. In three studies, the authors demonstrated that therapy was effective when it emphasized semantic information about people, and linked this knowledge to visual representations (imagery or photographs of faces); whereas therapy directed at processes that were not underpinning the impairment (i.e., name retrieval) was unsuccessful. In another case, Powell et al. (2008) investigated the rehabilitation of face recognition deficits in 20 adults who presented with a broad range of cognitive impairments following brain injury. The participants completed three training programmes targeted at the recognition of unfamiliar faces, comprised of (1) a semantic association technique that provided additional verbal information about faces, (2) caricatured versions of target faces for recognition, and (3) a part-recognition technique that drew participants' attention towards distinctive facial features. The patient group as a whole showed small improvements in each of the three training conditions compared to a control condition where participants were simply exposed to faces. However, when the techniques were applied to a single case of profound acquired prosopagnosia (patient WJ, described in McNeil and Warrington, 1993; see Table 1), little or no improvement was observed following the semantic association and caricaturing programmes, whereas the part-recognition technique yielded 25% greater accuracy than the control condition. This result may be explained by focussing on the

functional locus of impairment: WJ was impaired at the level of structural encoding, and relied on a feature-by-feature processing strategy that could be boosted by compensatory training. In some ways this is a surprising finding given that many prosopagnosics adopt this strategy in everyday life, and one might expect that WJ would naturally be using the technique even in the "simple exposure" condition. Nevertheless, this finding suggests not only that part recognition may be an effective method of circumventing damage to the typical face recognition system, but also that training in use of the technique may further boost a compensatory strategy that many individuals with prosopagnosia naturally adopt.

Clearly though, regardless of whether training is targeted at the impairment itself, other influences may prevent training success (e.g., KD, Ellis and Young, 1988). For instance, different levels of impairment may be more or less amenable to treatment: a number of authors have argued that prosopagnosia arising from perceptual deficits is most resistant to treatment and also least likely to show treatment generalization effects (Ellis and Young, 1988; Francis et al., 2002; Wilson, 1987). Polster and Rapcsak (1996) examined the effects of "deep encoding" – that is, incorporating personality judgements or providing names and other semantic information at the point of encoding – in patient RJ. They found that RJ, who showed face perception impairments, did not benefit from "shallow" encoding instructions to focus on facial features, yet performed relatively well with "deep" encoding instructions where he was required to rate faces in terms of their personality traits or was provided with semantic or name information during the study phase. The authors suggest that semantic information may aid recognition memory by establishing additional visually derived and identity-specific semantic codes. However, the gains did not generalize to novel viewpoints of the learned faces, and the authors conclude that the patient simply could not compensate for his inability to construct abstract structural codes that normally allow faces to be recognized from different orientations. Hence, even training in compensatory behavioural mechanisms could not circumvent the severity of the patient's face perception impairment.

While perceptual difficulties may well contribute to intervention success, it is of note that another study failed to rehabilitate an AP adult with higher-order impairments, patient PH. PH had profound face recognition impairments, but was found to display some covert recognition on several behavioural tasks, indicating he had a higher-level impairment affecting the FRUs or PINs, or the connection between them. Based on the knowledge that PH was capable of face recognition on an unconscious level, De Haan, Young and Newcombe (1991b) used a category-presentation method to try to improve the patient's face-processing skills. Specifically, PH was presented with the occupation performed by a set of famous people, and was asked to subsequently recognize their faces. Unfortunately, PH was only successful in recognizing faces from one of the six occupational categories that was used in the study, and the improvement was not maintained in a follow-up test two months later. This does not suggest that higher-order impairments cannot be remedied, but it does emphasise that, as discussed above, other factors such as age and lesion severity may contribute to the success of rehabilitation – it is pertinent to note that PH was an adult who had experienced bilateral damage to the temporo-occipital junction, and he did present with some perceptual impairments (see Table 1).

Finally, some cases of AP present with damage to more than one sub-process of the theoretical model. Francis et al. (2002) suggest that, when a patient's deficit is due to multiple impairments, intervention must target each of these in order for improvement to occur. For example, in their investigation described above, the authors found that therapy targeted at

only one of NE's deficits (the semantic problem) without considering the other (the prosopagnosia) was ineffective.

3.4. Implications for intervention: Compensatory or remedial training?

One of the critical debates in neurorehabilitation is concerned with whether training should encourage the formation of behavioural compensatory mechanisms, or attempt to strengthen normal behavioural mechanisms (remedial training). There has been only one attempt to restore normal processing in a case of AP to date, which unfortunately was not successful (KD, Ellis and Young, 1988). Clearly, no conclusions can be drawn on the utility of remedial methods for acquired cases on a single case alone, particularly given the unusual characteristics of the case (i.e. the age of acquisition, treatment option, and lesion size and location: see section 3.2).

While attempts at remedial training are currently very limited, three of the four published studies examining the use of compensatory strategies in AP report some success (see Table 1). It is of note that two of these studies describe individuals with similar perceptual deficits in face-processing, yet found success using different techniques. While Powell et al. (2008) found a benefit of part-based but not semantic encoding for WJ, Polster and Rapscak (1996) found a greater benefit for semantic or "deep" encoding than part-based encoding for patient RJ. It is unclear why featural and not semantic training helped WJ whereas the reverse pattern was observed in RJ, but these reports suggest both techniques may be beneficial, albeit for different individuals.

Of the studies presented in Table 1, only one of the four compensatory training studies had no effect - the study presented by De Haan et al. (1991b). Pertinently, the patient described in this study differs from those in the other studies, as they had a severe mnemonic rather than perceptual difficulty, and had also suffered bilateral damage. Based on the limited available evidence, compensatory training therefore appears to be more successful in AP than remedial techniques. Yet, further research is clearly required to examine the utility of remedial training in this form of the condition, and to assess which factors may influence the success of various training methods – for example, perhaps remedial training is more effective for patients with unilateral lesions, or for those with mnemonic deficits. Indeed, research into face-name encoding in Alzheimer's disease has had some success with remedial mnemonic techniques such as errorless learning and spaced retrieval (e.g., Haslam, Hodder, and Yates, 2011), but these techniques have not yet been applied in mnemonic cases of AP.

Understanding the conditions in which remedial techniques are effective is particularly important given that the wider neurorehabilitation literature suggests their benefits are larger than those of behavioural compensation (e.g., Sitzer et al., 2006). Within the AP literature, compensatory techniques show some limitations: NE (Francis et al., 2002) showed significant gains following training, but despite her success in the laboratory, she continued to encounter substantial problems in everyday life. She interpreted this as a case of competing demands – she was using a highly contrived method for remembering and recognizing new people, as well as coping with more general memory deficits. Such instances highlight the limitations of compensatory training, and should remedial training prove effective for at least some cases of AP, this may be a preferable option in terms of outcome.

4. Developmental disorders

4.1. DP and neuroplasticity

While we do not yet have a complete understanding of the genetic, neurological and cognitive underpinnings of DP, it is viewed by most as a parallel disorder to AP. Yet, some caution should be exercised in application of the principles of neurorehabilitation discussed above to the developmental form of the condition. Thomas (2003) notes that developmental disorders represent the limits of plasticity, given that spontaneous reorganization and compensation during the natural developmental process do not overcome whatever abnormalities are underpinning the condition, as they may do following focal damage in the peri- or postnatal period (e.g. Mancini et al., 1994). Granted, it would be very difficult to actually find any cases of spontaneous recovery in DP, and this is further complicated by our limited understanding of the developmental trajectory of the condition and the existence of any early biobehavioural indicators. Nevertheless, the persistence of deficits in developmental disorders suggest atypical limitations on plasticity rather than focal damage, perhaps because disruption to early brain development alters low-level neurocomputational constraints, which prevent certain neural regions from acquiring normal specialized functions (Thomas and Karmiloff-Smith, 2003). It has been suggested that DP can be attributed to a failure to develop the visuo-cognitive mechanisms required for successful face recognition (Susilo and Duchaine, 2013), although it is unclear whether this comes about via genetic influences (Kennerknecht et al., 2006) or unrelated neurological abnormalities (e.g. Behrmann et al., 2007; Garrido et al., 2009). Importantly, while there is some evidence for a genetic factor in DP, Pennington (2001) argues that the correspondence between genes and the complex behavioural phenotypes observed in heterogeneous disorders such as DP is many-to-many rather than one-to-one. Hence, it is unlikely that a specific gene or set of genes exists for certain cognitive functions, including face-processing.

Understanding the underpinnings of DP is an important issue when it comes to the design of intervention programmes: Karmiloff-Smith and colleagues warn that apparently normal behaviour in developmental disorders may be achieved by compensatory strategies that obscure underlying atypical processes (Karmiloff-Smith et al., 2002). In the context of face-processing this is evident in Williams Syndrome, a chromosomal disorder where face recognition skills are apparently normal (e.g. Wang et al., 1995), yet are underpinned by poor configural processing mechanisms (Karmiloff-Smith et al., 2004). It is also clear that individuals with DP develop complex and intriguing compensatory strategies that permit them to disguise their face recognition impairment in many real life scenarios (e.g. Yardley et al., 2008), and it remains unclear whether these techniques can sometimes obscure impaired processing strategies on behavioural tests of face and object processing. Thus, an important implication for the design of intervention programmes is that apparently specific cognitive deficits in developmental disorders do not necessarily imply a specific and localized site of neural impairment as has traditionally been observed in cases of adult brain damage.

This latter point has important implications for the notion that training should target the locus of functional impairment (see section 3.3). Several authors have attempted to interpret DP within the same theoretical framework that has traditionally been used for AP (e.g. Bruce and Young, 1986), and have used these findings to subsequently inform their rehabilitation programmes (e.g. Brunsdon et al., 2006; Schmalzl et al., 2008). However, some caution should be exercised when applying developmental deficits to adult frameworks of normal functioning. The traditional cognitive neuropsychological approach adopts the logic that implications about cognitive structure can be derived from the patterns of behavioural impairment that are observed in adults with acquired brain damage – for instance, the assumption that particular cognitive systems have modular structures allows for the possibility that highly selective patterns of impairment implicate relative independence of

different sub-processes. Interpretation of apparently similar patterns of deficits in developmental disorders is tempting, particularly as one might infer that specific impairments in acquired and developmental cases correspond to acquired damage to a particular module in the former, and failure to develop that module in the latter (notably, Temple, 1997, offers just such a characterisation for cases of DP). Yet, this inference is controversial, and some researchers have argued that development itself violates the basic assumptions of classic cognitive neuropsychological models, and there is no reason to suppose that abnormalities in development lead to the production of a cognitive system that simply maps onto the fully developed system (Bishop, 1997; Karmiloff-Smith, 1997).

Alternative explanations for DP may be found in the neurodevelopmental theories described in Section 1. For example, one might assume that the basic apparatus for the face-processing system are present, but an abnormality in development has prevented these brain areas from becoming specialized for faces. One theory that adopts this notion is the amygdala/fusiform modulation model (Schultz, 2005), which proposes that the preference for face-like stimuli seen in newborn infants is underpinned by functions in the amygdala that draw attention to social stimuli. This increased social attention is thought to consequently provide the scaffolding that supports social learning and modulates activity in the critical face-processing area of the brain, the fusiform gyrus (see Figure 2). This model has been used to explain the underpinnings of face-processing and socio-emotional deficits in autism spectrum disorder (ASD), based on the premise that faces have less emotional salience for these individuals.

< Insert Figure 2 >

The theory that face-processing deficits in ASD stem from a lack of social interest in faces has informed the development of face training programmes, such as the *Let's Face It* package (Tanaka et al., 2003). *Let's Face It* is a series of computerized games that target the child's ability to attend to faces, in addition to identity and expression recognition skills. Some gains have been noted in ASD participants following participation in the programme (Tanaka et al., 2010), although it is unlikely that similar gains would result in DP given the proposed visuo-cognitive rather than socio-attentional underpinnings of the condition (e.g. Duchaine et al., 2010). Although we do not have a clear understanding of the actual underpinnings and developmental trajectory of DP, the evidence from the ASD literature suggests that intervention can initiate specialization within a crude face-processing system, and that there may be potential for remedial training techniques in developmental conditions.

4.2. Compensatory or remedial training?

The more general neurodevelopmental literature casts doubt on the potential for remedial training in developmental disorders. For instance, Thomas (2003) concludes that only compensatory changes can take place in developmental disorders, as underlying abnormalities are built into the relevant neural structures preventing experience-dependent plasticity. De Haan (2001) presents an example of this argument using a group of individuals with ASD, none of whom could categorically perceive facial expressions. Yet, only those participants with lower IQs appeared to be impaired on an expression-recognition task, indicating that the individuals with higher IQs were using compensatory strategies to achieve good recognition by other means. She therefore allows that there is "a degree of plasticity in the developing system that allows for development of alternative strategies/mechanisms in face-processing" (p. 393), but little to no opportunity for remediation.

In the DP literature, there have been two attempts to improve face recognition via compensatory strategies, and two to remedy normal face-processing strategies (see Table 1). First, Brundson and colleagues (2006) attempted to improve face recognition skills in an eight year-old child (AL), who had problems perceiving and recognizing faces. The researchers gave AL a set of 17 personally known faces (i.e. those of friends and family) to learn on stimuli cards, while his attention was drawn to distinguishing features of the faces. AL continued training until he recognized all the faces in four consecutive sessions, which occurred after 14 sessions within a one-month period. A similar technique was adopted by Schmalzl and colleagues (2008), in their work with K, a four-year-old girl with DP. K achieved 100% accuracy in four consecutive sessions after nine attempts at training, and eye movement recordings indicated that she spent a longer time viewing the inner facial features after training. Both children reported benefits to their everyday recognition of the trained faces, although the benefits of training did not generalize to untrained faces in AL (generalization was not tested in K).

On the other hand, DeGutis and colleagues (2007) described a remedial training programme that suggests normal networks can be strengthened in DP. They report the case of an adult with DP, MZ, who had severe impairments in face perception. The training task was administered over 14 months in two separate intervals. Training required MZ to perform a perceptual classification task repeatedly over large numbers of trials. Specifically, facial stimuli were adjusted to vary in 2mm increments according to eyebrow height and mouth height. MZ was required to classify each face into one of two categories: those faces with higher eyebrows and lower mouths, and those faces with lower eyebrows and higher mouths. After training, behavioural evidence indicated that MZ's face-processing ability improved on a range of behavioural tasks. However, the most pertinent findings of the study came from changes in neurophysiological measures that were taken before and after training. Specifically, the authors used electroencephalography to investigate whether MZ displayed a selective N170 response for faces compared with watches. Although this face-selective component was not evident before training, its selectivity after training was normal. Further, levels of functional connectivity between key areas of the neurological face-processing system (see Figure 1) were increased after training. The authors suggested the training task was likely successful because it allowed MZ to become sensitive to spacing differences around the eye region and nose/mouth region and encourage her to integrate the spacing of these features into a coherent representation of the face. This gain was specific to training with upright faces: 8000 training trials with inverted faces improved MZ's ability to classify inverted faces but did not improve her performance with upright faces. However, there are some important caveats to these findings. MZ showed limited maintenance of training gains: she reported that the behavioural benefits faded after a few weeks without training, and post-training measures showed that her face-specific N170 had reverted back to its pre-training lack of face sensitivity after 15 weeks without training. Notably though, when the authors attempted to retrain MZ 15 weeks after training stopped, fewer trials were required than in the initial training to restore her improved performance on the assessment tests.

These findings were given weight by DeGutis et al. (in press) who showed that holistic processing improved in 13 out of 24 DPs who completed the same training programme over a three week period. Interestingly, the DPs who responded better to training only differed from those who achieved little gains according to the CFMT (a test of face memory: Duchaine and Nakayama, 2006) and not tests of face perception. In fact, the DPs who responded most to training were initially poorer at the CFMT (i.e. their prosopagnosia was more severe), although this comparison was not significant when a post-hoc correction was applied.

In sum, while at least some success was achieved in all four DP studies reported to date, it is difficult to draw general conclusions on the utility of each technique, particularly given the differences in age between the participants. The next section evaluates the factors that may have influenced treatment outcome in the studies described above.

4.3. Other influences on treatment outcome in DP

In the AP literature, a number of authors have argued that level of impairment in prosopagnosia is an important factor in treatment outcome, and particularly that prosopagnosia arising from perceptual deficits is more resilient to intervention and generalization (Ellis and Young, 1988; Francis et al., 2002; Wilson, 1987). Although it is currently unclear whether DP can also be partitioned into different functional subtypes, some individuals with DP do appear to present with deficits in face perception, whereas others do not (e.g. Bate et al., 2009). Interestingly, the two compensatory training studies used children who did have impairments in face perception, and while there was little evidence of generalization to other faces (analogous to the findings in the AP literature), the gains did translate to everyday life. These studies demonstrate that, in DP, the recognition of a set of familiar face photographs can be improved with relatively little but precisely targeted training, even in the context of severe face perception impairments. Perhaps more strikingly, everyday gains were also noted in the individual reported by DeGutis et al. (2007), who also had a severe face perception impairment. This finding indicates that it is possible to apply remedial programmes to individuals with perceptual impairments, at least in adults with DP. Critically, DeGutis et al. (in press) found that larger training gains appear to be associated with poorer face recognition performance, and were not related to perceptual abilities.

Given that DeGutis et al.'s (in press) remedial training programme was not successful in all DPs, it is likely that different subtypes of the condition are better suited to particular training methods. As only one (unsuccessful) remedial programme has been trialled with an AP participant, it remains unclear whether (a) DP is simply easier to treat than AP using remedial training, (b) perceptual deficits are not as severe in DP as in AP, (c) the methods used in the DP studies are simply more effective than those employed in the AP studies, or (d) the nature of the lesion in the AP participant precluded any improvement regardless of intervention strategy.

One might also question the influence of age in the DP studies (see section 3.1). From the available evidence it is very difficult to draw any conclusions on the suitability of remedial or compensatory training for different age groups, given the former were only carried in adults, and the latter in children. However, the studies reported by DeGutis and colleagues indicate that plasticity is retained in adult DPs, and provides encouraging evidence for the use of remedial programmes even in adulthood. Whether the same benefits will be exacerbated in children is unknown, but Dalrymple et al. (2012) briefly describe a DP child, TM, for whom remedial training was not successful. She notes several explanations for this, including the severity of his prosopagnosia, the intensity of training, and motivational factors (the training was quite tedious). It is clear that, although successful training strategies are beginning to emerge in adult studies, these strategies will need to be adapted and made age-appropriate for children, even if they target similar mechanisms.

If early intervention is critical in DP (before the development of unhelpful compensatory strategies and the passing of any critical periods), research needs to focus on early detection of the condition. Bradshaw (2001) argues that the consequences of atypical development may

not be observable on a behavioural level for some time after they have occurred, indicating that urgent work is required to establish the developmental trajectory of DP, and its biobehavioural markers and risk factors.

5. Further considerations of intervention programmes

5.1. Specificity of training

It is clear from the above discussion that the most successful training programmes (whether compensatory or remedial) are those that target the impairment itself. In particular, the studies reported by DeGutis and colleagues (2007, in press) indicate that training in holistic processing – a mechanism that is believed to be disrupted in both AP and DP – may be particularly fruitful. Pertinently though, it is possible to target such mechanisms using both facial (e.g. Maurer et al., 2002) and non-facial (e.g. Navon, 1977) stimuli. Such findings have important implications for training, given evidence that intervention using non-facial holistic processing techniques may not be beneficial for individuals with prosopagnosia. For instance, as mentioned in section 4.2, training with inverted face stimuli did not improve performance with upright faces in a participant with DP (DeGutis et al., 2007). A similar finding was reported in a study that attempted to train neurotypical participants in holistic processing using inverted faces (Robbins and McKone, 2003). While it is unclear exactly why this effect occurs, it is possible that training with inverted faces simply does not improve holistic processing strategies, and instead encourages processing strategies that are optimal for the recognition of inverted but not upright faces (Kanwisher, 2000; Farah, 1996). Alternatively it may simply be that there is a limit to the amount of transfer that is possible in perceptual learning, and upright faces are just too different from inverted faces for any gains to generalize (Fahle, 2005).

Perhaps the most striking demonstration of the need for face-specific training comes from a study reported by Behrmann et al. (2005). These authors describe the case of SM, a 24 year-old man with visual agnosia and concomitant prosopagnosia following damage to the right anterior and posterior temporal lesions, corpus callosum, and left basal ganglia. The authors trained SM to recognize Greebles (novel objects that require the integration of different 'features' composed of complex shapes; Gauthier and Tarr, 1997) over a 31 week period. As has been observed in previous studies (e.g. Duchaine et al., 2004; Gauthier and Tarr, 1997) SM showed a significant improvement in recognizing Greebles that also extended to untrained stimuli and common objects. However, his face recognition skills became even more impaired following training. When this became evident, the authors stopped the training programme and concluded that residual neural tissue with limited capacity may compete for representations. These findings indicate that, at least in the case of holistic processing, any attempts to remediate prosopagnosia must utilise faces in order to be effective.

5.2. Generalization, maintenance and transfer

Failure to elicit treatment generalization both to untreated items and also to alternative versions of the treated items has been common in the treatment of visual recognition difficulties, for both objects and faces (see Riddoch and Humphreys, 1994). In the AP studies that showed some success, there was only evidence of generalization in the study reported by Francis et al. (2002). In fact, these authors concur with Ellis and Young (1988) that level of impairment is an important factor in remediation outcome and particularly findings of generalization. Francis et al. (2002) propose that person-specific generalization in their study within the treated group of photos (i.e. generalization of trained images to other images of the same person) may have been related to the fact that NE did not exhibit perceptual deficits. They propose that failures to achieve this type of generalization in other cases may relate to

difficulties earlier in face-processing and particularly at a perceptual level (Ellis and Young, 1988).

However, a different pattern emerges in the DP literature. The one study that assessed generalization of the compensatory training programme within laboratory-based assessments found no evidence of generalization to untrained faces, although AL did show the benefits for different images of the trained faces (Brunsdon et al., 2006). However, response latencies were unusually long in AL, suggesting implementation of the strategy was laboured. This observation is akin to the report of NE (Francis et al., 2002), who also received benefits from compensatory training, but found the strategies were often inefficient to implement in everyday life. Nevertheless both AL and K (Schmalzl et al., 2008) reported improved recognition of the trained individuals in everyday life, and the gains were maintained at 3-month and 4-week follow-ups, respectively. K was also described in Wilson et al. (2010) when she was 7.5 years old, and continued maintenance of the gains was reported (but note that the authors suggest K may be on the autism spectrum). These observations suggest that in DP compensatory training may be rapid, suitable for adults and young children, suitable for individuals with perceptual impairments, and the gains may translate to everyday life (but only for trained faces) and be maintained.

On the other hand, the remedial holistic training programme reported by DeGutis and colleagues (2007, in press) also generalized to improvements in everyday face recognition (i.e. the gains were not restricted to the faces used in training), as evidenced by self-report diaries kept by the participants. However, MZ showed limited maintenance of training gains (DeGutis et al., 2007), which raises the possibility that while remedial training may bring about greater and more generalized gains, these benefits may quickly fade without continued rehearsal. Furthermore, training in the larger group study was only successful in 13 of the 24 participants, and was not linked to pre-training performance on perceptual tests. This indicates that gains from remedial training can vary significantly between individuals, and a more complex set of factors may influence treatment outcome.

5.3. Individual differences

Much evidence indicates that age may be an important variable in predicting success in neurorehabilitation. Although no clear patterns can currently be seen in the prosopagnosia literature, it is likely that participant age may dictate the choice of training technique. For example, although the DP studies indicate that compensatory training can be effective even in children, the case of TM (Dalrymple et al., 2012) raises the possibility that remedial training techniques are simply not age-appropriate. Given that the broader neurorehabilitation literature suggests that remedial training should be more effective in children, future work needs to develop adaptations of remedial programmes for specific age ranges.

The wider neurorehabilitation literature also suggests that other individual differences can influence intervention outcome, although it is too early to comment on whether these hold true for prosopagnosia. For instance, there is controversial evidence that gender predicts recovery from acquired damage in adulthood (Anderson et al., 2001), as hormones may cause the female brain to develop more rapidly and with a more diffuse organization, perhaps permitting greater plasticity and potential for reorganization of function (Kolb, 1995; Strauss et al., 1992).

In addition, individuals with higher intelligence and superior education are less affected by brain damage (Wilson, 2003), and Anderson et al. (2001) conclude that family function,

socioeconomic status, access to rehabilitation, and response to disability all make a powerful contribution to recovery. In the longer-term, it is environmental rather than organic factors that tend to predict recovery from acquired brain damage (e.g. Kolb, 1995). Hence, these factors may influence the outcome of rehabilitation studies, and should be taken into account when evaluating intervention success.

6. Future directions

Clearly future work needs to explore both compensatory and remedial training strategies in more depth, and match their suitability to both AP and DP, their potential subtypes, and properties of the individual participant. Future work should also investigate participants' emotional response to interventions – for example, whether training programmes can lead to negative outcomes (e.g., frustration or feelings of low self-worth if they are ineffective), and how these compare to the relatively modest behavioural gains reported to date. Future studies may also move beyond purely behavioural interventions: given huge gains in everyday face recognition have not been reported following any type of training, alternative methodologies may present with more fruitful means of boosting face recognition skills in prosopagnosia. Two methodologies in particular have the potential to supplement face training programmes: intranasal inhalation of oxytocin and non-invasive brain stimulation.

Recent evidence suggests that intranasal inhalation of oxytocin can temporarily improve face recognition skills in both typical participants and those with DP. Oxytocin is a neuropeptide that affects social cognition, potentially by increasing the perceptual salience of social cues (Bartz et al., 2011). Several studies of neurotypical populations have found better memory for faces (but not other, non-social stimuli) following inhalation of oxytocin (Guastella et al., 2008; Rimmele et al., 2009; Saskavan et al., 2008). More notably, a recent study found that participants with DP showed better performance on both a face matching and a face memory task following inhalation of oxytocin, compared with a placebo condition (Bate et al., 2014). Currently it is unclear why people with DP benefit from inhalation of oxytocin. On a neural level, findings from participants with typical face recognition suggest that oxytocin modulates activity in several regions implicated in face processing – namely, the FFA and the amygdala (Domes et al., 2010; Gamer et al., 2010). DPs show structural and connectivity abnormalities in the core face-processing system, around the fusiform and temporal gyri (Garrido et al., 2009) and within the ventro-occipital cortex (Thomas et al., 2009). Therefore, it is possible that oxytocin-related modulation of activity in these areas could underpin increased face recognition performance for the DPs in Bate et al.'s (2014) study. However, further work incorporating neuroimaging of DPs under oxytocin conditions is necessary to explore this possibility.

Inhalation of oxytocin has been found to increase fixations to the eye region of the face in typical participants (Gamer et al., 2010; Guastella et al., 2008). The eye region is considered optimal for face recognition (Peterson and Eckstein, 2012), and several studies have found that DPs spend less time looking at the eye region than typical controls (e.g., Schwarzer et al., 2007). It is possible that oxytocin encouraged DP participants to attend to the eye region more than usual, which may have increased their performance in face-processing tasks. Once again, further work using eye-tracking technology is necessary to explore this possibility. Future work may consider combining inhalation of oxytocin with behavioural training in an attempt to increase or speed up training gains, and/or to extend the benefits of oxytocin inhalation beyond a single session.

Another class of techniques that has been shown to improve face recognition performance, at least temporarily, is non-invasive brain stimulation. There are many types of non-invasive brain stimulation, but three in particular show promise for interventions in prosopagnosia: transcranial electric stimulation (incorporating transcranial direct current stimulation, or tDCS; and transcranial random noise stimulation, or tRNS) and galvanic vestibular stimulation (GVS). In transcranial electric stimulation, a weak current (usually 1-3 mA) is applied to the scalp via electrodes. tDCS involves the use of a constant current. Areas under the anode exhibit cortical excitability, whereas areas under the cathode show the opposite effect (Paulus, 2011). tDCS has been shown to improve performance in typical participants in a range of cognitive tasks, from low-level vision, executive functioning, memory, and language (Kuo and Nitsche, 2012). Notably, tDCS has also been used in stroke patients (generally those with aphasia), and, in concert with cognitive training, has been shown to improve speech and naming abilities (see Krause and Cohen Kadosh, 2013, for a review). This may occur because tDCS facilitates compensation in non-damaged regions, reduces activation in non-damaged regions that may inhibit activation in or around lesioned areas, or increases residual output of partially damaged areas (Cohen Kadosh, 2013). In other words, tDCS may be useful in conjunction with both remedial and compensatory training strategies, but choice of strategy and stimulation site (lesion area/contralateral lesion area) could vary patient-to-patient, depending on the site and extent of damage. To date, tDCS has not been applied to prosopagnosia, or in face perception tasks in typical participants. However, Ross et al. (2010) found that anodal tDCS over the right anterior temporal lobe significantly improved name recall for famous faces in a group of young adults with typical face recognition, indicating that anterior temporal tDCS may be useful in mnemonic cases of AP or DP.

tRNS involves the use of a current that changes several hundred times per second, taking its value from a random noise distribution centred around 0 (Paulus, 2011). Because the current oscillates between the two electrodes, there is no anode or cathode, and the areas under both electrodes show enhanced cortical excitability (Cohen Kadosh, 2013). Like tDCS, tRNS has been shown to improve cognitive abilities in a range of domains, including motor and perceptual learning (Fertonani et al., 2011; Terney et al., 2008). tRNS also shows long-term effects: when combined with five days of cognitive training for numerosity or mental calculation, stimulation resulted in increased training gains that remained evident between 16 weeks and six months later (Cappelletti et al., 2013; Snowball et al., 2013). Like tDCS, tRNS has not been applied in AP or DP as yet. However, evidence from training studies in other domains suggests that combining cognitive training (such as the techniques used by DeGutis et al., in press) with tRNS may enhance its effects, although work is needed to clarify which combination of training task and stimulation site is effective in various types of prosopagnosia.

GVS resembles tDCS of the vestibular nerve – electrodes are placed on the mastoid bones, which stimulates the vestibular nerve and, in turn, all vestibular relay stations upstream. fMRI studies have revealed that GVS activates a wide range of cortical areas including several associated with face-processing (e.g., the superior temporal gyrus and temporo-parietal cortex; Bense et al., 2001). Only one study has examined GVS in face recognition: Wilkinson et al. (2005) applied GVS to patient RC, who acquired prosopagnosia following damage to the right temporal lobe (amongst other areas). Short sessions of GVS improved RC's face discrimination performance to above-chance levels. However, the discrimination task was not strictly identity-matching – RC was required to choose a face that did not have its eyes and mouth inverted, rather than to choose between two typical faces. As such, it is difficult to say

whether the stimulation simply improved detection of abnormalities in a face, or whether the effects would carry over to other face processing tasks (e.g., face memory). Once again, further work is necessary to confirm whether GVS may also be beneficial for DPs, or in other cases of AP with different lesions or functional profiles.

7. Summary

In sum, while there have been few attempts to improve face recognition skills in either AP or DP, some tentative conclusions can be drawn from the available data and the wider neurorehabilitation literature. First, there is evidence to suggest that both forms of the condition respond to compensatory training, and that some adults with DP benefit from remedial training (although currently it is unclear precisely why some participants show benefits, whereas others do not). It is also unclear whether remedial programmes may be useful in AP, and in children with DP. While the benefits of compensatory training programmes appear to be that they are suitable for both adults and children and their gains are more long-lasting, they also promote more laboured processing strategies that are less likely to generalize to the recognition of untrained faces. On the other hand, remedial training techniques may promote more efficient "normal" processing strategies that are more likely to generalize to untrained faces, yet it takes more training to achieve these gains and they require continued rehearsal.

Given there have been very few studies in this area, further research into the duration, maintenance, and long-term benefits of remedial and compensatory training are necessary. It is likely that the suitability of these programmes for different individuals will have a complex interaction with age, the type of injury in acquired cases, the severity and nature of the prosopagnosia, and other environmental influences. In any case, gains are likely to be mild-to-moderate, and the utility of alternative methodologies (i.e. oxytocin inhalation or brain stimulation) should be considered. It is important to note that use of these techniques is in its infancy, and while single applications may bring about short-term gains in face recognition skills, there are likely to be significant safety considerations associated with everyday application of the techniques. Alternatively, performance of remedial training under oxytocin or stimulation conditions may bring about larger and longer-term benefits than the behavioural programme alone. Future work using more systematic methods and larger participant groups is clearly required, and in the case of DP, there is an urgent need to develop early detection and remediation tools for children in order to optimise intervention outcome.

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Table

Table 1: A summary of published research reports that have examined intervention techniques in acquired or developmental prosopagnosia.

Reference	Incident age (yrs)	Intervention age (yrs)	Lesion	Functional implication	Intervention technique	Success	Generalised gains (lab)	Gains to everyday life	Gains maintained
Acquired:									
Ellis & Young (1988)	3	8	Implied RH lesion & bilateral occipital damage	Perceptual	Remedial	No	-	-	-
De Haan et al. (1991b)	19	23	Bilateral temporo-occipital junction	Perceptual & mnemonic	Compensatory	No	-	-	-
Polster and Rapscak (1996)	61	68	Right temporo-occipital	Perceptual	Compensatory	Yes	No	Unknown	Unknown
Francis et al. (2002)	19	21	Right temporal	Semantic & Mnemonic	Compensatory	Yes	Yes	No	Unknown
Powell et al. (2008)	< 51	> 51	Bilateral occipital, left temporal & frontal	Perceptual	Compensatory	Yes	Unknown	Unknown	Unknown
Developmental:									
Brunsdon et al. (2006)	-	8	-	Perceptual	Compensatory	Yes	No	Yes	Yes
DeGutis et al. (2007)	-	48	-	Perceptual	Remedial	Yes	Yes	Yes	No
Schmalzl et al. (2008)	-	4	-	Perceptual	Compensatory	Yes	Unknown	Yes	Yes
DeGutis et al. (in press)	-	M=35, N=24	-	Various	Remedial	Yes	Yes	Yes	Unknown

Figure Captions

Figure 1: (a) The cognitive model of face-processing proposed by Bruce and Young (1986), and (b) an adaptation of the distributed model of face-processing proposed by Gobbini and Haxby (2007).

Figure 2: Schultz's (2005) amygdala/fusiform modulation model.

Figure 1.JPEG

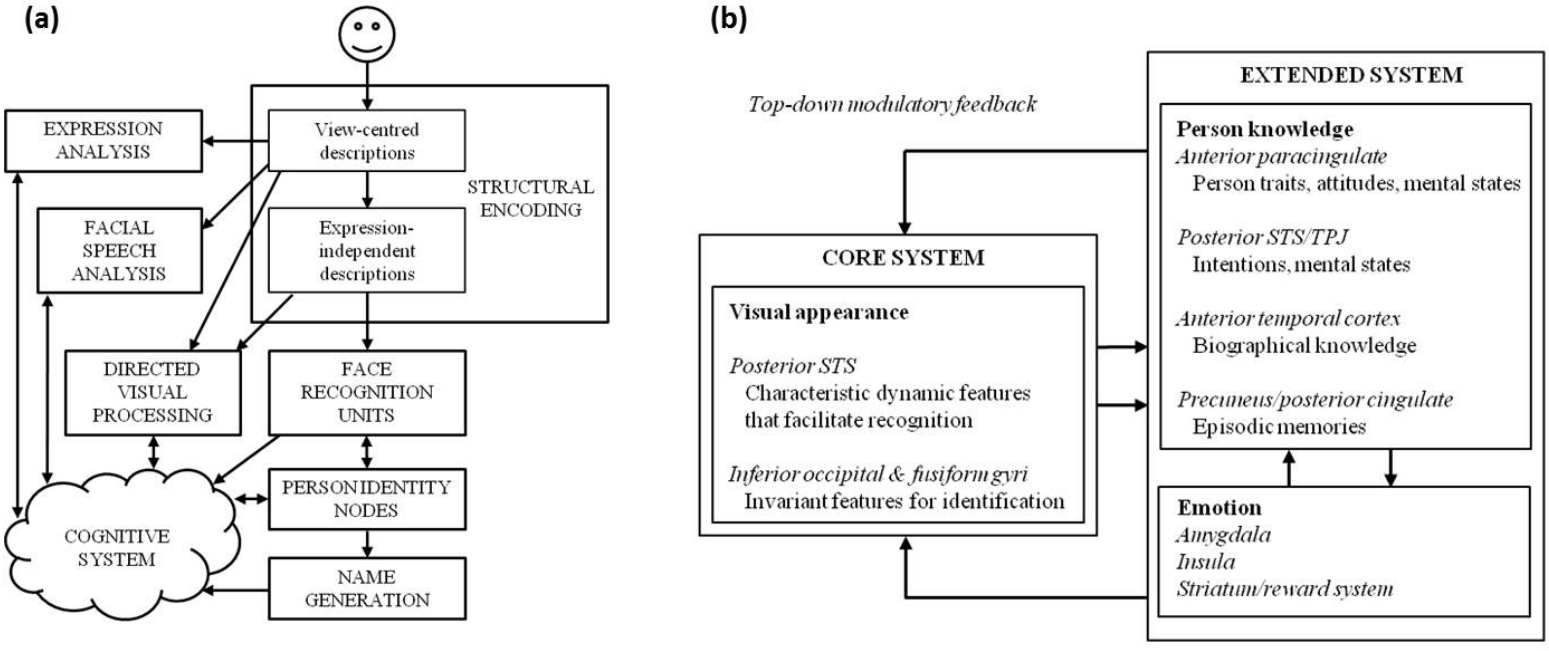
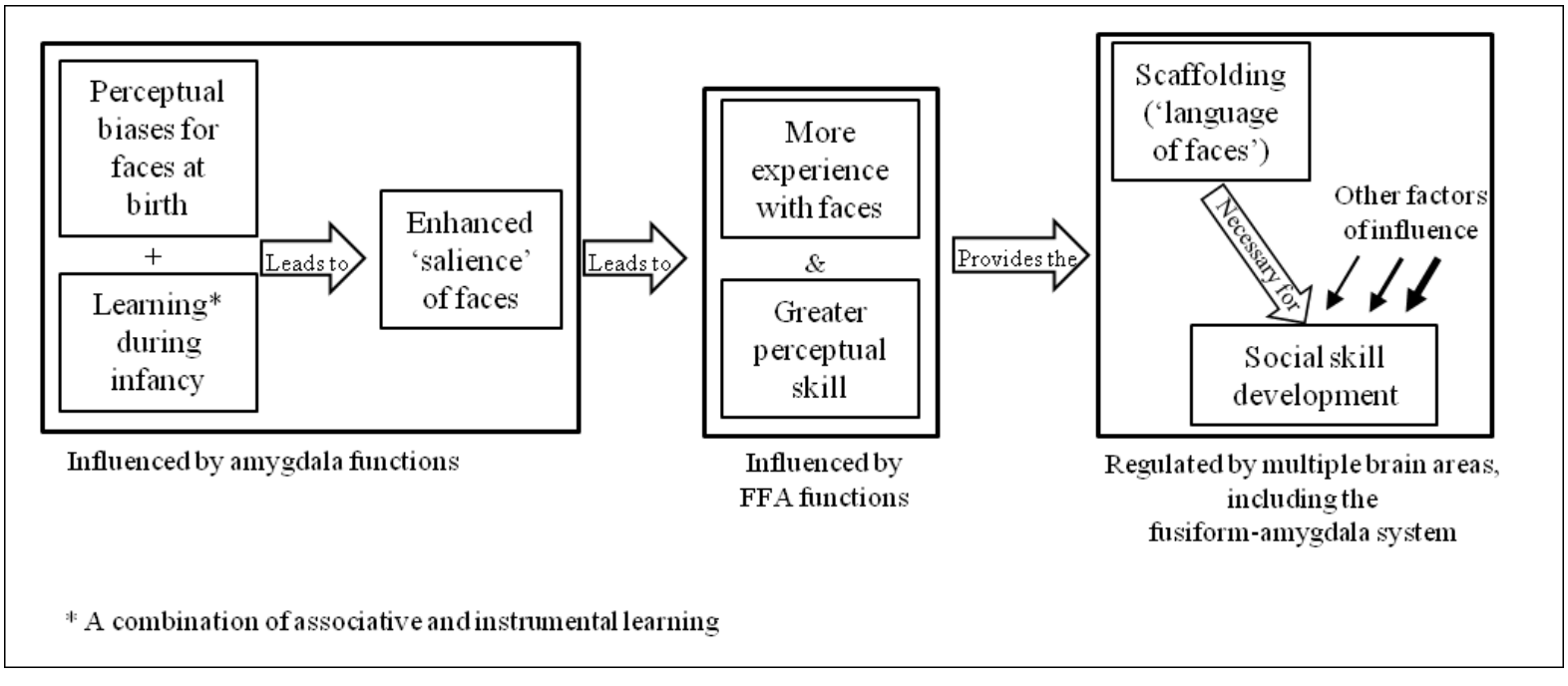


Figure 2.TIF


Perceptual biases for faces at birth
+
Learning* during infancy
Leads to
Enhanced 'salience' of faces
Leads to
More experience with faces
&
Greater perceptual skill
Provides the
Scaffolding ('language of faces')
Necessary for
Other factors of influence
Social skill development
Influenced by amygdala functions
Influenced by FFA functions
Regulated by multiple brain areas, including the fusiform-amygdala system
* A combination of associative and instrumental learning