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Disconnection in prosopagnosia and face processing

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ABSTRACT

Face perception is a function with significant complexity, reflected in cognitive models that propose a hierarchy of parallel and serial processing stages. Current neuroimaging data also show that face perception involves a core processing network of cortical modules, which are likely specialized for different functions involved in face processing. The core face processing network is further linked to an extended face processing network which is not solely involved in the perception of faces, but rather contains modules mediating the processing of semantic, biographic and emotional information about people. The segregation of these processes within discrete anatomic regions creates the potential for disconnection between regions to generate neuropsychological deficits involving faces. In this review we consider the types of disconnection possible both within the core face processing system and between the core and extended systems, the pattern of deficits that would be considered as evidence of such disconnections, the potential anatomy of lesions that would create them, and whether any cases exist that meet these criteria.

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Face recognition is an important perceptual skill: it enables the rapid recognition of hundreds, if not thousands, of unique faces, and enables appropriate social interactions. The loss of this skill is the key deficit in prosopagnosia, the inability to recognize familiar faces, which can be acquired in later life from a variety of cerebral lesions, or be present from birth as a congenital and sometimes inherited disorder. Although there were early proposals that this symptom might arise from the convergence of non-specific deficits of vision, memory and general mental processing (Bay, 1953; Cohn et al., 1977), it is apparent now that prosopagnosia is a selective visual agnosia resulting from damage to a cortical network devoted to the accurate perception of faces (Barton, 2003).

It is also apparent that prosopagnosia is not a single functional entity but a family of disorders. Face recognition is a complex process that involves both perceptual and memory

operations: dysfunction at a variety of levels may lead to the same end result of failure to recognize a familiar face. As with other visual agnosias (Barton, 2003; Lissauer, 1890), prosopagnosia has traditionally been divided into two broad subtypes (de Renzi et al., 1991). In apperceptive prosopagnosia, the patient is unable to form an accurate perceptual representation of the structure of a viewed face, a skill which is usually assessed by matching of unfamiliar faces (Benton and Van Allen, 1968). In associative prosopagnosia, formation of the facial percept is intact, but this information cannot be matched to facial memories in order to recognize that this is a face the subject has encountered before.

Just as there is more than one functional cause of prosopagnosia, there are also a variety of anatomic lesions that have been described in prosopagnosia. The two seminal small series of cases several decades ago noted an association with

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bilateral lesions of the lingual and fusiform gyri (Damasio, 1985; Meadows, 1974). Since then, there have been reports of anterior temporal lesions (Evans et al., 1995; Barton et al., 2002), unilateral right occipitotemporal lesions (de Renzi, 1986; Landis et al., 1986), and even rare left occipitotemporal lesions (Tzavares et al., 1973; Mattson et al., 2000; Barton, 2008). Likewise, recent functional imaging studies in healthy subjects have delineated a network of face processing regions rather than a single cortical region (Haxby et al., 2000; Palermo and Rhodes, 2007; Rossion et al., 2003a; Gobbini and Haxby, 2007; Ishai et al., 2005).

The fact that lesions in widely disparate locations can lead to forms of prosopagnosia lends support to network models of face processing (Haxby et al., 2000). These models consist of a core system of anatomic regions that are primarily responsible for face perception, with different perceptual roles assigned to different core modules (Haxby et al., 2000). Beyond the core system of face processing is a large extended system responsible for other functions relevant to the perception of a face, such as accessing biographical, semantic or emotional information related to the face (Gobbini and Haxby, 2007; Haxby et al., 2000). An important distinction between the core and extended systems is that the former is specialized for the perception of faces, whereas the latter is multimodal, and can be accessed by a wide range of stimuli other than faces (Gobbini and Haxby, 2007; Haxby et al., 2000).

The involvement of multiple cognitive processes and multiple anatomic regions in face recognition raises the distinct possibility that some cases of prosopagnosia may be not due to damage to specific processes or regions, but due to disconnections between processes and regions (i.e., topological vs hodological damage; see Catani and Ffytche, 2005). In this review we first consider historical proposals of disconnection in prosopagnosia. We then summarize current cognitive and anatomic frameworks of face processing and discuss where disconnections could arise within these frameworks, what behavioral findings would suggest such disconnections, and whether there are existing cases in the literature that fulfill these predictions. We will focus on three potential disconnections. First, we will examine the core disconnection of associative prosopagnosia, and discuss whether associative prosopagnosia can be shown to be due to disconnection between perceptual mechanisms and facial memory stores, and not simply due to damage to the memory stores. Second, we will examine the potential for a disconnection between the core face processing system and other regions involved in processing stored semantic and biographic information related to people, namely the anterior temporal lobes and the precuneus. Finally, we will discuss affective ‘visual-limbic’ disconnections, as reported in a hypoemotionality syndrome associated with prosopagnosia (Bauer, 1982; Gomori and Hawryluk, 1984; Habib, 1986) and in Capgras syndrome (Barton, 2003).

1. Historical concepts of disconnection as the basis for prosopagnosia

The revival of the concept of disconnection as the basis for dysfunction in alexia, aphasia and other behavioral syndromes

(Geschwind, 1965) led naturally to many considerations of whether disconnection could also account for at least some cases of prosopagnosia (Aptman et al., 1977; Kay and Levin, 1982; McNeil and Warrington, 1991; Ross, 1980; Takahashi et al., 1995; Bauer, 1982; Gomori and Hawryluk, 1984; Habib, 1986). Two main proposals emerged, one focusing on *intra-hemispheric* disconnection, the other on *inter-hemispheric* disconnection.

First, regarding *intra-hemispheric disconnection*, it was noted that the bilateral lesions of the fusiform and lingual gyri described in early studies would also likely compromise the inferior longitudinal fasciculus (Catani and Thiebaut de Schotten, 2008, *this issue*; Catani et al., 2003), which connects regions of the occipital and temporal cortices (Benson et al., 1974). Damage to such a tract might disconnect visual processing in the occipital lobe from memory processing in the temporal lobe (Habib, 1986; Kawahata and Nagata, 1989; Kay and Levin, 1982; Meadows, 1974; Takahashi et al., 1995). If so, this *intra-hemispheric disconnection* might create a form of associative prosopagnosia, in which the products of intact perceptual processing of facial structure could not access residual facial memories (see also Ross, 2008, *this issue*). Such patients should show relatively preserved perceptual abilities and, ideally, relatively preserved facial memories as well.

Second, proponents of *inter-hemispheric disconnection* raised analogies with the syndrome of alexia without agraphia (Aptman et al., 1977). *Inter-hemispheric disconnection* accounts of alexia without agraphia postulate that left hemispheric regions specialized in decoding visual word forms lose access to visual input when a lesion both causes a right hemianopia and also interrupts callosal fibers from the right occipital lobe (Epelbaum et al., 2008, *this issue*), which process data in the remaining left hemifield (Dejerine, 1892; Geschwind, 1965). Could prosopagnosia represent the mirror-image deficit of alexia without agraphia, from deafferentation of a face processing region or network predominantly located in the right hemisphere? The initial reports of bilateral occipitotemporal damage as a prerequisite for prosopagnosia (Meadows, 1974; Damasio, 1985) would appear to cast doubt on this mechanism. However, subsequent reports of prosopagnosia with lesions limited to the right hemisphere (Landis et al., 1986; de Renzi, 1986) and functional magnetic resonance imaging studies showing more face-related activity in the right hemisphere (Haxby et al., 2000; Kanwisher et al., 1997) indicate a right-sided dominance in face processing. Thus the notion of prosopagnosia as the mirror image of alexia without agraphia cannot be so easily dismissed. Furthermore, the more variable nature of the left-sided lesions in cases with bilateral damage has suggested to some that the role of the left-sided lesion is to disconnect the left hemisphere’s visual input (i.e., right visual hemifield) from face processing regions in the right hemisphere, much as splenic lesions do (Habib, 1986; Kay and Levin, 1982; Meadows, 1974). This mechanism would be particularly plausible in prosopagnosic patients with a left hemianopia. Theoretically, this *inter-hemispheric disconnection* could result in either an apperceptive or associative prosopagnosia, depending upon one’s view of what aspects of face processing are lateralized to the right, whether it is perceptual encoding of face structure or the storage of facial memories.

These two disconnectionist accounts have been superseded to some degree by more current concepts of prosopagnosia as a selective visual agnosia due to loss of higher-level object recognition mechanisms from cortical lesions rather than tract damage. In particular, the account of occipitotemporal disconnection from damage to the inferior longitudinal fasciculus has suffered from the discovery of a face-selective region in the lateral portion of the mid-fusiform gyrus, the ‘fusiform face area’, or FFA (Kanwisher et al., 1997), which is also in the vicinity of many of the occipitotemporal lesions described in the prosopagnosic literature (Barton et al., 2002). (Likewise, disconnectionist accounts of alexia without agraphia have been challenged by concepts of this disorder as a visual agnosia from damage to a visual word form area in the left fusiform gyrus (Kleinschmidt and Cohen, 2006). Nevertheless, these alternative explanations do not exclude the possibility of disconnection variants in the heterogeneous family of deficits within prosopagnosia. To place such disconnectionist accounts in a modern perspective, however, it is useful to first review current concepts of the cognitive mechanisms and neuroanatomy of face recognition.

2. Pre-requisites for disconnection: face processing networks and functional stages

Disconnection as a cognitive mechanism has a number of pre-requisites. First, there should be a defined series of functional processing stages, so that a disruption in information transfer between stages can be detected. Second, in order for physical disconnection on a macroscopic scale to be possible, the cognitive process must involve a network of discrete anatomic structures. Third, functional processing stages should be relatively segregated in different anatomic structures: if all cognitive operations were performed equivalently by all anatomic components of a network, it would be very difficult if not impossible to detect the functional signature of physical disconnection between these components. Fourth, one must have experimental tests capable of probing the individual cognitive operations performed by these anatomic components. Proof of disconnection is most clear when the individual cognitive operations of anatomic modules can be shown to be intact, despite the disruption of functions that emerge from the coordinated action of the network.

How well does the process of face recognition meet these requirements? First, cognitive models of face processing (Fig. 1) have long postulated distinct modules in face processing, with parallel streams and a hierarchy of processing stages (Bruce and Young, 1986; Damasio et al., 1990). An early stage involves the perceptual encoding of the face, which may include (i) a view-dependent representation of the face (pictorial encoding) and (ii) a view-invariant representation of the face (encoding of three-dimensional structure). Processing of dynamic aspects of facial representations is required for (iii) interpretation of expression and (iv) interpretation of facial speech patterns, for example. On the other hand, processing of motion-invariant aspects of facial structure contributes to (v) categorization of the face by gender or race, and is key for extracting the identity of the face. Thus the distinction between dynamic and motion-invariant facial properties

may represent an early bifurcation in face processing. For recognition, motion-invariant properties then require (vi) matching to facial memories to evoke a sense of prior familiarity. A successful match can then lead to access of person-related information that is not specific to faces or vision, such as (vii) the name, (viii) semantic or episodic biographic information, and (ix) associated affective responses (Bruce and Young, 1986; Gobbini and Haxby, 2007).

Second, functional neuroimaging has confirmed an anatomic network of face processing areas, as discussed above (Figs. 2 and 3). In addition to the FFA, which has been found bilaterally but predominantly in the right hemisphere (Kanwisher et al., 1997), other face-responsive occipitotemporal areas include regions in the inferior occipital gyrus (occipital face area, OFA), and within the superior temporal sulcus (STS) (Haxby et al., 2000). These three regions comprise what is sometimes called the “core system” for face perception. Beyond these core regions an “extended system” includes regions of cortex that can be activated not only by faces but also by other person-related stimuli, such as the anterior paracingulate cortex, amygdala, anterior temporal cortex and precuneus/posterior cingulate cortex (Gobbini and Haxby, 2007).

The third criterion, that different functional operations be supported by different anatomic structures, remains a topic of ongoing research, particularly in studies using fMRI adaptation techniques. Current models postulate that the FFA is involved in the encoding of structural properties related to identity processing, whereas the STS is involved in the processing of facial expression (Haxby et al., 2000). The OFA may be involved in the encoding of early facial representations common to both identity and expression processing, but this issue is not yet settled. Some recent formulations have proposed that dynamic facial structure relevant to expression processing is represented solely in the STS, and that the OFA and FFA function as a unit in the perceptual encoding relevant to identity (Gobbini and Haxby, 2007); if so, it is not clear whether the OFA and the FFA make distinct contributions. Beyond the perceptual encoding stage, the data are less clear. An area containing facial memory stores should show influences of familiarity: known faces should have representations in such stores that novel faces lack. Familiarity effects are inconsistent or non-existent in the FFA (Eger et al., 2005; Elfgren et al., 2006; Kosaka et al., 2003; Pourtois et al., 2005; Gobbini and Haxby, 2006), but can be found in anterior and medial temporal regions (Sergent et al., 1992; Gorno-Tempini et al., 1998; Leveroni et al., 2000; Nakamura et al., 2000). However, personally familiar faces also have semantic and emotional processing, making it difficult to know if familiarity effects represent facial memory stores or alternatively ‘person identity nodes’ that contain semantic information. To clarify this, one study used recently learned faces without semantic or name associations to show familiarity effects in the right inferotemporal cortex (Rossion et al., 2001). Lesion data also suggest that recognition memory for faces may be selectively localized to the perirhinal cortex of the temporal lobe (Taylor et al., 2007). The person-related information located in ‘person identity nodes’ in older models has been fractionated into different types of information about people, which are also postulated to be represented in different anatomic compartments in the extended system.

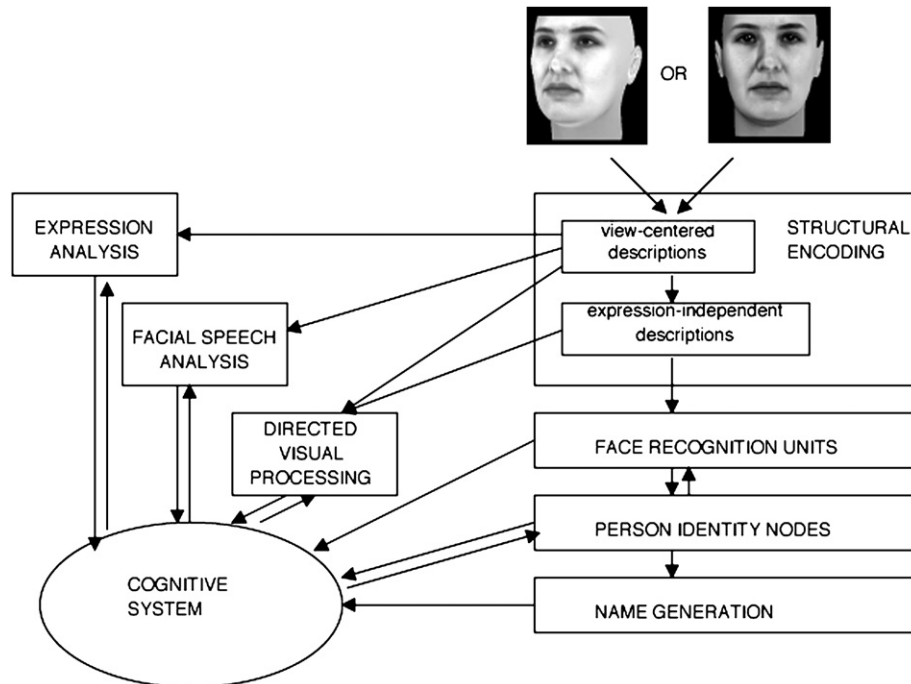


Fig. 1 – The classic cognitive model of face processing (modified version of Bruce and Young, 1986). Structural encoding feeds perceptual data into several streams of information processing. That involving recognition of identity is represented in the right column, where perceptual input is linked to face recognition units (facial memory stores), which then activate person identity nodes and further access to data like names.

Thus information about personality traits are tentatively assigned to anterior paracingulate cortex, biographical memory to anterior temporal cortex, episodic memory about people to the precuneus, and inferring the intentions of others

to the temporoparietal junction (Gobbini and Haxby, 2007). Likewise, expression processing extends beyond the STS, to include structures involved in general emotional processing such as the amygdala, insula, and striatum.

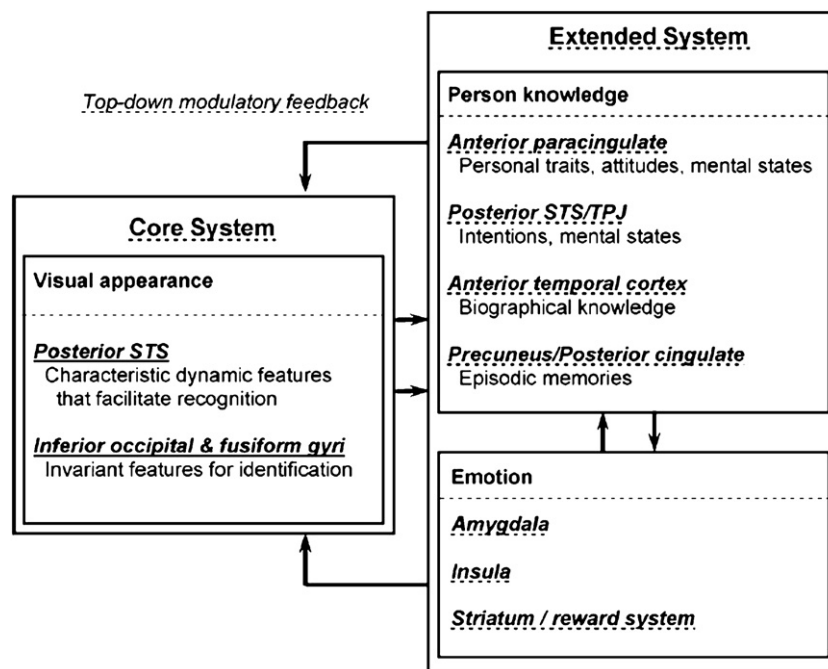


Fig. 2 – A model of face processing incorporating neuroimaging data (Gobbini and Haxby, 2007). A core face processing system on the left is primarily responsible for face recognition: outputs of this system feed into an extended system on the right that links faces to various types of information about people, which are distributed in different anatomic regions. Reprinted with permission from Neuropsychologia® Elsevier Ltd.

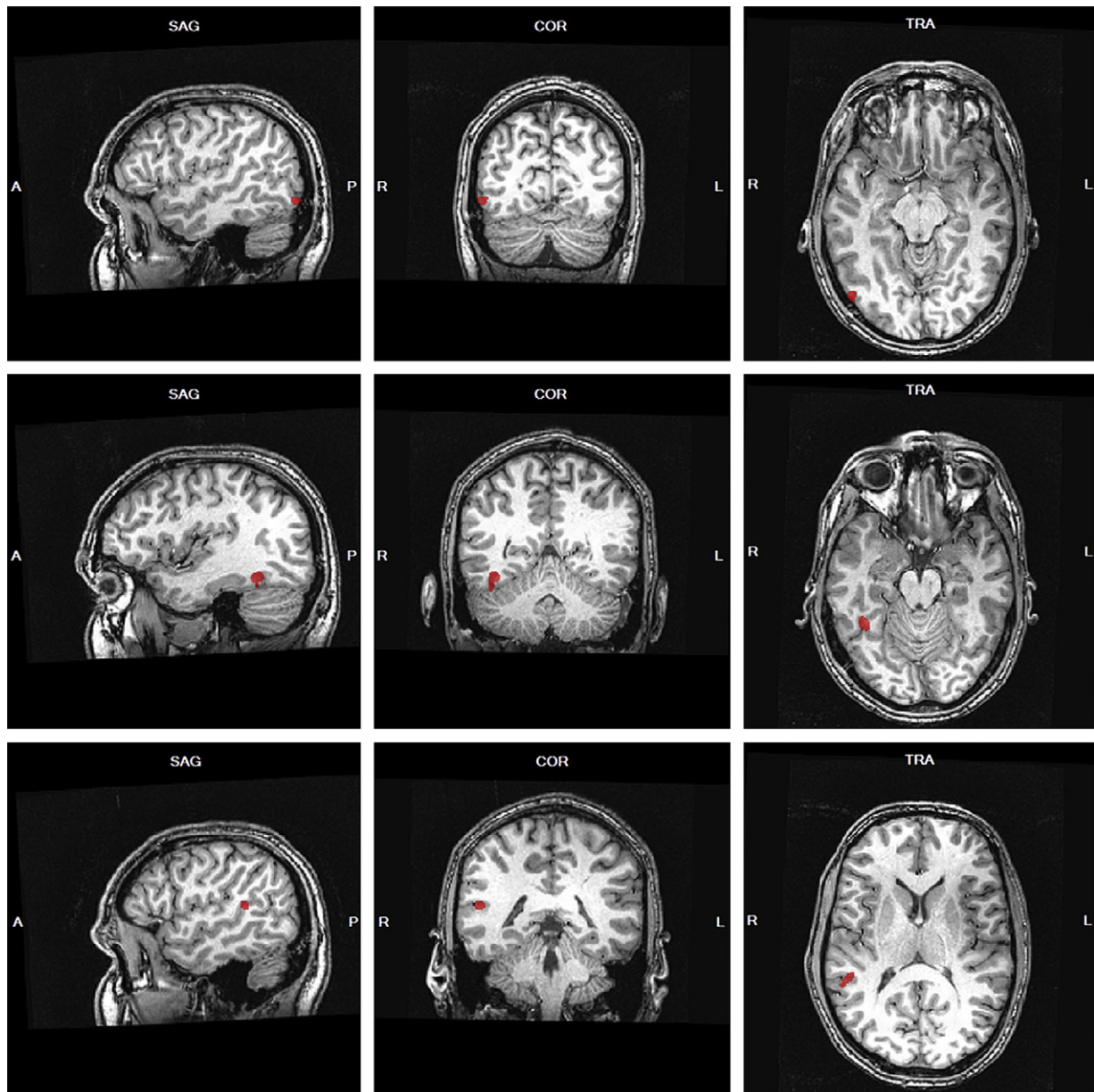


Fig. 3 – Core anatomic areas in the right hemisphere of the face processing network. The images show sagittal (left), coronal (middle) and axial (right) images from a single subject. Top row: occipital face area (OFA), middle row: fusiform face area (FFA), bottom row: superior temporal sulcus (STS).

Thus, current concepts of the face processing system suggest that specific anatomic structures may be arranged in a hierarchical processing tree, with different structures performing specific cognitive operations. These functional and structural aspects make it reasonable to consider the existence of disconnection in prosopagnosia on theoretical grounds. The next question is a pragmatic one: do we have the means to detect the functional signatures of a disconnection in this cognitive/anatomic network? In the following sections we will discuss several possible disconnections both within the core system and between the core and extended systems of face processing. For each disconnection we will first discuss its functional signature and tests that may be used to assess both intact and impaired processes

associated with this disconnection. We will then discuss potential sites of damage that could lead to such a disconnection. Finally, we will review any prior reports of patients with symptoms consistent with this form of disconnection.

3. Disconnection in the core face processing system: the case of associative prosopagnosia

A key step of face recognition in cognitive models (Bruce and Young, 1986) is the transition from perceptual encoding of facial structure to the matching of this information against a store of facial memories (also known as ‘facial recognition units’, FRU). A successful match generates a sense of familiarity

and subsequent activation of semantic information about that person in 'person identity nodes' (PIN). Disconnection between perceptual encoding and facial memories is one proposed mechanism for associative prosopagnosia: indeed, this is the cognitive mechanism hypothesized in classic reports (Habib, 1986; Kawahata and Nagata, 1989; Kay and Levin, 1982; Meadows, 1974; Takahashi et al., 1995), and in some recent network models of prosopagnosia (Burton et al., 1990; Young and Burton, 1999) (Fig. 4). However, damage or loss of facial memories is another potential mechanism for associative prosopagnosia (McNeil and Warrington, 1991). Therefore, the functional signature of a disconnection variant of associative prosopagnosia requires, in addition to the failure to recognize familiar faces, demonstration of first, intact perceptual encoding of facial structure, and, second, intact stores of facial memories (Table 1).

Probes of perceptual encoding generally involve match-to-sample or discrimination tasks, which require subjects to detect similarities and differences between facial images without any need for subjects to remember these faces or report familiarity. These can involve test items that include variations in lighting or viewpoint, so that perception of three-dimensional structure is stressed. The Benton Face Recognition Test (BFRT) (Benton and Van Allen, 1968) is the most widely used of such tests, although other tests with similar principles exist (Delvenne et al., 2004; Takahashi et al., 1995). Matching or discrimination tasks can also be constructed to test what types of facial information the subject fails to process, by using target faces that differ in features, the spatial arrangement of features, external contour, and other elements (Barton et al., 2002; Malcolm et al., 2004).

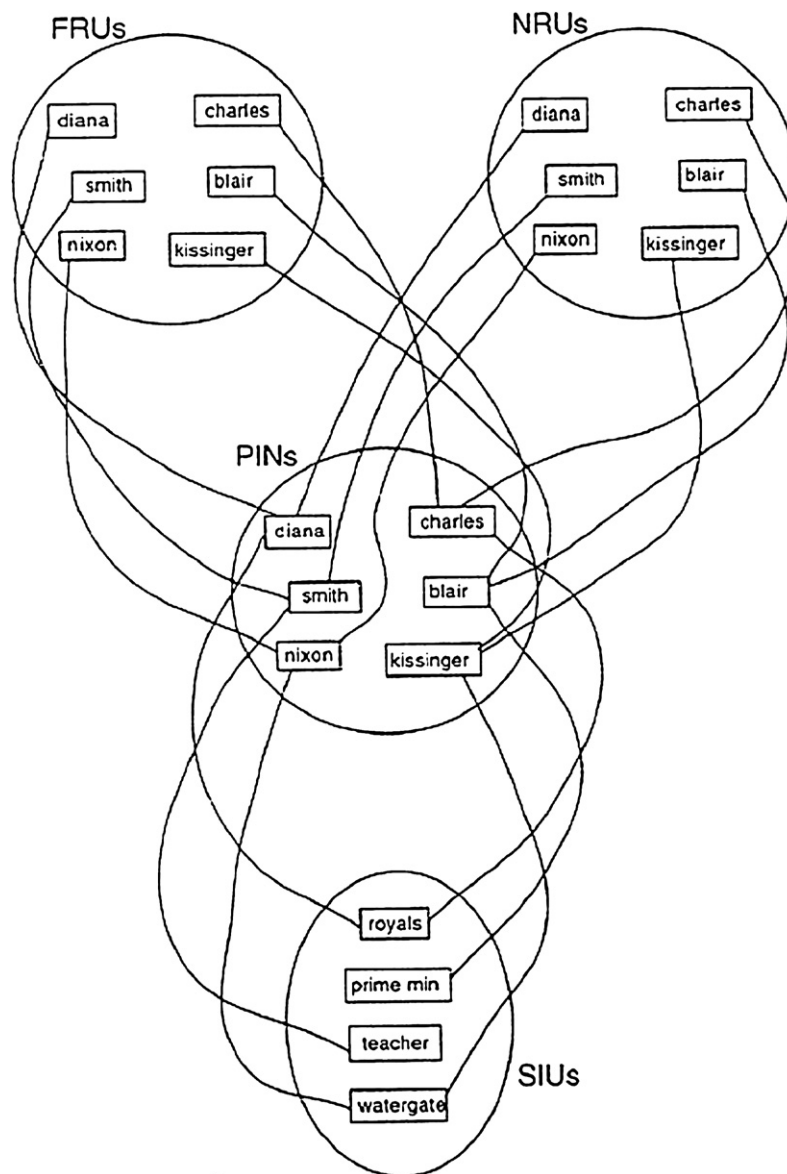


Fig. 4 – A neural network model of face processing (Young and Burton, 1999). Associated prosopagnosia in this model is visualized as a disruption of the connecting links between the FRU (face recognition units, or facial memories) and PIN (person identity nodes). SIU = semantic information unit; NRU = name recognition unit. Reprinted with permission from Cognitive Neuropsychology® Taylor & Francis Ltd.

Table 1 – Core disconnection

Cognitive function	Status	Experimental test
Perceptual encoding	Intact	Face matching (e.g., Benton Face Recognition Test) Face discrimination
Recognition	Impaired	Famous face recognition Short term familiarity (e.g., Warrington recognition memory test)
Facial memory stores	Intact	Facial imagery Covert recognition (?)

Probing the integrity of facial memory stores is more problematic since, to evaluate this independent of the function of perceptual modules, it would be desirable to assess this without requiring perceptual processing of any test stimuli. Some have suggested that covert recognition may depend upon facial memory stores, and therefore serve as an indirect probe of such stores (De Haan et al., 1992; McNeil and Warrington, 1991). However, this is open to debate, as others argue that the status of perceptual modules is more relevant to covert recognition (Bruyer, 1991). Tests of facial imagery – asking a subject to mentally recall aspects of faces known to them – may be a better method for assessing the integrity of facial memory stores (Takahashi et al., 1995; Young et al., 1994; Barton and Cherkasova, 2003). Imagery tests do not require perceptual input and therefore impaired performance on tests of facial imagery cannot be attributed directly to impairments in perceptual mechanisms. For this reason, tests of facial imagery may be the best current method for assessing the status of facial memory stores (Barton and Cherkasova, 2003; Takahashi et al., 1995; Young et al., 1994).

Given what we have learned from functional neuroimaging, where would we find a lesion disconnecting facial memory stores from perceptual encoding? The historical suggestion of the inferior longitudinal fasciculus is compatible with the lesion in the case of Takahashi et al. (1995), but is the proposal that an occipitotemporal disconnection causes this functional disconnection consistent with current neuroimaging data? Certainly, fMRI adaptation studies have provided significant data showing that the OFA and the FFA are regions sensitive to changes in facial structure (Rotshtein et al., 2005), and lesion data suggest that damage in the vicinity of these regions causes a severe deficit in the perception of facial structure (Barton et al., 2002): hence it is plausible that perceptual encoding involves occipital and posterior temporal regions. Neuroimaging data are less conclusive about the location of facial memory stores, however; the most consistent fMRI effects of face familiarity occur in anterior and medial temporal regions (Sergent et al., 1992; Gorno-Tempini et al., 1998; Leveroni et al., 2000; Nakamura et al., 2000) and right inferotemporal cortex (Rossion et al., 2001). Overall, these data lend credence to the hypothesis that damage to a tract connecting posterior occipitotemporal perceptual regions like the OFA and FFA with more anterior temporal regions that may contain facial memory stores could result in associative prosopagnosia (Fig. 5).

This cannot yet be considered a definitive account, however. A contrary view is that facial memories may indeed be

represented in the FFA. Two pieces of evidence suggest this. First, when familiarity is experimentally induced through repeated exposures (minimizing the contribution of semantic overtones that are invariably present with faces familiar from real life), previously trained faces elicit weaker responses than novel faces in the right FFA and OFA (Rossion et al., 2001, 2003b). In other similar studies, as familiarity increased through the course of the experiment, the fMRI signal increased in the precuneus and decreased in the FFA and amygdala (Gobbini and Haxby, 2006; Kosaka et al., 2003), leading to suggestions that changes in the FFA with familiarity may be due to “the development of a sparser encoding or a reduced attentional load when processing stimuli that are familiar” (Gobbini and Haxby, 2006). Second, an fMRI adaptation study examined categorical effects for face images created by morphing between celebrity face pairs (Rotshtein et al., 2005). While the OFA showed release from adaptation with a change in the stimulus, the FFA showed release only when the change caused the stimulus to cross a category boundary between identities (Rotshtein et al., 2005). This suggests that FFA activity is not only sensitive to facial structure, but also has knowledge about identity.

It is possible that these effects in the FFA reflect top-down modulation from more anterior temporal regions that are the true site of facial memory stores, an interpretation that is supported by lesion data suggesting that anterior temporal lesions rather than fusiform lesions are associated with the most severe deficits in facial imagery (Barton and Cherkasova, 2003). Nevertheless, if facial memories are located in the FFA, then disconnection of the FFA from the OFA may be an alternative candidate for the neural correlate of the disconnection between perceptual encoding and facial memory stores in associative prosopagnosia (Fig. 5). Intriguingly, a lesion overlap meta-analysis of prosopagnosia cases in the literature suggests that the most frequent damage in the right hemisphere in prosopagnosia affects either the OFA or the region between the OFA and FFA (Bouvier and Engel, 2006). However, more information is required to determine whether the functional profile of cases with lesions located between the OFA and FFA meet the proposed requirements for a disconnection form of associative prosopagnosia.

To what extent have prior reports claiming disconnection as a cause for associative prosopagnosia met the two functional criteria discussed above? Regarding perceptual encoding of faces, evidence for its preservation varies in the early reports. Some claim preserved face matching without providing much data (Habib, 1986; Kay and Levin, 1982), while others document normal scores on the BFRT (Bauer, 1982). Some report impaired face matching on the BFRT (Aptman et al., 1977), while others report face matching deficits in their patients but assert that since a non-prosopagnosic control patient had similar deficits, such data do not indicate an encoding problem sufficient to cause prosopagnosia (McNeil and Warrington, 1991) (note, however, that this argument does not prove the presence of perceptual encoding sufficient to support face recognition). Others provide no evidence regarding encoding (Gomori and Hawryluk, 1984; Kawahata and Nagata, 1989).

Regarding facial memory stores, the older literature often contains the assumption that damage to facial memories could only occur as part of a more widespread amnesic disorder: therefore, loss of memories confined to faces or the visual

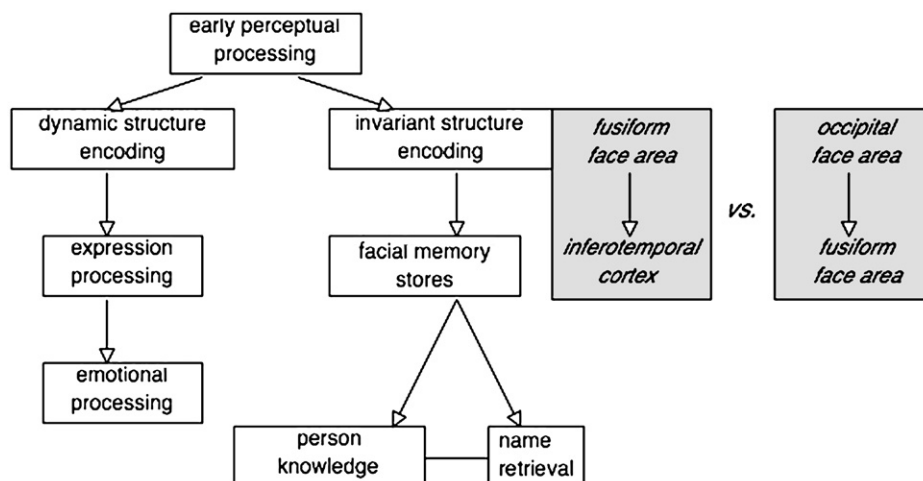


Fig. 5 – Potential anatomic correlates of a disconnection form of associative prosopagnosia, in which perceptual data cannot be linked to facial memory stores. Depending upon where one believes facial memory stores to be located, this may occur from damage to connections between the FFA and inferotemporal cortex, perhaps involving the inferior longitudinal fasciculus, or from damage to connections between the OFA and the FFA.

modality (Ross, 1980, 2008, *this issue*) must indicate a disruption between visual input and memory processing in the temporal lobe (see also Ross, 2008, *this issue*). Preserved encoding of faces and the absence of a general amnesic disorder is thus claimed as sufficient proof of disconnection. More specific probes of the status of facial memories would be desirable, however. Unfortunately, many studies did not attempt such assessments (Gomori and Hawryluk, 1984; Kawahata and Nagata, 1989; Kay and Levin, 1982). One study suggested that the covert ability of patients to learn to associate famous faces with their correct names more quickly than with incorrect names is proof of the existence of residual facial memories, and can be used to distinguish disconnection versus destruction of facial memory stores (McNeil and Warrington, 1991). Face imagery has seldom been used. Interestingly, some reports claiming disconnection contain statements that actually suggest degraded facial memories: “visual evocation of faces was also very poorly performed” (Habib, 1986). Perhaps the most plausible report of disconnection causing associative prosopagnosia is a man with bilateral infarcts of the lingual and fusiform gyri (Takahashi et al., 1995). Normal perceptual encoding of faces was demonstrated on tasks of same/different face discrimination and unfamiliar face matching. The authors concluded that facial memory stores were intact on the basis of normal general memory function and the patient’s claim that he could imagine the faces of familiar individuals. This claim was tested by verbal descriptions and a drawing task, admittedly subjective forms of evidence.

4. Disconnection from the extended system: conscious awareness

Although not a component of current concepts of the extended system, an older disconnection account of associative prosopagnosia also deserves mention. This hypothesis postulates that associative prosopagnosia may sometimes arise from disconnection between the intact normal output of the

core face processing system and a system mediating conscious awareness (De Haan et al., 1992). It is modeled on concepts within the “dissociative interactions in conscious experience” (DICE) model (Schacter, 1989), which proposes that the outputs of specialized stimulus-specific modules – such as a face processing module – are integrated by a ‘conscious awareness system’ that generates the experience of recognition and identification. This hypothesis predicts that patients with this disconnection would show intact functions of the face processing system, including normal structural encoding of faces, and intact facial memory stores, the latter of which they proposed to be indexed by residual covert recognition of faces with behavioral or autonomic tests, such as measures of skin conductance. On the other hand, patients with associative prosopagnosia due to damage to facial memory stores rather than disconnection of facial memory stores from the conscious awareness system would show lack of covert recognition in this hypothesis (Fig. 6).

This model was advanced as an explanation for covert face recognition. We suggest that it would predict that covert recognition (1) correlates with facial imagery, which we propose as another index of the integrity of facial memory stores, and (2) is never present in patients with impaired structural encoding of faces. Current data for covert behavioral indices of face processing do not support either prediction (Barton and Cherkasova, 2003), but there are no data on whether covert autonomic indices are consistent with these assertions. Anatomically, it is not clear if there is a discrete structural correlate of either this conscious awareness system or the proposed elements that link face processing with it.

5. Disconnection from the extended system: amnesic face-related deficits

In the cognitive model of face processing, achievement of a successful match between perception and facial memories may suffice for preserved familiarity with faces, but may not

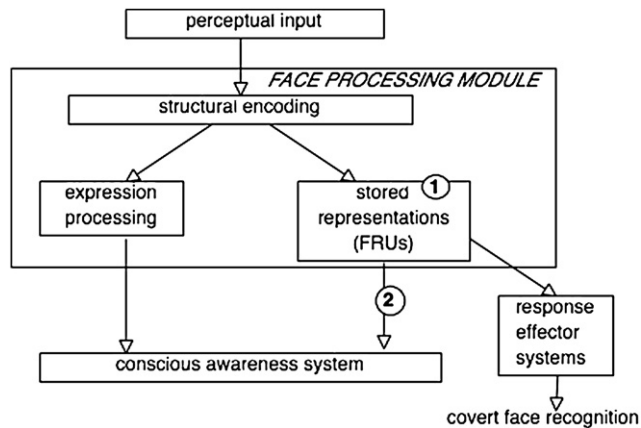


Fig. 6 – An alternative disconnection account of prosopagnosia, as proposed in (De Haan et al., 1992). Damage to FRUs (locus 1) causes an associative prosopagnosia with additional loss of covert recognition. Disconnection of FRUs from a conscious awareness system (locus 2) causes an associative prosopagnosia with preserved covert recognition. Reprinted with permission from Cortex® Elsevier Ltd.

support further processing required for recognition, which requires participation of the extended system. (There are dissenting views, however, that propose that “visual representations as such do not contain information related to familiarity or identity” and that conscious recognition only arises when facial representations are linked with knowledge or memories *Sergent and Poncet, 1990*; see also *Fig. 4*.) This would be akin to the common occurrence of seeing someone whom you realize is familiar, but whom you can’t quite place (*Young et al., 1985*). Current models suggest that this access problem can be further differentiated by the type of person-related information being accessed, such as the person’s name, other semantic information (e.g., their job), episodic memories pertaining to the person, or emotional connotations associated with them, all of which might involve different anatomic structures (*Gobbini and Haxby, 2007*) (*Fig. 2*). If so, there may be a number of different types of disconnection that could occur within this extended system.

What would be the functional signature of these disconnections? First, if the current distinction between core and extended processing systems is correct, common to all and distinguishing them from classical prosopagnosia would be an intact ability to judge facial familiarity, which can be done by presenting patients with a series of famous and anonymous faces and asking them to indicate which ones are familiar, without requiring them to name the faces (*Barton et al., 2001*).

Second, impaired ability to use the faces of celebrities or personally familiar faces to access specific person-related information should be found. Ideally, tasks should probe whether, when presented with a face that they acknowledge as familiar, the patient can provide (1) a name, (2) semantic information (e.g., job, nationality), and (3) episodic biographical data (e.g., historical event associated with the person). Furthermore, if these types of person-related information are

really encoded in different anatomic structures (*Gobbini and Haxby, 2007*), a specific disconnection in the extended system should show problems with performing one of these three tasks but not the other two.

Third, one must demonstrate that the person-related information that cannot be retrieved from viewing a face can be accessed through some other route, such as hearing voices. Access between these systems may be an alternative method: e.g., the ability to provide semantic information about a name (What was John F Kennedy’s job?), or the ability to provide a name for specific episodic information (Which president was assassinated in Dallas, Texas?). This is required to prove that the information still exists, but cannot be accessed from the outputs of the face processing system (*Table 2*).

Predicting the location of lesions that would generate these potential mnemonic disconnections between the core and extended systems is hampered by the debate over the localization of facial memory stores. Definitive assignment of anatomic structures to the processing within the extended system is also tentative at present (*Fig. 2*). Semantic information about people may be stored in the anterior temporal lobes (*Douville et al., 2005*; *Gobbini and Haxby, 2007*; *Snowden et al., 2004*; *Tsukiura et al., 2002, 2006*), possibly with some lateralization to the right hemisphere (*Thompson et al., 2004*) (see also *Catani and Mesulam, 2008b, this issue*). The precuneus and/or posterior cingulate cortex seems to be more involved with episodic memories associated with face familiarity (*Gobbini and Haxby, 2006, 2007*; *Kosaka et al., 2003*) and its multimodal nature is shown by the fact that it is activated by both personally familiar faces and voices (*Shah et al., 2001*). However, others suggest that these elements of the retrosplenial cortex may actually be more involved with a ‘familiarity check’ than episodic memory (*Shah et al., 2001*).

Name storage and retrieval, on the other hand, may lateralize to the left anterior temporal lobe. In semantic dementia, greater right-sided atrophy is linked to difficulty identifying faces as familiar, but greater left-sided atrophy impairs the ability to identify names as familiar (*Snowden et al., 2004*). While patients with right anterior temporal lobectomy are impaired in processing the familiarity of a face, patients with left anterior temporal lobectomy have a normal sense of familiarity with faces but have difficulty naming these faces (*Glosser et al., 2003*; *Seidenberg et al., 2002*). Other studies show that the deficit for name retrieval after left anterior temporal lobectomy is multimodal, in that subjects cannot

Table 2 – Mnestic disconnection

Cognitive Function	Status	Experimental test
Face familiarity	Intact	Unfamiliar/familiar face sorting
Face access to person information	Impaired	Access from famous faces to (A) name, (B) semantic information or (C) episodic/biographic information
Person information	Intact	Access from famous names or famous voices to (A) name, (B) semantic information or (C) episodic/biographic information.

provide the name when given either the face of or semantic information about the person (Fukatsu et al., 1999; Tsukiura et al., 2002). These neuropsychological conclusions are supported by neuroimaging studies showing that the long-term retrieval of names associated with faces is accompanied by activation in the left anterior temporal lobe (Douville et al., 2005; Tsukiura et al., 2003), which may be further enhanced when name retrieval is linked to semantic information (Tsukiura et al., 2006).

It is not clear whether there are any neuropsychological cases with data that meet the above criteria for a disconnection between the core and extended face processing systems. Nevertheless, this review suggests that, of all these hypothetical disconnections, a face-selective anomia for people may be the most plausible deficit, and might occur with an inter-hemispheric disconnection between the right and left anterior temporal lobes. Selective left amygdalohippocampotomy may provide such a scenario, as it preserves much of the anterior temporal lobe, but may destroy some of the white matter tracts.

6. Disconnection from the extended system: affective processing

Viewing a familiar face is often associated with affective responses and corresponding autonomic reactions (Herzmann et al., 2004; Tranel and Damasio, 1988; Tranel et al., 1985). Disconnection of the outputs of the core processing system to processes mediating these affective responses would result in intact familiarity of faces – and probably intact access from faces to names and semantic data, if other aspects of the extended system remain accessible – without the appropriate emotional overtones. This would result in the subjective experience of a face that ‘looks’ familiar but doesn’t ‘feel’ familiar.

The functional signature of such an affective disconnection would first consist of intact recognition or at least familiarity for known faces. Second, the affective response to faces must be impaired. While many indices can be devised, this has been most often indexed by the galvanic skin response, which is greater for familiar than novel faces (Herzmann et al., 2004; Tranel and Damasio, 1988; Tranel et al., 1985). Third, normal generation of an affective response to other stimuli or modalities, such as familiar names (Bauer, 1984) or sounds (Tranel et al., 1995) must be present (Table 3).

Anatomically, emotional processing involves a network that includes the amygdala and insula. Studies of galvanic skin conductance show loss of this autonomic index of affective processing in patients with lesions of the amygdala (Tranel et al., 1995). Thus it is conceivable that a ‘visuo-limbic disconnection’ could occur from bilateral lesions of projections from the occipital to the anterior temporal regions, possibly in the inferior longitudinal fasciculus (Catani and Thiebaut de Schotten, 2008, this issue).

Visuo-limbic disconnections have been hypothesized in cases of visual hypoemotionality associated with prosopagnosia (Bauer, 1982; Habib, 1986). Habib (1986) reported a prosopagnosic woman who had a ‘lack of emotive reaction elicited by visual stimuli’ but exhibited normal emotional responses to

Table 3 – Affective disconnection

Cognitive function	Status	Experimental test
Face recognition	Intact	Famous face recognition
Face-induced affective response	Impaired	Autonomic response (i.e., galvanic skin response) to view famous faces.
Voice- or name-induced affective response	Intact	Autonomic response (i.e., galvanic skin response) to famous names or heard famous voices.

auditory stimuli (see also Ross, 2008, this issue). More objective data were provided by Bauer (1982), who studied skin conductance changes in a male prosopagnosic patient and found increased autonomic responses to sexual narratives but not to the viewing of female nudes. However, such cases of visual hypoemotionality are not truly disconnections of the core face processing system from limbic processing, as the hypoemotionality affects many visual stimuli, not just faces: hence they are a parallel disconnection that is associated with prosopagnosia, likely because of anatomic proximity, rather than a disconnection involving face processing (Fig. 7).

Disconnection between face processing and limbic systems has also been advanced as an explanation for the Capgras delusion, a misidentification syndrome in which

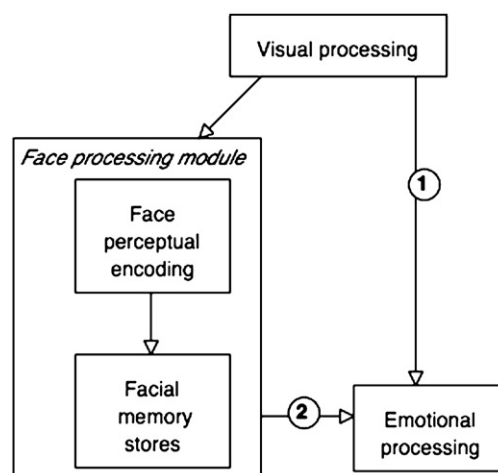


Fig. 7 – Visuo-limbic disconnections. Classic reports of visuo-limbic disconnection (Bauer, 1982) reflect a general loss of emotional responsivity to all visual stimuli, not just faces, and hence represent a disconnection between visual processing and emotional processing (locus 1) that can occur together with prosopagnosia (damage to modules on the left side of the diagram) possibly through damage to the inferior longitudinal fasciculus. A hypothetical face-related visuo-limbic disconnection may be envisioned between the outputs of a face processing module to the emotional processing system (locus 2). In this case, face recognition, the product of the face processing module, may be intact, but lack emotional overtones. Such a disconnection has been proposed as an explanation of Capgras syndrome (Ellis et al., 1997).

the subject claims that familiar people are impostors (Capgras and Reboul-Lachaux, 1923). The subject states that the ‘impostor’ looks similar to the people they are replacing, often describing them as ‘doubles’, but does not accept them as the real person (Lucchelli and Spinnler, 2007). On occasion this can be selective to the visual domain, as some patients do not show a similar delusion for the voices of the same people they consider to be imposters visually (Hirstein and Ramachandran, 1997). In essence, the Capgras delusion represents the combined effects of a (1) discordance between some degree of recognition at one level (otherwise they would claim the familiar person was a stranger, not an impostor) and failure of recognition on another, along with (2) failure of decision-monitoring systems, possibly involving the frontal lobe, so that the source of the discordance is attributed to the stimulus. One possible discordance (note that other hypotheses exist; Ellis and Lewis, 2001) is that, while conscious face recognition is intact, allowing subjects to see the similarity between the person before them and someone they know, affective responses to that face are lacking, with the result that the encounter does not feel quite ‘real’. In support, studies using skin conductance have shown that patients with Capgras delusion fail to show an affective response to familiar faces (Brighetti et al., 2007; Ellis et al., 1997). Thus Hirstein and Ramachandran (1997) postulate that Capgras delusion could result from a lesion affecting connections between face processing systems in the temporal lobe (inferior temporal cortex and STS) and the limbic system including the amygdala (Fig. 7). Their patient DS had Capgras delusion following a right parietal fracture, with bifrontal encephalomalacia evident on a CT scan, and showed normal face matching and famous face recognition but reduced galvanic skin response to familiar faces (Hirstein and Ramachandran, 1997).

7. Assessing connectivity in vivo with MRI

The main assumptions of any disconnection syndrome are that different brain regions are anatomically connected and that damage to connections may impair the information transfer between those regions, resulting in a selective cognitive dysfunction. Older reports of disconnection have relied on theoretical cognitive models or anatomical findings in post-mortem brains. Neuroimaging techniques are beginning to allow assessment of brain connectivity *in vivo*. First, functional MRI studies can determine whether fluctuations in signal intensity are correlated between different cortical regions, either during a resting state or while the subject is engaged in processing some stimulus or performing some task. These analyses of ‘functional connectivity’ (Rogers et al., 2007) interpret a high correlation as evidence that different regions are working in concert as part of a processing network and have recently been applied to the study of face processing systems (Fairhall and Ishai, 2007). Second, ‘structural connectivity’ can be assessed by diffusion tensor imaging (DTI) tractography (Le Bihan, 1991), which uses the fractional anisotropy of water diffusion to re-create the course of white matter projections (Basser et al., 1994; Pierpaoli and Basser, 1996; see also Jones, 2008, this issue).

Use of these techniques in both patients and healthy controls has the potential to validate neuropsychological hypotheses of disconnection based upon cognitive models (see also Rudrauf et al., 2008, this issue; Thiebaut de Schotten et al., 2008, this issue). DTI tractography in healthy controls may be used to demonstrate connectivity between different regions included in both extended and core systems of face processing. The most likely fiber pathway for connecting regions of the core system of face processing is the inferior longitudinal fasciculus (Catani and Thiebaut de Schotten, 2008, this issue), long proposed as a possible substrate for prosopagnosia (Benson et al., 1974; Habib, 1986; Kawahata and Nagata, 1989; Kay and Levin, 1982; Meadows, 1974; Takahashi et al., 1995). This fiber pathway courses along the inferior surface of the brain from the occipital pole to the temporal pole and is present in both humans (Catani et al., 2003) and non-human primates (Martin-Elkins and Horel, 1992). Damage to the inferior longitudinal fasciculus may disconnect the OFA and FFA from each other or from regions in anterior temporal lobe and the precuneus (Catani et al., 2003). Projections connecting the anterior temporal lobe with regions in the frontal lobes, such as the anterior paracingulate cortex, may be present in the uncinate fasciculus (Catani et al., 2002; Catani and Thiebaut de Schotten, 2008, this issue; Kier et al., 2004). In addition to these intra-hemispheric tracts, callosal fibers (see also Glickstein and Berlucchi, 2008, this issue; Doron and Gazzaniga, 2008, this issue; Catani and Thiebaut de Schotten, 2008, this issue) may play a role in transferring information between right and left homologues of certain modules of the core system and the anterior temporal lobes (Habib, 1986; Kay and Levin, 1982; Meadows, 1974). Finally, in addition to long projection fibers, U-shaped projections connect adjacent gyri along the inferior surface of the temporal lobes (Catani et al., 2003; Tusa and Ungerleider, 1985), and lesions affecting these may disconnect adjacent face modules such as the OFA and FFA from each other.

While DTI studies have begun to delineate these pathways in humans (Catani et al., 2003; Kier et al., 2004), more work is needed to integrate these data with functional imaging and behavioral data in patients to determine the types of information utilizing these tracts and the patterns of disconnection associated with their disruption. Work in this direction is already being conducted in congenital prosopagnosia. Preliminary results from DTI tractography have shown a reduction in fibers connecting the temporal and frontal lobes in these patients (Thomas et al., 2006), who not only lack visible lesions but show intact activation of the FFA and OFA. Such a finding may indicate a hodological disruption of connection fibers, as suggested by Catani and Ffytche (2005). It would also be of interest to determine whether similar disruptions in connectivity between modules of the face processing systems are present in other conditions with impaired face processing and grossly normal cerebral structure, such as autism spectrum disorders (Barton et al., 2004).

Finally, it should be emphasized that the behavioral patterns of deficits hypothesized above for theoretical dissociations in models may not be as clean and precise in living patients. Underlying many of these predicted patterns are assumptions that each cognitive step emerges from the function of a single anatomic module independent of the functional status of other modules. It is quite possible that, even though

different anatomic modules make different contributions to different cognitive stages, the full product of each stage may require interactions between separate modules. (It may be, for example, that perceptual encoding may occur predominantly in the FFA and OFA, but that there is a minor contribution from anterior temporal regions. This could explain the observation that a prosopagnosic patient with anterior temporal damage had not only severe deficits in face imagery, but also subtle perceptual defects in encoding face structure; [Barton et al., 2003](#).) If so, anatomic disconnection may result in deficits to processing stages that the current formulations suggest should be intact: hence a disconnection in the core processing system causing associative prosopagnosia may cause some deficit in both encoding and facial imagery, rather than no deficit (see also [Catani and Mesulam, 2008a, this issue](#)). One might hypothesize that such deficits would be less severe than the deficits resulting from damage to the primary cortical structures involved in perceptual encoding or facial memories, but this remains to be proven. The ability to visualize anatomic connectivity with modern neuroimaging will provide a very useful test of the type and pattern of behavioral disconnections suggested in current cognitive models.

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