Acquired prosopagnosia: structural basis and processing impairments

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1. ABSTRACT

   Cognitive models propose a hierarchy of parallel processing stages in face perception, and functional neuroimaging shows a network of regions involved in face processing. Reflecting this, acquired prosopagnosia is not a single entity but a family of disorders with different anatomic lesions and different functional deficits. One classic distinction is between an apperceptive variant, in which there is impaired perception of facial structure, and an associative/amnestic variant, in which perception is relatively intact, with subsequent problems matching perception to facial memories, because of either disconnection or loss of those memories. These disorders also have to be distinguished from people-specific amnesia, a multimodal impairment, and prosop-anomia, in which familiarity with faces is preserved but access to names is disrupted. These different disorders can be conceived as specific deficits at different processing stages in cognitive models, and suggests that these functional stages may have distinct neuroanatomic substrates. It remains to be seen whether a similar anatomic and functional variability is present in developmental prosopagnosia.

2. INTRODUCTION

   Prosopagnosia is the impaired ability to recognize familiar faces or to learn to recognize new faces (1, 2). Individuals with prosopagnosia have a problem discriminating known from unknown faces, and in the absence of useful information about face identity they experience most faces as unfamiliar (which contrasts with the bias to experiencing most faces as familiar that is seen in patients with “false familiarity for faces” (3). Because of the pre-eminence of faces in social interactions, prosopagnosia is one of the most well-known and well-studied deficits of person recognition. Although impaired face recognition can be a symptom of more general problems of perception, cognition, and memory, as in macular degeneration (4), Alzheimer’s dementia (5-7), mild cognitive impairment (8), Huntington’s chorea (9), and Parkinson’s disease (10, 11), the term ‘prosopagnosia’ should be reserved for a specific dysfunctional state in which there is a relatively selective deficit in face recognition that cannot be explained by more general problems of perception, cognition or memory. Therefore, diagnosing this condition requires detailed
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Figure 1. Model of face processing. Damage to posterior regions of the inferior occipito-temporal cortex can result in difficulties with early perceptual encoding and perceptual encoding of static structure, resulting in apperceptive prosopagnosia (blue). Damage to the anterior inferior temporal cortex can result in difficulties retrieving face memories, or linking static structure to the memory of faces (red). Meanwhile, damage to the anterior temporal pole can result in difficulties with biographical information which results in person-specific amnesia (green).

Why and how people can acquire a deficit that seems to affect mainly the ability to recognize faces is the subject of substantial research. One important point deserving emphasis is that prosopagnosia is not a disorder but a family of disorders. Face recognition is a complex cognitive process, and like all such processes it cannot be reduced to a single function or a single anatomic region in the brain. Rather, it requires participation of several perceptual, memory and cognitive operations that take place in a distributed network of interconnected cerebral regions. As a result, the lesions of acquired prosopagnosia can vary significantly between patients, as can the precise nature of their dysfunction and associated defects.

Structurally, it has long been known that prosopagnosia can arise from a very diverse set of lesions, ranging in size from posterior occipitotemporal regions to anterior temporal cortex (15). While early reports described prosopagnosia after bilateral occipitotemporal lesions (16, 17), others suggested that a right hemispheric lesion could be sufficient to cause prosopagnosia (18, 19). This was supported by later work with neuroimaging indicating that some patients had unilateral lesions, almost always on the right side (19, 20). Of the few subjects with unilateral left lesions, most were left-handed (21-24), suggesting that they may have had anomalous hemispheric asymmetries to begin with. A right hemispheric bias for cases of prosopagnosia accords with data from functional magnetic resonance imaging studies in healthy subjects, which show that faces activate more voxels with greater significance in the core face–processing network of the right hemisphere, compared to those components in the left hemisphere (25, 26). At this point, though, it is not clear how prosopagnosia with bilateral lesions differs from prosopagnosia with unilateral right-sided lesions. Although there is some suggestion from functional neuro-imaging that the components of the face network in the left hemisphere may be involved more with perception of local features of the face (27), it is not known for certain whether these components perform redundant operations or forms of processing that are complementary to their right-sided counterparts. Nevertheless, there are occasional reports of patients who suffered right-side damage but did not report prosopagnosia until after a second left-sided lesion (28), suggesting that in at least some human subjects the contribution of the left hemisphere to face recognition is significant.

Functionally, concepts of the nature of the dysfunction in prosopagnosia are closely linked to models of normal face recognition. One enduring and influential model (29) contains a number of key aspects. First, a prominent feature is the proposal of two parallel mechanisms – one involved in processing the changeable aspects of faces, such as emotional expression, viewpoint, lip-reading, and gaze direction, and another involved in the perception of stable aspects of faces, particularly identity (Figure 1). This is supported by evidence from functional imaging and primate electrophysiology that there may indeed be separate areas for encoding facial identity and
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Facial social signals (30-32). If so, this raises the possibility that deficits in the processing of identity and social signals could be dissociated in patients with lesions, and that not all types of facial information may be affected in prosopagnosia. Although the literature is mixed on whether prosopagnosic patients are also impaired on aspects of face perception like expression and lip-reading (see (33) for a review), there is some evidence for a double dissociation between identity and expression processing (34).

A second important feature is that face processing involves a hierarchy of stages (35, 36). In the case of identity, visual processing generates a face percept, which is then matched to a memory store of previously encountered faces, sometimes referred to as ‘face recognition units’, or FRUs. A successful match activates person-identity nodes (PINs), which in turn activate name recognition units (NRUs) and semantic information units (SRUs) containing biographical information about the person. PINs, SRUs and NRUs are multimodal in nature, in that they can also be accessed through other non-facial cues, such as voice or gait. Top-down processing can also occur. For example, matching of the face percept to face recognition units may be enhanced by top-down semantic activation from person identity nodes, as when the subject already knows the name of the person or some contextual information about them (eg. actor, family, workmate).

Reflections of this hierarchical model are also evident in some of the clinical aspects of prosopagnosia. First, there is evidence of functional subtypes of prosopagnosia, in which either the creation of the face percept or its subsequent matching to facial memories is the critical deficit (15, 37, 38). Second, patients with prosopagnosia can identify people by voices or non-facial visual cues such as voice or gait. Top-down processing can also occur. For example, matching of the face percept to face recognition units may be enhanced by top-down semantic activation from person identity nodes, as when the subject already knows the name of the person or some contextual information about them (eg. actor, family, workmate).

One of the important goals of research in prosopagnosia is to correlate the structural variations with functional subtypes, to better understand the anatomic basis of the different cognitive processes involved. Most of the evidence that has been collected has been performed on cases with acquired prosopagnosia, which will be the major focus of this article. A developmental form of prosopagnosia has only been recognized more recently: it is increasingly a topic of study, and is more extensively reviewed in the article of Avidan and Behrmann in this issue.

3. ACQUIRED PROSOPAGNOSIA

Acquired prosopagnosia is the loss of the ability to recognize familiar faces following some cerebral injury (44). Most often this affects both the recognition of familiar faces as well as new faces. However, there is a rare anterograde form, in which the deficit is limited to faces encountered since the onset of the lesion (45-47).

As mentioned above, whether or not the face-processing deficit is limited to the recognition of identity is of theoretical interest to cognitive models. The older literature is replete with contradictory claims. Some prosopagnosic subjects are purportedly impaired in processing gaze direction, emotional expression, age, ethnicity and gender (41, 42, 48-51), while in others the face processing deficit is stated to spare at least some of these other types of facial information (39, 52-55). One simple explanation for these divergent claims may be variations in lesion extent and location: however, assessing this is difficult with the information provided in older cases from different researchers. Recent advances in neuroimaging and the ability to identify the functional network involved in face-processing in single subjects (56) will advance this issue. A report that used functional magnetic resonance imaging to describe the impact of lesions on the face network noted a double dissociation (Figure 2). This tested the ability of subjects to discriminate changes in faces morphed along either an identity or expression continuum, with the level of difficulty kept equivalent between the two. The updated data from this study shows that, while a few subjects are impaired in neither or impaired in both, some patients do show dissociated performance on this test. Prosopagnosic patients can be impaired in discriminating changes in identity but not changes in expression in morphed facial images. Conversely, a patient with a lesion that eliminated the right superior temporal sulcus had the reverse deficit (34).

The existence of at least two functional subtypes of prosopagnosia is best established for this acquired form (15, 37, 38). In ‘apperceptive prosopagnosia’ the defect is an inability to form a sufficiently accurate representation of the face’s structure from visual data. This results in a degraded match to facial memory stores, with weak activation that may not be sufficient to achieve a threshold to trigger either a familiarity signal or access to further information about the person. In contrast, in ‘associative prosopagnosia’ the patient can perceive facial structure well; rather, the defect lies in the process of matching this high-fidelity facial information to facial memories. In some cases it is postulated that this is due to a disconnection between perception and memory (57). In other cases, it may be simply because facial memories have been lost, a scenario which some would term an ‘amnestic variant’ of prosopagnosia (15). Of course, given the variable location and extent of naturally occurring lesions in humans, and the fact that complex cognitive operations are seldom reducible to single anatomic loci, pure versions of these subtypes may be the exception rather than the rule. Indeed, the data show that patients with severe perceptual deficits in face perception often have milder impairments in face imagery, while those with severe impairments of memory for faces have milder problems on perceptual discrimination tests for faces (38). This is consistent with the concept that face recognition emerges from the coordinated action of a

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Figure 2. Contrast between recognition of identity and expression in morphed facial images. Used with permission from (34).

The four prosopagnosic patients in the yellow zone have impaired perception of morphing-induced changes in identity, but are accurate in discriminating similar changes in expression. In the blue zone is one subject with a lesion of the right superior temporal sulcus, who had the reverse, impaired perception of expression changes but intact discrimination of identity changes. A number of prosopagnosic subjects are normal on both tests (clear area), including some patients with occipitotemporal lesions. (However, some of these admitted later to using a feature-based strategy to solve the identity part of the test, R-IOT4 by concentrating on the eyebrows, for example.) Only two prosopagnosic subjects had problems with both identity and expression (pink zone). L-IOT1 had a left fusiform resection for epilepsy but also had an atrophic right fusiform region: he showed activation by faces of only the left occipital face area and the right superior temporal sulcus of his core network. B-ATOT1 had extensive bilateral fusiform and anterior temporal lesions from herpes encephalitis.

distributed network, though one in which the different nodes of the network have different contributions. Thus, the terms apperceptive and associative/amnestic may be best used to indicate the predominant rather than the sole functional deficit in a given patient, with an anterior-posterior gradient in which occipital lesions cause more problems with perception than memory for faces, while anterior temporal lesions cause more problems with memory than with perception of faces, as discussed below.

3.1. Apperceptive prosopagnosia

In apperceptive prosopagnosia, the subject cannot form an accurate perceptual representation of the facial structure that is specific to identity. This can occur following either unilateral (most often right) or bilateral occipitotemporal damage (Figure 3). Older reports suggest that this is most often correlated with damage to the right or bilateral fusiform gyri (37, 58). More recent evidence from structural MRI suggests that the responsible lesions often occur in the vicinity of the right fusiform face area (59, 60), an assertion that receives support from functional MRI studies confirming loss of the right fusiform face area in some patients (34). However, others have suggested that the most common lesioned site for prosopagnosia is around the right OFA (61), and is supported by patient findings such as PS, whose lesions involved the right occipital face area and the left fusiform face area, but spared a right fusiform face area (62, 63). This is consistent with face recognition emerging from activity across a cortical network rather than a single region, and suggests that both the occipital and fusiform face areas contribute to the perceptual encoding of faces.

Apperceptive prosopagnosia is diagnosed by showing that patients are impaired not only in familiarity or recognition of known faces, but also impaired in perceiving the difference between faces. The Benton Face Recognition Test (64) asks a subject to choose which face in an array of six images matches a target face, in some items across changes in viewpoint and lighting. However, this test can be failed by non-prosopagnosic patients (65-67), and some prosopagnosic patients may achieve normal accuracy rates but take a long time to do the test, suggesting abnormal perceptual strategies (68). The Cambridge Face Perception Test (69) presents a face at the top of the screen and asks a subject to arrange in order of resemblance six faces that a morphing program has made gradually more different from the top face, within a time limit. Experimental tests can also examine the amount of difference between morphed faces required to support discrimination (34), or examine the ability of subjects to perceive changes to facial shape (70).

The precise nature of the processing deficit that can result in impaired perception of faces but leave basic object recognition intact remains unclear. One hypothesis is that some sort of holistic perceptual mechanism is disrupted. A number of observations in healthy subjects show substantial influences of whole-object structure on face perception (71-74) and studies have shown that some prosopagnosic patients are deficient in the perception of
Figure 3. Axial images from T1-weighted magnetic resonance imaging of two patients with ‘apperceptive’ prosopagnosia. A) Unilateral inferior occipital damage in a 61 year-old man (R-IOT4) presenting with prosopagnosia, topographagnosia, and left quadrantanopia. B) MR axial images of bilateral inferior occipital damage in a 60 year-old man (B-IOT3) presenting with prosopagnosia, topographagnosia, dyschromatopsia and right hemianopia.

whole faces and instead rely on a feature-by-feature strategy in face perception (58, 75-77). Another related hypothesis is that the configuration or spatial relations between individual facial features in this whole-object structure may be particularly important in specifying the structure of a unique face (78-80). In monkeys, electrophysiological recordings have shown that cells in inferior temporal cortex are selective for faces that differ in these spatial relations (81, 82). Studies have shown that prosopagnosic patients with occipitotemporal lesions are impaired in perceiving the configuration of facial features (38, 83, 84). Ultimately, though, it may be that these spatial relations are merely a convenient metric for studying the precision of a subject’s perception of the complex shape of faces, which need to be processed rapidly and in aggregate across the entire face to support efficient recognition of identity.

A third aspect of face perception is the fact that some regions are more salient than others (85). Numerous studies show that subjects pay more attention to the eyes than to the lower face, particularly when the subject is trying to identify the face (86), and that the eye region contains the information most useful for identification (87-91). Prosopagnosic patients may be particularly impaired in using information from the eye region. Their scanning eye movements show a reduced number of fixations in the eye region (92), their discrimination of structural changes in the eye region is particularly poor (93), and they are more impaired in deducing identity from the eyes than from the mouth (60, 94-96). Loss of normal patterns of saliency in how prosopagnosic subjects process faces may reflect loss of optimal perceptual strategies in deriving identity, which normally should emphasize the eyes.

Whether deficits in perception of more elementary aspects of vision may contribute to prosopagnosia has been considered. Brightness and contrast are important cues to the orientation of surfaces when lighting casts shadows, and therefore are potent sources of information about the shape of complex objects with multiple surfaces. Studies with photonegatives confirm an important role for brightness information in face recognition (97), and reduced brightness perception was reported in one subject with developmental prosopagnosia (98). Impaired face perception in Alzheimer’s disease has been attributed to reduced contrast sensitivity at low spatial frequencies (7), but one study of seven patients with acquired prosopagnosia found more consistent deficits at higher spatial frequencies (99). Curvature perception has also been studied. The face has a myriad of curved surfaces, and impaired curvature perception was reported in a subject with developmental prosopagnosia (100, 101). However, in the series of subjects with acquired prosopagnosia, a deficit in curvature perception was found in only one subject, who also had the most difficulty on tests of basic-level object recognition (99).
The problems with judging the spatial relationship between features demonstrated in apperceptive prosopagnosia (83) has raised the question of whether this is a deficit in perceiving fine spatial structure that extends to other visual stimuli. Some studies have shown that patients with acquired prosopagnosia have problems perceiving the spatial relationships between dots arranged in face and non-face-like configurations (99). This deficit was specifically linked to judgments about object shape, as their perception of the spatial relationships between different objects was not affected (102). Interestingly, their difficulty with the spatial arrangement of dot patterns continued to show influences of whole-object perception (103). Their ability to perceive local spatial relationships improved when more dots were available, suggesting that they gained by being able to reference dots to multiple points in the whole arrangement, when size or orientation changed between stimuli, which emphasized referencing to the whole object, or when the global arrangement had a more regular structure. Similarly, it has been reported that some patients with acquired prosopagnosia show normal influences of global whole-object structure with Navon letters (103, 104). Thus, while their impairment with judging the fine spatial metrics between parts of an object may be impaired not just for faces but also for other stimuli (but see case GG for an exception; (105)), any impairment in holistic processing may be specific for faces. This may also be an important distinction from congenital prosopagnosia, where differences in holistic processing for non-face objects like Navon letters have been demonstrated (106, 107), as discussed in the article by Avidan and Behrmann in this issue.

3.2. Associative/amnestic prosopagnosia

In this variant, face perception is relatively intact, but there is a failure of this perceptual information to gain access to face memory stores (face recognition units) (37, 45, 108). This type of prosopagnosia is associated with anterior temporal lesions (39, 109, 110), and may be due to either a disconnection between facial percepts and the memory stores (43, 57), or a loss of facial memories. Similar to apperceptive prosopagnosia, associative/amnestic prosopagnosia can occur following either right unilateral damage, or bilateral damage (Figure 4).

To demonstrate intact or relatively preserved face perception, one can use the Benton Face Recognition Test or the Cambridge Face Perception Test. It should be noted that experimental tests of face discrimination can still show some perceptual deficits that are generally milder than those seen in patients with occipitotemporal damage. For example, even though patients with anterior temporal lesions do better at perceiving the spatial relations between facial features, some may fail to integrate these spatial relations with each other across the entire face: again, a type of whole-face processing deficit (110). Also, tests with morphed faces show that at least some patients with anterior temporal lesions have difficulty appreciating subtle variations in facial shape (Figure 2).
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To probe the status of face memory, one can use probes of facial imagery, where the subject has to answer questions based on what they can recall about famous faces, without actually seeing them (43, 109). Failure to do this better than chance suggests a severe loss of facial memories, and has been noted in prosopagnosic patients with anterior temporal lesions and relatively preserved facial perceptual skills, while patients with posterior occipitotemporal lobe lesions show only mild impairments, despite their much more degraded face perception (60). Nevertheless, the fact that even occipitotemporal lesions do cause milder impairments in face imagery reinforces the point that the difference between these two groups of patients is often a relative rather than an absolute dichotomy. Hence prosopagnosic subjects with anterior temporal lesions are relatively better at facial perception and relatively worse on tests of facial imagery, compared to prosopagnosic patients with occipitotemporal lesions (38).

It has been argued by some that loss of facial memories should be considered an ‘amnestic’ deficit and distinct from inability to access facial memories through disconnection, with the term ‘associative’ reserved for the latter (15). In common, both amnestic and associative variants would show intact performance on encoding of facial structure on experimental tests or clinical assessments like the Benton Face Recognition Test or Cambridge Face Perception Test, and show no recognition or sense of familiarity on tests like the Warrington Recognition Memory Test or the Cambridge Face Memory Test. However, facial memories would still be intact in the disconnection scenario, and so these subjects should still perform well on tests of facial imagery, while those with the amnestic variant would fail (57). At this point, there are no known patients with impaired familiarity but both preservation of perceptual encoding of faces and also normal facial imagery: hence the pure associative non-amnestic variant remains a theoretical construct. For this reason, we tend to refer to prosopagnosic patients with preserved perceptual encoding and impaired facial imagery as having an associative variant, or sometimes an associative/amnestic variant, to stress the loss of facial memories.

While the classic disconnection proposed for associative prosopagnosia lies between perceptual processes and face memory stores in the face recognition units, another disconnection between face memories and person-identity nodes may also occur. This allows the patient to recognize that the face is familiar, because of a successful match between the percept and the correct facial memory, but they fail to retrieve the name or any biographical information about that person, because of failure to activate the corresponding person-identity node, even though name and biographical information can be accessed through other routes such as voice. Hence this condition may be better termed “prosop-anomia”, and has been described in a patient with an unusual left hemispheric lesion (111) and in another with bilateral temporal damage (47). Of note, in the first case, the defect was not specific to faces, as the patient also had anomia for places and other objects. It is of interest to speculate how a prosop-anomic patient would do on tests of facial imagery: if the top-down connection between person-identity node and facial recognition units is also severed, then they should have as much difficulty in conjuring up the face to a name as do patients with the associative/amnestic variant of prosopagnosia.

As a last point, it is important to distinguish associative prosopagnosia from people-specific amnesia. Unlike associative prosopagnosic subjects who can still recognize people from other sensory cues, damage to the person identity nodes can result in the inability to recollect other people via any cues, including spoken names or voices. Although these patients present with a memory deficit specific to people with other types of memories intact, these patients are not prosopagnosic. People-specific amnesia has been described in patients with right temporal pole lesions (39, 40, 112, 113), and is consistent with neuroimaging studies showing that both name and face recognition activate the anterior middle temporal gyrus and temporal pole (114, 115). Although many prosopagnosic subjects claim to recognize others by voice, this has seldom been verified by formal tests, which may be particularly important in those with anterior temporal lesions.

3.3. Impairments of other functions

In addition to their difficulties with face recognition, prosopagnosic subjects often have other deficits, most often because naturally occurring damage is not limited to the face network but also involves neighboring structures. Damage to the optic radiations or striate cortex is common in those with occipitotemporal lesions, and causes visual field deficits, often in the left or bilateral upper quadrants, or sometimes a left hemianopia (2, 43, 99). Additional damage to the lingual and medial fusiform gyri causes achromatopsia. Also, many prosopagnosic patients with occipito-temporal damage have topographagnosia, or difficulty in navigating in familiar surroundings (20, 39, 41, 48, 53, 116, 117). Functional imaging studies show that buildings and places activate a specific region in occipito-temporal cortex, the ‘parahippocampal place area’, which is adjacent to the fusiform face area (118). Lesions here may cause a form of topographagnosia related to impaired recognition of landmarks. Field defects and problems with colour vision or navigation are less likely in prosopagnosic patients with anterior temporal damage, but these subjects may have minor visual or verbal memory disturbances (20, 119).

3.4. Face specificity versus expertise

Related to the issue of associated deficits is the controversy about whether prosopagnosia is a truly face-specific deficit caused by damage to a module or network dedicated to the processing of faces alone (120), or if this reflects damage to an expertise network, required for making subtle differentiations between similar exemplars of the same object category, of which faces are merely the most dramatic and universal example (121). Although some prosopagnosic subjects may also have a mild visual object agnosia (41, 48), it is generally agreed that they can identify objects at a basic level or category, for example being able to distinguish faces from cars, and from flowers.
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What is argued is how well they do at more subtle distinctions, particularly within object categories, for example, distinguishing between types of cars or species of flowers. In support of face modularity are those reports of prosopagnosic subjects who can still identify personal belongings (122), individual animals (52, 123), specific places (39, 52), cars (52, 124, 125), flowers (39), vegetables (124, 126), and eyeglasses (127). In support of the expertise hypothesis are reports of prosopagnosic subjects who cannot identify types ("subordinate categories") of cars, food, or coins, or specific unique exemplars of buildings, handwriting, or personal clothing (17, 48, 128, 129).

There are many logical difficulties in settling this issue. On the one hand, impairments with recognizing other types of objects may simply be due to damage to other visual association cortex adjacent to face-processing regions, as is the case for achromatopsia and topograhphagnosia. On the other hand, claims of preserved recognition for another object class may be met with objections that either testing did not include a sufficient range of other object categories or else it did not test in sufficient detail. For example, some prosopagnosic subjects can show apparently normal accuracy rates on tests of their recognition of other objects, but analysis of reaction times or signal detection measures may reveal an impairment (130). Finally, a significant issue is that, while it is reasonable to assume nearly universal expertise for faces among human subjects, the same assumption cannot be made for most other visual objects. Hence, to evaluate the expertise hypothesis correctly, one must take into account how proficient a prosopagnosic subject was with the object type being tested before the onset of their problem (131). For example, the average person should be able to tell a hawk from an eagle, but a bird-watcher should be able to do better, perhaps distinguishing the buteo from accipiter genera of hawks. Showing intact hawk/eagle discrimination on a test may be evidence for preserved bird discrimination in the average person, but if this was the best discrimination a prosopagnosic bird-watcher could achieve after their lesion, one would suspect that they had impaired bird recognition as well.

In most situations, there is no opportunity to assess pre-morbid visual expertise with objects prior to the onset of acquired prosopagnosia. To deal with this difficulty, one might try to find a category for which subject interest and experience may be nearly as universal as with faces: this was the motivation for one study that found that most prosopagnosic subjects were also impaired in vegetable and fruit recognition (60, 132). However, for most object categories a degree of expertise homogenous across the population is unlikely and varying expertise will almost certainly be reflected in performance on tests. Even for food items, one might expect that a professional chef would be better than the average person. What is needed is some surrogate post-lesion measure that is highly likely to be correlated with pre-morbid visual expertise for other objects. Based on the assumption that semantic processing should be unaffected in a perceptual disorder such as prosopagnosia, one study examined the relationship between verbal semantic knowledge and visual recognition of cars. These two measures are highly correlated in healthy subjects (133). This tight relationship allows one to predict from a prosopagnosic subject’s semantic score what their visual recognition score should be if other object processing was indeed preserved. Based on this adjustment for pre-morbid expertise, our updated results in a group of 10 prosopagnosic subjects show that most subjects fell below the visual performance predicted by their verbal semantic score (Figure 5). In fact, convincing evidence for spared visual car recognition was found in only one subject, who had a right anterior temporal lesion from herpes encephalitis (Figure 4A).

3.5. Covert face recognition

Despite the professed inability of prosopagnosic subjects to recognize faces, in some there remains an unconscious or ‘covert’ face recognition (134-136). Covert face familiarity in prosopagnosia has been demonstrated with a wide variety of techniques, for which a taxonomy has been proposed (136). There are psychophysologic measures such as electrodermal skin conductance (45, 117, 119), and electrophysiological measures such as visual evoked potentials (137). Behavioural methods can be direct, as with name-cued forced choice guessing of identity (12, 58, 138), learning of paired face-name associations (52, 58, 138, 139), and eye movements when viewing famous versus anonymous faces (92, 140). Finally, indirect behavioural techniques seek to determine if faces that subjects do not recognize overtly nevertheless influence the way subjects perform other tasks that do not involve recognizing the identity of the face. Classic examples include studies of priming and interference effects of faces on tasks involving names, such as sorting famous names according to occupation (141-143), or indicating whether the names are familiar or not (139). These studies show that whether the face matches the name in the task can influence the speed of performance, even though the subjects do not recognize the face.

The mechanisms responsible for covert recognition continue to be debated. One possibility, the dissociated dual-pathway hypothesis, is based on disconnection models, and proposed that covert recognition represents surviving processing in an intact dorsal occipitoparietal pathway to the amygdala that parallels the damaged occipitotemporal structures that support explicit recognition (144). Another possibility, the residual network activity hypothesis, is that it represents residual weak function of a damaged face-processing network, as supported by computer simulations (145-147), as well as observations that covert priming effects are correlated with the degree of residual overt recognition in prosopagnosia (143), a finding that is predicted by the residual network activity hypothesis but not by the dissociated dual-pathway hypothesis.

4. DEVELOPMENTAL PROSOPAGNOSIA

Before concluding, it is worth devoting a few words to developmental prosopagnosia, a condition that has received increasing attention since its first report in 1976.
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Figure 5. Car recognition in prosopagnosia, adjusted for semantic knowledge as an index of pre-morbid expertise. Visual recognition (naming the manufacturer of a car whose image is shown on the screen) is plotted as a function of verbal semantic knowledge (naming the manufacturer of a car whose name is given, without showing its image). In healthy controls the visual and verbal scores are highly correlated (solid line shows linear regression). The scores for 10 prosopagnosic patients are shown (blue = right anterior temporal, green = bilateral anterior temporal, red = right occipitotemporal, orange = bilateral occipitotemporal). The relationship between visual and verbal scores is lower for prosopagnosic subjects (dashed line) than it is for controls (solid line), indicating that their visual recognition of cars is worse than predicted by their verbal semantic knowledge. Only one prosopagnosic subject (RAT3) has convincing evidence of intact car recognition.

(148), in particular regarding its parallels with acquired prosopagnosia. Again, it is important first to draw some distinctions within the variety of face processing deficits that may originate in early life. In some cases prosopagnosia can be acquired because of brain injury during early childhood, when face expertise is still developing, while in other cases there is visual evidence of a cerebral malformation or an in utero insult (149). Also, impaired face recognition may be part of another congenital disorder, such as autism or Asperger syndrome (150). However, the term developmental prosopagnosia is best preserved for those patients in whom impaired face recognition is the chief or sole deficit, and in whom imaging does not reveal any evidence of a structural lesion: other cases may be referred to as early-onset acquired prosopagnosia.

Previously studies have estimated that up to 2-2.9% of the population may have developmental prosopagnosia (151, 152). However, when the diagnosis is based on the simple statistical criterion that a subject’s score on a face recognition test lies more than 2 standard deviations below the mean (151), this estimate is tautological. (If the scores of a healthy population follow a normal distribution, 2.5% of its members will by definition score worse than 2 standard deviations below the mean.) Hence these figures are almost certainly an over-estimation of the true incidence of developmental prosopagnosia. Such liberal diagnostic criteria confound healthy subjects who are just worse than average with faces and those with a truly pathological problem.

Nevertheless it is undoubtedly true that there are some subjects born with extremely poor face recognition, which may reflect anomalous cerebral development. In some cases there may be a genetic contribution, as some individuals have family members with similar face recognition problems (107, 153, 154). This has led to the suggestion that developmental prosopagnosia may be an autosomal dominant trait (152). However, here again having several family members with poor face recognition is not necessarily evidence of a pathologic entity. Normal variation in face recognition abilities may also have a genetic component, as shown by twin studies that show greater correlation between face recognition abilities in monozygotic than in dizygotic twins (155). Besides genetic defects, other factors such as the failure to orient towards faces in early life (156), and certain personality traits such as shyness (157), may influence the development of face recognition abilities, given that these continue to evolve during early life.

The structural and functional parallels between acquired and developmental prosopagnosia are of interest. Neuroimaging studies have suggested a variety of subtler structural, functional, and connectivity anomalies in developmental prosopagnosia, with no consensus yet. Some studies have found reduced activity or face-selectivity in components of the core face network (106, 158-160), while others found relatively normal activation (161-165). Despite normal activation, one study did find reduced grey matter volume in portions of the inferior temporal cortex associated with face processing, which correlated with
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facial identification performance (166). Similarly, the degree of face-selectivity of the right fusiform face area in developmental prosopagnosia has been shown to correlate with performance on face identification measures (160). Others suggest that the abnormality in developmental prosopagnosia lies not in the core face network but beyond it. A reduction in grey matter volume in the right anterior fusiform gyrus (anterior to the fusiform face area) and a corresponding increase in the right middle temporal gyrus, has been reported in developmental prosopagnosia, with this reduction correlating with face recognition deficits (167). Reduced structural connectivity in occipitotemporal cortex has also been shown in developmental prosopagnosia (168), and has been followed by demonstrations of reduced functional connectivity between the core face network and anterior temporal regions involved in processing identity (165).

Of course, it is not necessarily the case that all subjects with developmental prosopagnosia have the same structural anomaly, given the variety of lesions in the acquired form. It may be that some subjects have reduced activity of the core face-network, while others have reduced connectivity from this network to anterior temporal structures, perhaps due to different genetic defects. If so, this may also be paralleled by functional subtypes just as found in acquired prosopagnosia. However, at present the question of functional subtypes of developmental prosopagnosia has only recently begun to be addressed (169, 170), and further confirmatory studies of larger series of subjects with uniform test batteries of diverse face processing functions would be welcome. See Avidan and Behrmann (this issue) for more discussion on this topic.

5. SUMMARY

Prosopagnosia is a family of disorders that differ in the responsible cognitive deficit and accompanying structural lesions. In the acquired form, difficulties perceiving facial structure is characteristic of apperceptive prosopagnosia, which is associated with right or bilateral occipitotemporal lesions that involve the fusiform and/or occipital face areas. The perceptual problem may lie in extracting the fine spatial metrics of the complex shape that is the face, which is usually done rapidly in a holistic fashion. Whether this type of perceptual analysis is specific to faces or affects other object categories continues to be debated: current evidence suggests that some impairment for other object classes, particularly those for which the subject has some expertise, may be the rule rather than the exception. Difficulties accessing facial memories because of disconnection or loss of those memories is typical of associative/amilotic prosopagnosia, which involves more anterior structures in the right or both temporal lobes. As mentioned, most of the preceding points have been learned from cases of acquired prosopagnosia. Developmental prosopagnosia is a specific deficit that is present from birth, with evidence for some genetic contribution. Whether there are similar structural and functional parallels between acquired and developmental prosopagnosia is not yet known.

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