

SUBCORTICAL FACE PROCESSING

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Abstract | Recent functional imaging, neuropsychological and electrophysiological studies on adults have provided evidence for a fast, low-spatial-frequency, subcortical face-detection pathway that modulates the responses of certain cortical areas to faces and other social stimuli. These findings shed light on an older literature on the face-detection abilities of newborn infants, and the hypothesis that these newborn looking preferences are generated by a subcortical route. Converging lines of evidence indicate that the subcortical face route provides a developmental foundation for what later becomes the adult cortical 'social brain' network, and that disturbances to this pathway might contribute to certain developmental disorders.

NEGLECT

A neurological syndrome (often involving damage to the right parietal cortex) in which patients show a marked difficulty in detecting or responding to information in the contralesional field.

BLINDSIGHT

The ability of a person with a lesion in the primary visual cortex to reach towards or guess at the orientation of objects projected on the part of the visual field that corresponds to this lesion, even though they report that they can see nothing in that part of their visual field.

PROSOPAGNOSIA

The inability to visually recognize faces that were previously familiar, usually after a brain injury.

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During the past decade there has been increasing evidence that subcortical structures are important for perceptual and cognitive functions. For example, the cerebellum has been implicated in complex aspects of language processing and other cognitive operations^{1,2}. Evidence such as this has begun to move cognitive neuroscience away from the prevailing 'cortico-centric' perspective on brain function. One of the domains in which a cortico-centric perspective has prevailed until recently concerns the perception and processing of faces. However, cognitive neuroscience, electrophysiological and neuropsychological studies of adults have provided evidence for a rapid, low-spatial-frequency (LSF), subcortical face-detection system in adults that involves the superior colliculus, pulvinar and amygdala. Although these brain structures have different functions (some of which are discussed here), it is useful to consider them as an integrated system or route for information processing. From a cortico-centric perspective, subcortical structures are often viewed as slaves to cortical activity. However, several lines of evidence indicate that the subcortical face-processing route does not simply respond to top-down influence from the cortex. On the contrary, it seems to modulate the cortical processing of faces.

In this article, I review evidence from cognitive neuroscience studies of adults that supports the existence of a subcortical route for face processing that is rapid, operates on LSFs, and modulates cortical processing. Although many of these experiments involve presentation of fearful faces, it is proposed that the subcortical

route has a broader function than fear detection. Following on from this, results from studies of the face-related preferences of newborn human infants are discussed. This analysis indicates that newborn preferences might rely on the same subcortical route as that described in adults, or a precursor of it. This pathway might be important for establishing the network of cortical regions that make up the adult social brain. Finally, it is proposed that disturbances to the subcortical route result in specific types of atypical development.

The subcortical face route in adults

Initial evidence for the existence of a subcortical face-processing route in adults came from neuropsychological studies, and specifically from evidence for residual face-processing abilities in patients with hemispatial NEGLECT, BLINDSIGHT or PROSOPAGNOSIA. For example, patients with hemispatial neglect normally show VISUAL EXTINCTION to stimuli in their neglected field, but not if the elements are arranged in the pattern of a face^{3,4}. Similarly, blindsight patients with extensive damage to the visual cortex show a residual ability to detect faces and some facial expressions, an effect that does not seem to be due to residual cortical vision⁵. Although adults with prosopagnosia resulting from cortical damage are poor at identifying faces, most of them can detect the presence of faces, and certain facial expressions⁶. This neuropsychological evidence supports the idea that there are separate routes for face detection and face identification, with face detection being supported by

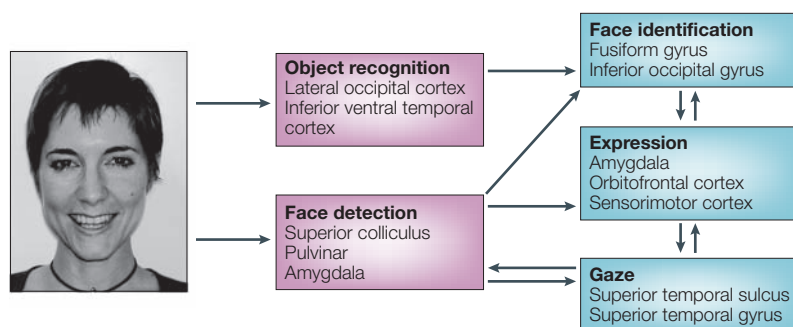


Figure 1 | The dual route model of face processing in adults. The model illustrates how faces are processed through both a subcortical face-detection route (involving the superior colliculus, pulvinar and amygdala) and a cortical route. The subcortical route modulates processing in structures that are fed by the cortical pathway and are involved in face identification (fusiform gyrus and inferior occipital gyrus), facial expression (amygdala, orbitofrontal cortex, sensorimotor cortex) and eye gaze (superior temporal sulcus). Modified, with permission, from REF. 6 © (2003) National Academy of Sciences USA.

a subcortical route. Data from functional imaging, electrophysiological and patient studies have implicated the superior colliculus, pulvinar and amygdala as the main structures on this route⁶ (FIG. 1). Building on this initial evidence for a subcortical route for face processing, several laboratories with different methodologies and patient groups have generated data that are consistent with a pathway that is fast, operates on LSF visual information and modulates cortical face processing.

Rapid. Although there are likely to be reciprocal interactions between cortical and subcortical face processing, to determine which system has a causal effect on the other, it is useful to consider their relative time courses of activation. Converging evidence from EVENT-RELATED POTENTIAL (ERP) and MAGNETOENCEPHALOGRAPHIC (MEG) studies shows that components associated with a 'fast pathway' for face processing can occur at much shorter latencies (less than 100 ms) than those that are generally associated with the 'structural encoding' stage of cortical face processing, such as the N170 and M170 (REFS 7–10). One possibility is that these early components indicate a fast, magnocellular cortical route that provides top-down facilitation from prefrontal areas for later, more detailed processing by the VENTRAL VISUAL PATHWAY¹¹. However, in some cases, a face-selective response occurs even before the activation of the primary visual cortex (V1)^{9,12}, which raises the hypothesis that the fast face-processing pathway originates in a subcortical route.

The idea that subcortical responses to faces might precede those in the cortex is supported by intracranial ERPs recorded from patients with epilepsy who have depth electrodes implanted in the amygdala. Such recordings show short latency responses to faces in the amygdala that become selective to fear after a latency of 200 ms¹³. After 200 ms, a sustained activation in the amygdala spreads to the occipito-temporal, anterior temporal and orbitofrontal cortex¹³. So, in this case, the subcortical route helps to spread selective face responses to cortical regions, including parts of the prefrontal cortex.

Low spatial frequency. Different neural pathways in the brain process different frequencies of visual information. Higher spatial frequencies (which reveal the details of faces, such as expression-related wrinkles) are carried mainly by parvocellular channels to the cortical ventral visual stream^{14,15}. This pathway potentially offers fine resolution, but at the cost of a slow response. By contrast, the lower spatial frequencies (associated with the general configuration of the elements of a face) are carried to the superior colliculus and pulvinar via magnocellular channels¹⁶. This pathway potentially offers a 'quick and dirty' route of visual processing that is best suited to detecting stimuli in the periphery, or those that indicate potential danger.

In event-related functional MRI (fMRI) studies of adults, responses in the fusiform cortex were sensitive to broad-band or high-spatial-frequency (HSF) information about faces, and retained these representations over time¹⁷. This HSF information is likely to be important for encoding the identity of faces. By contrast, activation of the pulvinar, amygdala and superior colliculus related to LSF information about faces, and in particular fearful faces. This subcortical route was insensitive to HSF information. The authors concluded that: "...the amygdala and cortical systems might operate on different subsets of visual information that are both available simultaneously in naturalistic images of faces"¹⁷. A caveat to this conclusion is that the fusiform cortex might also show enhanced responses to fearful facial expressions driven by LSF information¹⁸.

Modulates cortical processing. Given the evidence for a rapid, LSF system for face processing, the next issue to consider is what effect, if any, this has on the cortical processing of faces. The evidence that the subcortical route is activated rapidly makes it unlikely that this pathway is merely a slave to cortical activity. However, the question remains as to whether the cortical and subcortical routes are independent streams of processing, or whether the faster, subcortical system modulates, inhibits or enhances the slower, HSF cortical route. It has been suggested¹⁹ that activation of the amygdala is associated with the modulation of cognitive processes, including attention and memory. Also, evidence from several functional imaging studies indicates that the degree of activation of structures in the subcortical route (amygdala, superior colliculus and pulvinar) predicts or correlates with the activation of cortical face-processing areas^{20,21}. For example, correlational and 'functional connectivity' fMRI analyses found that amygdala activation correlates with activity in several relevant cortical regions during the processing of emotional and neutral faces²², and of faces with a direct, as opposed to averted, gaze²³. In one study, the fusiform face area (FFA) showed significantly greater coupling (functional connectivity) with portions of the amygdala during direct gaze (eye contact between the viewer and the viewed face) than averted gaze. Furthermore, significant correlations between activity in the two regions occurred only during direct gaze²³.

VISUAL EXTINCTION

This is often associated with damage to the parietal cortex. The patient can see a stimulus presented alone in the contralateral visual field, but cannot see it if it is presented at the same time as a stimulus in the ipsilateral visual field.

EVENT-RELATED POTENTIALS (ERPs)

Electrical potentials that are generated in the brain as a consequence of the synchronized activation of neuronal networks by external stimuli. These evoked potentials are recorded at the scalp and consist of precisely timed sequences of waves or 'components'.

MAGNETOENCEPHALOGRAPHY (MEG)

A non-invasive technique that allows the detection of the changing magnetic fields that are associated with brain activity. As the magnetic fields of the brain are weak, extremely sensitive magnetic detectors, known as superconducting quantum interference devices, that work at low, superconducting temperatures (–269 °C) are used to pick up the signal.

This evidence raises the hypothesis that the initial rapid activation of the subcortical route modulates the activity of cortical areas before or during their processing of cortical-stream visual input. This putative short-latency modulation of cortical processing of faces does not mean that cortical areas, in turn, cannot modulate amygdala activity. For example, it is known that a region of the prefrontal cortex can regulate the response of the amygdala to negatively versus positively cued (for example, she just lost US\$500 versus she just found US\$500, respectively) surprised faces²⁴.

Stimuli for the subcortical route. During the past decade, a common viewpoint has been that the subcortical pathway has a specific role in threat detection, as it seems to be most activated by fearful facial expressions²⁵. However, several authors have recently commented that this is probably an inadequate description. As the subcortical pathway also responds to positive-affect expressions, such as smiling¹⁹, one characterization is that the pathway is important for directing 'emotional attention'¹⁷. Evidence from adult patients with bilateral amygdala damage indicates that, unlike control participants, they are more accurate at identifying emotional scenes when information from faces is obscured. Adolphs and Tranel²⁶ conclude from this finding that the amygdala is important for recognizing emotions from faces, and not from scenes and events in general. A similar conclusion was reached in an fMRI study in which subjects viewed facial expressions or emotional scenes²⁷. The amygdala showed stronger responses to the faces than to the scenes (for an alternative view, see REF. 28). However, neutral faces activate the amygdala more than scrambled images²⁹. This suggests a broader function in which biologically salient face inputs activate the pathway and this, in turn, can enhance relevant cortical processing.

One possibility (discussed below) is that the face stimuli that best activate the subcortical route are those that can be best discriminated on the basis of LSF information, or that provide maximal LSF input to a face-configuration detector. For example, a fearful face involves open eyes and mouth and might be more discriminable on the basis of LSF information than other expressions¹⁷.

A related aspect of the sensitivity of the subcortical route is that information from the eyes of the face being viewed might be particularly important. Although the details of the eye cannot be detected from LSF information at short distances from the viewer, widening of the eyes and coarse direction of gaze can be. In one patient with bilateral amygdala damage, the impairment in the ability to recognize fear from facial expressions is attributable to an inability to make use of information from the eyes when judging emotions. This defect, in turn, was traced to a lack of spontaneous fixation on the eyes of faces during free viewing³⁰. The authors³⁰ concluded that the impaired fear recognition in this patient was due to a failure of the amygdala to direct fixation towards the eyes. This result is in agreement with other recent findings that the amygdala helps to process information

about the eye region of faces^{31–33}, and that perceiving direct gaze increases the correlation between activity in the amygdala and in cortical face-processing areas²³. In a recent study, the extent of white scleral field around the pupil of the eye was shown to regulate amygdala responses, with the larger scleral field associated with fearful faces eliciting greater activation³⁴.

An issue that will require further research concerns the differential roles of the amygdala, pulvinar and superior colliculus in the subcortical route. These structures are often co-activated and usually share common stimulus-related response properties, indicating that they are components of one functional system¹⁷. Nevertheless, the differential roles of these structures, and their functional interactions, need to be better specified. Although the possible functions of the amygdala and superior colliculus in relation to face processing have been debated at some length^{6,35}, the pulvinar has been less commonly associated with face detection. Our knowledge of this brain structure has increased rapidly over the past decade³⁶, and the descriptions of its function make it a prime candidate for involvement in the subcortical route. Specifically, portions of the pulvinar receive input directly from the superior colliculus (as well as from the retina and, at least in adults, the striate and extrastriate visual cortex)^{37,38}. The pulvinar nuclei may also receive direct retinal inputs³⁹ and project to the amygdala⁴⁰. Additionally, in adults, there are reciprocal connections between the pulvinar and frontal, temporal and parietal regions, as well as the anterior cingulate cortex³⁸. The exact functions of the pulvinar remain unclear, but it seems to have an important role in the direction of attention and eye movements to 'salient' (biologically relevant) multimodal stimuli that are important to the animal³⁶.

The newborn response to faces

One of the most long-standing debates in developmental psychology has surrounded the evidence for face detection in newborn babies. A study published in 1991 replicated earlier reports that human newborns preferentially orient towards simple schematic face-like patterns⁴¹. On the basis of this and other findings, it was proposed that this preference was supported by a subcortical processing route, and that it served to bias the visual input to developing cortical circuits to ensure the development of a specialization for faces^{42,43}. At the time, the idea that infants were born with face-related information had been rejected by most in the field, largely on the basis of experiments with 1- and 2-month-old infants that failed to show face preferences (for a review, see REF. 35). However, Johnson and Morton³⁵ showed that this failure to detect a preference was due to inappropriate testing methods that did not engage subcortical visuomotor systems.

The idea that infants possess some information about the characteristics of faces from birth^{42,43}, and that this is largely supported by subcortical processing, has come under continuing scrutiny over the past decade^{44–46}. The early experiments with newborns indicated that a stimulus with three high-contrast blobs

N170/M170

The N170 is a well-studied ERP component, the latency and amplitude of which are modulated by the presence of faces in the visual input to the participant. It is a negative peak that is usually recorded at ~170 ms after stimulus onset over lateral occipital and temporal recording sites. The M170 is a similar component recorded during MEG studies of face processing, and might share common generators with the N170.

VENTRAL VISUAL PATHWAY

Visual information coming from the primary visual cortex is processed in two interconnected but partly dissociable visual pathways, a 'ventral' pathway, which extends into the temporal lobe and is thought to be primarily involved in visual object recognition, and a 'dorsal' pathway, which extends into the parietal lobes and is thought to be more involved in extracting information about 'where' an object is or 'how' to execute visually guided actions towards it.

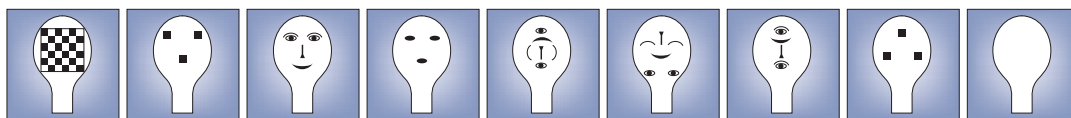


Figure 2 | Both schematic and realistic stimuli have been used to test newborns' preferences for face-related stimuli. The figure illustrates a selection of the schematic stimuli that have been used to test newborns' face preferences in several experiments. Some of the stimuli are designed to test the importance of the spatial arrangement of a face (configuration), and others the importance of particular features. Newborns will preferentially attend to patterns that contain the basic configuration of high-contrast areas of a face (for example, the second, third and fourth stimuli from the left are preferred to those on the right). The mechanisms that underlie this preference are still the focus of debate (see BOX 1).

corresponding to the approximate location of the eyes and mouth might be sufficient to elicit the newborn preference. This stimulus is reminiscent of an LSF image of a face (FIG. 2).

Several studies of face-related behaviour in human newborns have been published since 1991 (BOX 1). The findings of most of these studies provided some evidence for the discrimination of face-like patterns, in the sense that the stimulus preferences observed were argued to be sufficient to elicit a preference for real faces in the natural environment of the newborn. The current prevailing view (but see BOX 1 for alternative views) on the mechanisms that underlie the preference of newborn babies for face-like stimuli is that newborns have one or more biases in visual processing that are sufficient, in their natural environment, to ensure that they fixate faces. Johnson and Morton³⁵ proposed that a stimulus equivalent to the LSF components of the configuration of a face is optimal for eliciting the

preference (FIG. 2). Recently, it has been proposed that the configuration of high-contrast areas associated with the eyes and mouth are not required, but that newborns might prefer up-down asymmetrical patterns with more elements or features being contained in the upper half of a bounded object or area⁴⁷. Although such preferences are sometimes said to be due to several 'domain-general' biases, such as a putative upper visual field bias⁴⁸, experiments indicate that there is a crucial interdependency between the borders of the stimulus and the elements within it⁴⁸, signifying that there is some complexity to the bias. Experiments that independently manipulate upper visual field elements and bounded areas, and experiments that measure eye movements sufficiently to control presentation in the upper or lower visual field, have not yet been published.

Recent results indicate that the phase contrast of stimuli is also important for newborns' preferences⁴⁹. In these experiments, newborns showed a preference for an upright face (with both schematic and naturalistic images) only under positive (face-like) contrast conditions. If phase contrast is added to the previous requirements for the 'top-heavy bias' underlying newborn face preferences, it is clear that a more complex representation is required than just an upper visual field bias.

When recent evidence is considered, we are left with two candidate stimuli that could best elicit newborn face-related preferences. One of these is a raised surface or area with more indentations or dark areas in the upper half, and the other involves indentations or darker blobs corresponding to the approximate locations of eyes and mouth (FIG. 3). At a distance, or in the periphery, a mechanism activated by these stimuli would direct attention towards faces. When closer to the infant, the same mechanism might direct attention to the eyes of a face.

The neural basis of newborn looking preferences. Although there is an increasing literature on the neural basis of face detection in human infants aged 2 months and older (reviewed in REF 50), for various technical and ethical reasons, it has not yet proved possible to use fMRI, MEG or positron emission tomography (PET) to study face perception in healthy newborns. However, several converging lines of evidence support the view^{35,43} that face-related looking behaviour in newborns is mediated largely by a subcortical pathway. First, neuroanatomical, functional imaging, electrophysiological and behavioural evidence indicates that although visual cortical areas can be partially activated

Box 1 | Face preferences in newborns

During the past decade, more than a dozen papers have been published on the face-related looking preferences of newborn infants^{41,46,48,59,60,61,93–95,99–107}. Although most of these papers concluded that newborns are biased to attend to stimuli that possess certain characteristics of faces, two alternative views have been expressed.

The first of these views (the 'sensory hypothesis') is that all newborn visual preferences, including those for face-related stimuli, can be accounted for simply in terms of the relative visibility of the stimuli. The newborn visual system is restricted to the lower part of the range of spatial frequencies that is visible to adults. It has been proposed that newborns prefer to look at faces merely because the amplitudes at different frequencies of these stimuli happen to best match the sensitivity of the newborn visual system¹⁰⁸. The sensory hypothesis has fallen out of favour because, even when amplitude is controlled, phase information (configuration) still influences the newborn preference towards faces^{35,109}. In addition, attempts to simulate newborn preferences with neural network models based on the sensory hypothesis¹¹⁰ are unlikely to account for other experiments involving realistic faces in the complex visual scenes to which newborns are exposed¹¹¹.

The second alternative view is that we have complex face-processing abilities from birth¹¹². The findings used to support this claim include a preference for images of attractive faces^{94,95}, data indicating that newborns are sensitive to the presence of eyes in a face⁹⁹ and evidence that they prefer to look at faces that engage them in eye contact¹⁰². In addition to the immaturity of the cortex at birth⁶³, all of these results could be accounted for by a low-spatial-frequency face-configuration detector (see main text). For example, older infants prefer more attractive faces because these faces are closer to an average or prototypical face¹¹³. Inspection of realistic face images through the appropriate spatial frequency filters for newborns reveals that a mechanism that is sensitive to the configuration of a face could be preferentially activated by the most prototypical face configuration presented; the presence (or absence) of open eyes and direct rather than averted gaze¹⁰² (FIG. 4).

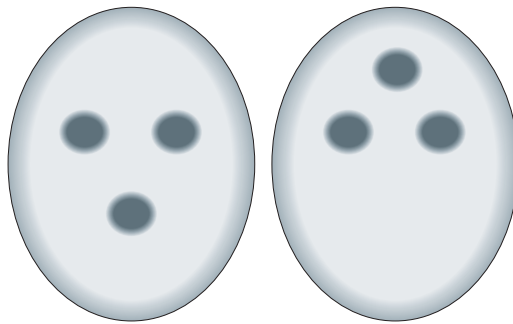


Figure 3 | Schematic illustration of the stimuli that might be optimal for eliciting a face-related preference in newborns. These hypothetical representations were created by putting together the results of several experiments on newborns' face-related preferences. Conclusions were combined from experiments showing the importance of the number of elements in the upper half of a bounded area or surface, the importance of a face-relevant pattern of phase contrast, and the importance of the basic face configuration as viewed at low spatial frequencies.

in newborns, they are relatively immature^{41,51–53}. In addition, the partial activation of visual cortical areas in the first months might have little influence over the visually guided behaviour of the infant⁵⁴. Compared with the cortical visual route, structures on the subcortical route seem to be more developed around the time of birth (reviewed in REFS 51,53).

A second line of evidence that supports the view that newborn face preference is subcortical comes from other species. Almost all vertebrates can recognize biologically relevant stimuli at, or shortly after, birth. In avian, rodent and primate species, a subtelencephalic route is involved in innate stimulus recognition⁵⁵. Filial imprinting in chicks⁵⁶ is a particularly well-studied example. In chicks, an early predisposition to orient to, and approach, conspecifics interacts with a subsequent learned preference for a particular stimulus. Whereas learned preference depends on certain regions of the avian telencephalon, the early tendency to approach conspecifics does not⁵⁶. So, evidence from various species supports the existence of a subcortical route involved in conspecific detection from birth.

As the nasal and temporal visual fields feed differentially into the cortical and subcortical visual routes in humans^{57,58}, it is possible to gain converging evidence for subcortical processing by presenting stimuli in either the temporal or nasal visual fields only. Specifically, stimuli presented in the nasal field feed differentially into the cortical route, whereas those in the temporal field feed into the subcortical route. In one experiment, newborns wore patches on one eye while face-like stimuli were presented to the other eye in either visual field. Consistent with the view that face preferences in newborns are due to the action of subcortical processes, the face-related preference was observed only when stimuli were presented in the temporal visual field^{59,60}. Similar conclusions were reached in a study of the GAP EFFECT in newborns⁶¹.

GAP EFFECT

A commonly observed phenomenon is that a saccade to a peripheral target is significantly slower when a central fixation stimulus is still present, compared with when the fixation point is removed at, or just before, the onset of the peripheral target. One explanation for this gap effect is that participants have to disengage from the fixation point before initiating their saccade to the target.

The subcortical pathway and development

The converging lines of evidence discussed above support the hypothesis that the adult subcortical face-processing route functions in newborns, and is responsible for the patterns of face-related stimulus preference that are seen at that age. This hypothesis generates predictions, for both adult and infant experiments and for both typical and atypical development (see below). The working hypothesis suggests that the subcortical route not only detects the presence of faces, and orients the newborn towards them, but might also activate relevant cortical regions such as the lateral occipital, fusiform and orbitofrontal cortices. It is possible that the projection pattern to the cortex from the subcortical route partly determines which cortical regions become incorporated into the social brain network during development (BOX 2). Although the amygdala has widespread projections to cortical areas, it is notable that most of the cortical areas associated with the 'social brain' network receive input from this structure⁶². If the subcortical LSF pathway operates from birth in humans, then it could enhance the activity of cortical areas that, at this stage, receive only poor input through the cortical visual route. Such early enhancement of activity in selected cortical areas, together with other architectural biases⁶³, might assist in the recruitment of these specific cortical areas for face processing and social cognition (BOX 2).

Consistent with a role for the subcortical system in selecting and structuring the cortical social brain network, one possibility is that cholinergic afferents enhance cortical processing of relevant stimuli⁶⁴. However, acetylcholine concentrations are also crucial for experience-dependent organization of the cortex during development⁶⁵. Therefore, modulation of acetylcholine might be an important regulatory factor, both for short-term modulation in adults and longer-term modulation during development.

Another developmental change in the relationship between the subcortical pathway and cortical areas might relate to the types of face that best activate the subcortical route. As discussed above, fearful faces tend to elicit greater activation in the adult amygdala than do neutral faces. However, this pattern of activation is not observed in children, who show at least equal activation in response to neutral faces⁶⁶. One explanation for such functional changes could be that amygdalo-cortical connectivity continues to mature into adolescence⁶⁷.

Atypical development

If the subcortical face-processing route is important for the development of the adult social brain network, then disruption of this pathway by congenital factors could have important knock-on consequences for the social brain network as a whole. Several studies have implicated the amygdala in autism spectrum disorder (ASD), leading to speculation that early disruption of amygdala function by congenital or acquired lesions, or by genetic anomalies, can result in the atypical development of a network of regions involved in the

Box 2 | Why does the fusiform cortex develop a face area?

A central debate in cognitive neuroscience concerns the origin and specificity of the fusiform face area (FFA) and other face-sensitive regions of the cortex. One view is that the FFA is selectively activated by faces owing to genetically specified and domain-specific computational properties of that region⁸⁷. By contrast, others have proposed that the region is involved in processing visual stimuli in domains of perceptual expertise¹¹⁴, and most human adults become experts in face processing. From the developmental perspective taken in this article, an alternative ‘middle-way’ account of the FFA emerges — parts of the fusiform cortex become specialized for processing faces as a result of several constraining factors. First, the subcortical route described in this article ensures that newborns preferentially orient to faces and therefore foveate them, thereby providing input to cortical visual pathways. Second, the cortical projection patterns of the subcortical route might enhance the activation of specific areas, including the fusiform cortex, when faces are in the visual field of the young infant. Third, the parts of the fusiform cortex that become face-sensitive receive foveal cortical visual input, and are at the ‘object level’ of visual stimulus processing in the ventral pathway¹¹⁵. Therefore, information from both face routes might converge in the FFA. These and other possible constraints, such as multimodal inputs, and general biases in gene expression levels between the right and left cerebral cortex¹¹⁶, combine to ensure that certain developing cortical circuits become specialized for face-related stimuli. By this developmental account, it is inevitable, barring some disruption to the normal constraints, that parts of the fusiform cortex will specialize for faces. However, this inevitable outcome is achieved without genetically specified domain-specific patterns of connectivity within the FFA.

processing of socially salient stimuli⁶⁸. Similar proposals have been made for Turner syndrome⁶⁹ and Williams syndrome⁷⁰.

The association between ASD and amygdala deficits^{71–73} is based on several sources of evidence. Post-mortem neuroanatomical and structural MRI studies from patients with ASD report abnormalities in the amygdala^{71,74}, and lesions of the amygdala in monkeys induce some of the symptoms of autism⁷⁵. In addition, patients with acquired damage to the amygdala show deficits in aspects of social cognition that are reminiscent of those observed in ASD⁷⁶. Finally, functional imaging studies of patients with ASD have shown atypical patterns of activation in the FFA and other face-related cortical areas, particularly in response to the recognition of facial expressions^{77,78} and social attributions⁷⁹. In one study, the atypical activation of the FFA and related cortical areas was specifically associated with a failure to activate the amygdala in a task that required the application of ‘social intelligence’ to face stimuli⁸⁰.

Although the above evidence indicates that amygdala function is probably disrupted in ASD, it is important to note that most of the other cortical and subcortical regions associated with the ‘social brain’ have also shown abnormalities in these patients (for a review, see REF. 81). If a defining feature of ASD is the inappropriate or atypical activation of the social brain network, then one candidate causal mechanism for this is early disruption of the subcortical face-processing pathway. This could prevent the development of appropriate patterns of regional enhancement of cortical activity in response to faces (BOX 2). This, in turn, could alter or delay the emerging specialization of cortical components of the social brain⁸².

Another developmental consequence of this atypical specialization might be that visual cortical processing is less tuned to the lower spatial frequencies that determine activity in the subcortical pathway. The reduced association between LSFs (subcortical) and HSFs (cortical) during developmental plasticity in the cortex could lead to an unrestrained specialization of these cortical circuits for HSF information (without regard to LSF components). Behaviourally, this could be reflected in a bias towards featural, rather than configural, processing⁸³. There is evidence that autistic children depend more on HSFs for the processing of faces, unlike typical individuals, who depend on middle spatial frequencies and LSFs⁸⁴.

Further evidence that a fast face-processing pathway is altered in autism comes from a MEG study of face processing in typical and autistic individuals¹². In this study, control subjects had a fast face-processing pathway that showed specificity for faces before the activation of V1. This pathway showed unusual response properties in autistic individuals. The authors suggested that this aberrant fast pathway might also disrupt the cortical response to faces that occurs later in processing time¹². Finally, the subcortical route hypothesis could potentially unite the previously separate perceptual cognitive deficits in face processing with the motivational/affective disturbances in ASD⁸⁵.

The subcortical route hypothesis might also shed light on another disorder, developmental prosopagnosia. As discussed above, although adult prosopagnosics have severe deficits in most measures of face processing, they also have residual face detection abilities that are thought to be supported by the subcortical route⁶. Recently, cases of developmental prosopagnosia have been described. Whereas some of these cases can be traced to damage acquired in infancy^{86–89}, a substantial number of cases (sometimes referred to as ‘congenital prosopagnosia’) lack apparent damage to the cortex during infancy or later in life⁹⁰. One of several ways in which such congenital prosopagnosia could arise is from an early defect in the subcortical route that results in a lack of appropriate cortical specialization for face processing during development.

If this view is correct, then measures of subcortical pathway function should reveal a dissociation between face processing in developmental prosopagnosics and that in adult-acquired prosopagnosia. This hypothesis was tested in an ERP experiment that focused on the face-sensitive N170 component⁵⁸. In typical adults, the N170 can be elicited by the presentation of faces in either the nasal or temporal visual hemifields, and can be of greater amplitude when faces are presented in the temporal field⁵⁸. The activation of the cortical generators of the N170 by presentation of stimuli in the temporal visual field is interesting because it could represent the activation of cortical structures through the subcortical route. In a case of developmental prosopagnosia, the N170 showed the opposite pattern to that of controls, in



Figure 4 | How newborns see faces. a | Realistic images of faces as viewed through the visual system of newborns at a typical distance for face-to-face interaction (~50 cm). A neutral face with direct gaze, averted gaze and eyes closed, as well as a fearful face, are shown. These images support the view that, at close viewing distances, information around the eyes could activate the subcortical route. **b** | The same realistic images of faces as viewed through the visual system of newborns, but from ~2 m. When viewed from a greater distance than in **a**, or in the periphery, the configuration of shadowed areas that is characteristic of a naturally (top)-lit face could also activate the subcortical route.

that it was greater after presentation of stimuli in the nasal visual field, indicating that the subcortical system might have failed to activate cortical processing, or maybe a lack of orientation to faces in the periphery⁵⁸. Consistent with a possible disturbance in the function of the subcortical pathway in some cases of developmental prosopagnosia is the observation that the residual discrimination abilities seen in adult-onset prosopagnosics are more limited in developmental cases⁹¹ and that the covert face-detection abilities described earlier are absent in at least some developmental cases^{88,91}.

Clearly, the putative causal role of disruption of the subcortical route cannot explain the marked differences between developmental prosopagnosia and ASD. The differences between these phenotypes might reflect differences in the timing of developmental events. Alternatively, it might mean that the putative disruption to the subcortical route is just one of several necessary predisposing factors in these conditions, or that different structures on the subcortical route are disrupted. It is possible that damage to the amygdala could yield the wider range of symptoms in ASD, whereas damage to other parts of the subcortical route, or its connections to the cortex, produce the more specific deficits in face processing seen in congenital prosopagnosia.

Conclusions

Evidence from various cognitive neuroscience and neuropsychological studies in adults supports the existence of a subcortical face-processing route. Analysis of the evidence relating to the bias of newborn infants to orient towards faces and face-like patterns indicates that this process might rely on the same subcortical face-detection route or a precursor of it. The basic attributes of this system make it well suited for a developmental role in helping to establish the network of cortical structures involved in the adult 'social brain'. Disturbances to the functioning or developmental timing of the subcortical route might result in specific types of atypical development.

For both adults and infants, there is controversy about the optimal stimuli for activating the subcortical route. One possibility is that at close viewing range (suitable for social interaction) the pathway responds best to information associated with the dark of the eye surrounded by the white sclera. By this account, fearful faces provide optimal stimuli for activating the pathway because the wide eyes expose a greater extent of the sclera³⁴ (FIG. 4a). When faces are viewed at a greater distance, or in the periphery, LSF information about the face under naturalistic top-lighting conditions yields dark shadowed areas for the eye sockets, surrounded by the illuminated areas of the cheeks, nose and forehead (FIG. 4b). The importance of the other features of the face,

such as the mouth, and of the outline of the head against a background, remains to be determined.

Future work is required to address several issues. First, to what extent are the stimulus conditions that elicit the bias in newborns the same as those that elicit maximal activation of the subcortical route in adults, and vice versa? With one exception, the stimuli for eliciting newborn preferences have yet to be studied in adult functional imaging studies. Caldara and colleagues (R. Caldara, M. Seghier, B. Rossian, L. Francois, C. Michel, and C.-A. Havert, unpublished observations) have conducted a preliminary experiment in which adults viewed some of the stimuli used in newborn studies^{48,92,93}. Region-of-interest (ROI) fMRI analyses revealed that the right FFA showed the largest response to the stimulus that was most preferred by infants. However, as the ROI did not include any subcortical structures, we do not know whether the increased FFA activity reflected enhancement by the subcortical pathway. A counter-intuitive prediction that has yet to be tested is that newborns might respond preferentially to fearful faces. Furthermore, as newborns prefer attractive, more typical faces^{94,95}, modulation of subcortical face processing in adults might also be sensitive to this stimulus dimension.

A second line of work that merits future research is direct measurement of the neural basis of face processing in young infants. On the basis of the adult studies

discussed here, activation of the FFA and related cortical areas in the social brain network in young infants might arise mainly through the subcortical pathway. Although the FFA can be active in infants as young as 2 months⁹⁶, and other cortical correlates of face processing have been observed at 3 months⁹⁷, these cortical activations could be partly a consequence of activation of the subcortical route rather than visual input through the geniculostriate pathway.

A third issue for future work concerns the degree of overlap between the subcortical route and a proposed cortical fast route for object processing¹¹. This fast cortical route is said to project LSF visual information directly from early visual cortical areas to parts of the prefrontal cortex. This allows the prefrontal cortex to feed back a likely interpretation of the input image to structures on the ventral pathway before they receive detailed higher-frequency information. As the amygdala is deemed important for this route, owing to its extensive reciprocal connections with the orbitofrontal cortex^{11,98}, it is conceivable that the subcortical route projects to the orbitofrontal cortex to provide appropriate feedback and activation for further cortical processing of faces.

Finally, it is important to continue to determine the properties of the different structures on the subcortical face route. This line of work might shed light on the developmental causes of ASD and developmental prosopagnosia.

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