The social brain in adolescence

Sarah-Jayne Blakemore

Abstract | The term 'social brain' refers to the network of brain regions that are involved in understanding others. Behaviour that is related to social cognition changes dramatically during human adolescence. This is paralleled by functional changes that occur in the social brain during this time, in particular in the medial prefrontal cortex and the superior temporal sulcus, which show altered activity during the performance of social cognitive tasks, such as face recognition and mental-state attribution. Research also indicates that, in humans, these parts of the social brain undergo structural development, including synaptic reorganization, during adolescence. Bringing together two relatively new and rapidly expanding areas of neuroscience — social neuroscience and the study of brain development during adolescence — will increase our understanding of how the social brain develops during adolescence.

Conspecifics
Individuals of the same species.

Humans are inherently social. A large proportion of the human brain is involved in social interaction and understanding other people. The brain regions that are involved in social cognition are collectively referred to as the 'social brain' (REF. 1) (FIG. 1). Certain regions in the social brain undergo structural and functional changes during development. Recently, neuroimaging studies have focused on adolescence — usually defined as the period of physical, psychological and social transition between childhood and adulthood — as a time of significant functional development of the social brain. This research points to continued development throughout adolescence of social processes such as the recognition of conspecifics and the understanding of others' emotions, intentions and beliefs. This fits with evidence from social-psychology studies that suggests that adolescence is characterized by social change, including heightened self-consciousness, increased importance and complexity of peer relationships and an improved understanding of others[2]. Social-brain development during adolescence is probably influenced by multiple factors, including changes in hormone levels and changes in the social environment. In addition, significant neuroanatomical changes occur in parts of the social brain that are likely to affect cognition and behaviour.

In this Review I describe the social brain and its functional development during adolescence, and attempt to explain how these functional changes relate to the structural changes that occur.

The social brain

The social brain is defined as the complex network of areas that enable us to recognize others and evaluate their mental states (intentions, desires and beliefs), feelings, enduring dispositions and actions[1,3]. Brain areas that are involved in social cognitive processes include the medial prefrontal cortex (mPFC), the anterior cingulate cortex (ACC), the inferior frontal gyrus, the superior temporal sulcus (STS), the amygdala and the anterior insula[3] (FIG. 1). Over the past two decades, research has begun to shed light on how the brain enables the diverse set of functions that allow humans to understand and interact with each other. These functions include recognition of faces and bodily gestures, evaluation of what another person is thinking or feeling, prediction of what that person is about to do next and communication with the person. In this Review I focus on a subset of these functions, namely those that are involved in understanding others, from the recognition of conspecifics to the understanding of emotions and mental states — because these processes have been investigated in adolescence.

Recognition of conspecifics. A fundamental component of social interaction is the ability to recognize conspecifics. Newborn babies seem to be equipped with the ability to detect human faces: at birth, babies prefer to look at photographs and cartoons of faces than at other objects or inverted faces[4]. This early face recognition probably relies on subcortical structures[5], but in adults face recognition relies on additional cortical areas. Single-cell studies in monkeys have identified neurons in the STS that respond selectively to faces[6]. Evidence from various sources, including electroencephalograms, functional MRI (fMRI) and brain lesions, indicates that the posterior STS (pSTS) is one of the regions that is specialized for the detection of faces[7] and eye gaze[8] in humans.

Institute of Cognitive Neuroscience, University College London, 17 Queen Square, London, WC1N 3AR, UK.
e-mail:
e-mail:
s.blakemore@ucl.ac.uk
doi:10.1038/nrn2353

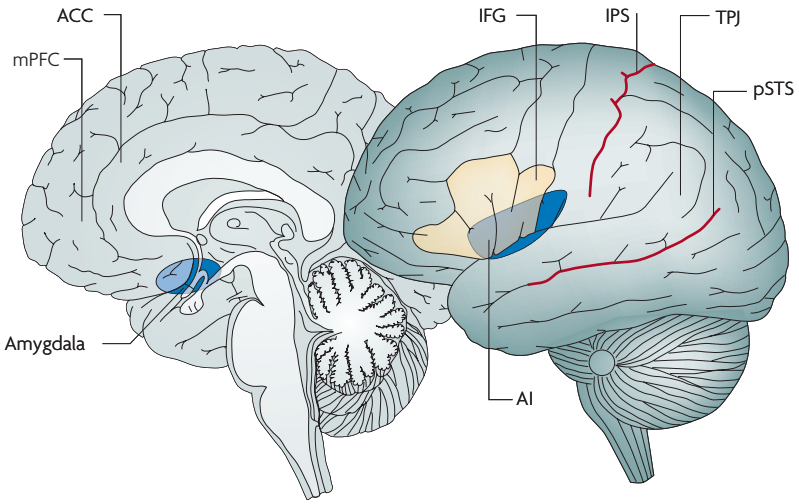


Figure 1 | **Regions of the social brain.** Regions that are involved in social cognition include the medial prefrontal cortex (mPFC) and the temporoparietal junction (TPJ), which are involved in thinking about mental states[19–29], and the posterior superior temporal sulcus (pSTS), which is activated by observing faces[6–8] and biological motion[11–13]. Other regions of the social brain on the lateral surface are the inferior frontal gyrus (IFG) and the interparietal sulcus (IPS). Regions on the medial surface that are involved in social cognition include the amygdala, the anterior cingulate cortex (ACC) and the anterior insula (AI). Anatomical image adapted, with permission, from REF. 100 © (1996) Appleton & Lange.

Another aspect of recognizing other individuals is the detection of motion of conspecifics. Research on biological motion often uses point-light displays (recordings of a person with light sources attached to the joints of their body moving in a dark room[9]), which result in a schematic representation of biological motion that consists of a moving set of dots. The ability to detect biological motion from point-light displays is present from an early age: infants as young as three months of age show a preference for upright point-light displays compared with both inverted point-light displays and displays in which the absolute motion is normal but the spatial relationship between the points of light is changed[10]. In both monkeys[11] and humans, the pSTS is involved in the perception of biological motion[12–14].

As well as recognizing a stimulus as a conspecific, we automatically evaluate its emotional state. A complex network of regions is involved in the recognition of basic emotions, such as disgust and fear[15], and in the recognition of more complex emotions, such as trustworthiness[16], guilt and embarrassment[17]. This network includes the amygdala, the anterior insula, the STS and the PFC. The mPFC is involved in understanding social emotions, such as guilt and embarrassment[17]. Posterior regions of the inferior frontal gyrus (IFG) are involved in emotional judgement and might have a role in top-down aspects of emotion recognition, such as deciding what action to take based on someone's emotion or predicting what someone is about to do[18].

Attribution of mental states. Another aspect of social cognition, which enables us to predict the future actions of others, is the ability to work out a conspecific's mental state, including their intentions, desires and beliefs — this ability is known as 'theory of mind' or 'mentalizing'. Using functional imaging and a wide range of stimuli, several independent studies have shown remarkable consistency in identifying the brain regions that are involved in mentalizing. These studies used stimuli such as stories[19–21], sentences[22], words[23], cartoons[24] and animations[25] (BOX 1) that were designed to elicit the attribution of mental states. In each case the mentalizing task resulted in the activation of a network of regions that included the pSTS at the temporoparietal junction (TPJ), the temporal poles and the mPFC. Lesion studies have consistently demonstrated that the superior temporal lobes[26] and the PFC[27–29] are involved in mentalizing, as damage to these brain areas impairs mentalizing abilities. It is interesting to note that one study reported a patient with extensive PFC damage whose mentalizing abilities were intact[30], suggesting that this region is not necessary for mentalizing. However, there are other potential explanations for this surprising finding. It is possible that, owing to plasticity, this patient used a different neural strategy in mentalizing tasks. Alternatively, it might be that in some cases damage to this area during adulthood spares mentalizing abilities, whereas damage that occurs earlier in life might always be detrimental. This kind of pattern has also been reported in relation to orbitofrontal cortex (OFC) damage: whereas patients with adult-onset OFC lesions showed no impairment on social–moral reasoning tasks, two patients whose OFC lesions occurred before 16 months of age showed significant impairment[31].

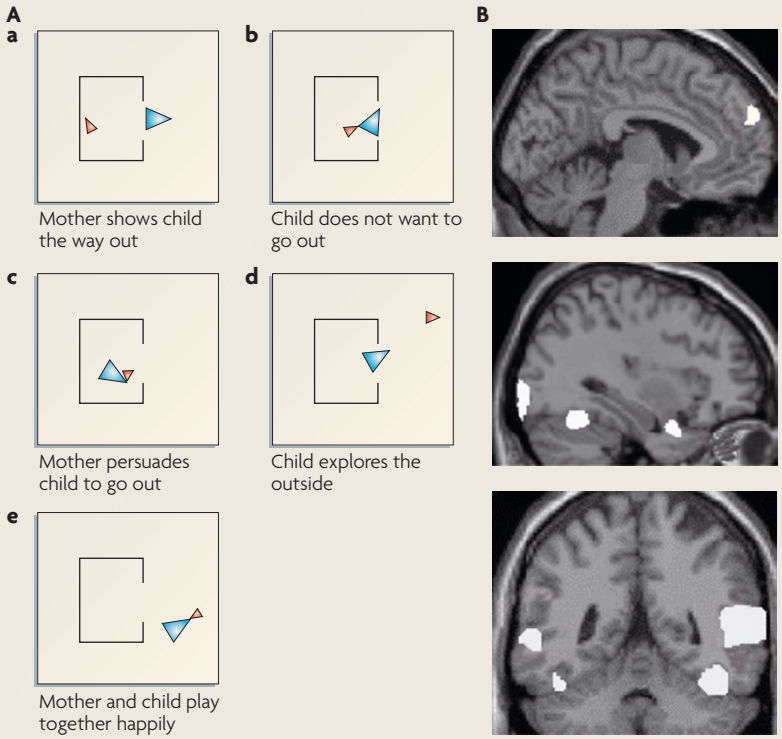
Recent meta-analyses of mPFC activation by different mentalizing tasks indicate that the peak activation lies in the dorsal mPFC[32,33] (FIG. 2). This region is activated when one thinks about psychological states, regardless of whether these psychological states are applied to oneself[34–37], one's mother[38], imagined people[39] or animals[40]. Competitive games that involve surmising an opponent's mental state also activate the mPFC[41,42]; thus, it has been proposed that the mPFC is involved in the necessary decoupling of mental states from physical reality[43]. Although the mPFC is activated during tasks that require mental-state attribution relative to matched control tasks, activity in the same region is often highest during low-demand baseline conditions, such as simply looking at a fixation cross[44]. In other words, the mPFC is deactivated during mentalizing tasks relative to low-demand baseline conditions. However, this is probably an artefact of using rest or low-demand tasks as a baseline. Such baseline conditions allow participants to indulge in a maximum degree of spontaneous mentalizing — that is, they might naturally start thinking about mental states (what they want to eat for lunch, whether they enjoy the experience of lying in a noisy brain scanner, *et cetera*)[32].

Given the role of the pSTS in the perception of faces and biological motion (described above), Frith has suggested that the nearby region of the pSTS/TPJ, which is implicated in mentalizing, is involved in predicting what movement a conspecific is about to make[43]. Saxe, on the other hand, makes the case that the pSTS/TPJ is specifically involved in understanding other people's mental states[45]. However, a recent fMRI study showed that the specific region of the pSTS/TPJ that is activated

Box 1 | **Early development of mentalizing**

Signs of social competence develop during early infancy, so that by approximately 12 months of age infants can ascribe agency to a system or entity[81]. The understanding of intentions emerges at approximately 18 months, when infants acquire joint attention skills — that is, the ability to follow an adult's gaze towards a goal or to look to where an adult is pointing[82]. 'Pretend play', which usually starts at approximately 18 months, involves differentiating between belief and reality[83]. These early social abilities precede more explicit mentalizing, such as 'false-belief understanding', which usually becomes apparent by four or five years of age[84]. In a typical false-belief task, the child is asked where a person (for example, Sally) will look for a toy that she left in a certain place and that was moved by another person (for example, Anne) when Sally was out of the room. Understanding that Sally will not know the new location of the toy relies on the ability to distinguish between Sally's false belief and reality. Recently, Onishi and Baillargeon provided evidence that infants as young as 15 months of age can correctly evaluate the mental states of others[85]. They investigated whether infants can predict an actor's behaviour on the basis of the actor's true or false belief about a toy's hiding place. The infants were surprised (they looked for longer) when the actor reached for the toy in its actual hiding place rather than in the location where they believed the toy to be.

Children with autism spectrum disorder tend to fail false-belief tasks[86]. Recent paradigms that have been used to test people with autism include the animations task[87] (see part **A** of the figure), during which participants watch silent animations in which two triangles move around in such a way that they seem to have mental states, such as intentions and desires. Children with autism spectrum disorder do not generate appropriate mental-state terms to describe the triangles' patterns of movement[87]. Regions of the social brain, including the medial prefrontal cortex (top panel in part **B** of the figure), the temporal poles (middle panel) and the superior temporal sulcus (bottom panel), are activated when healthy participants observe this type of mentalizing animation (relative to a control task in which they observe animations that do not evoke mental-state attributions)[25]. Parts **A** and **B** of the figure reproduced, with permission, from REF. 25 © (2000) Academic Press.



by mental-state attribution is also activated by a non-social attentional reorienting task[46]. Based on this finding, Mitchell has proposed that the pSTS/TPJ might have a more general role in representing beliefs about, or attention to, stimuli (social or otherwise).

The agreement between neuroimaging studies in terms of the localization of activity in both the pSTS/TPJ and the mPFC during mentalizing tasks is remarkable because subtracting a control condition from a mentalizing condition isolates a high-level cognitive process rather than a low-level sensory one. For example, in the task described in BOX 1, participants viewed animations that depict triangles moving in such a way that they seem to possess mental states and emotions. Participants' brain activity during this condition was compared with the activity that was elicited when they observed animations of the same triangles moving in patterns that did not elicit the attribution of mental states or emotions. Brain activity that was associated with processes common to viewing both types of animation (processing visual motion, paying attention, following instructions, *et cetera*) was subtracted in the comparison between these two conditions to leave only the brain activity that was associated with the attribution of mental states and emotions. Such a high-level cognitive process might not be expected to have a modular functional architecture, as it presumably involves multiple component processes that might not be domain-specific[47]. The consistent localization of activity to a network of regions that included the pSTS/TPJ, the mPFC and the temporal poles suggests that these regions are key to the process of mentalizing.

In the next section I describe the functional development during adolescence of brain regions that are involved in mentalizing and other aspects of social cognition.

Functional changes in the adolescent social brain

There is a large body of literature on the development of social cognition in infancy and childhood that points to step-wise changes in social cognitive abilities during the first five years of life (BOX 1). However, there has been surprisingly little empirical research on social cognitive development that takes place beyond childhood. Only recently have studies focused on the development of the social brain beyond early childhood, and these studies support evidence from social psychology that adolescence represents a period of significant social development.

Most researchers in the field use the onset of puberty as the starting point for adolescence[48]. The end of adolescence is harder to define and there are significant cultural variations. However, the end of the teenage years represents a working consensus in Western countries[2]. Adolescence is characterized by psychological changes that affect an individual's sense of identity, their self-consciousness and their relationships with others. Compared with children, adolescents are more sociable, form more complex and hierarchical peer relationships and are more sensitive to acceptance and rejection by their peers[2,49]. Although the factors that underlie these social changes are most likely to be multi-faceted, one possible cause is development of the social brain. Some neuroimaging experiments have investigated the development of the social brain during adolescence, focusing on face processing and mentalizing.

Agency
The capacity of an individual to make conscious choices and impose those choices on the world.

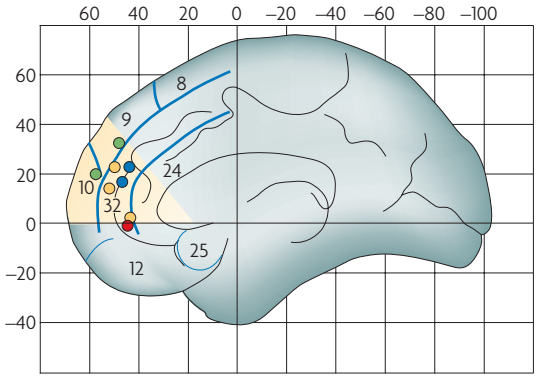


Figure 2 | **Activation of the medial prefrontal cortex (mPFC) during mentalizing tasks decreases during adolescence.** The yellow shaded area indicates a section of the dorsal mPFC that is activated in studies of mentalizing: Montreal Neurological Institute 'y' coordinates range from 30 to 60; 'z' coordinates range from 0 to 40 (REF. 32). The coloured dots indicate voxels in which altered activity is observed between late childhood and adulthood during participation in social-cognition tasks. The red dot represents an area of activation that is higher in adolescents than in adults during the animations task described in BOX 1 (REF. 59). The green dots represent areas of activation that are higher in adolescents than in adults during an irony-comprehension task[56]. The blue dots represent areas of activation that are higher in adolescents than in adults during intention understanding[57]. The yellow dots represent areas of activation that are higher in children than in adults in a self–other evaluation task[58]. The blue lines indicate approximate borders between Brodmann areas, which are numbered on the diagram. Figure modified, with permission, from REF. 32 © (2006) Macmillan Publishers Ltd.

Development of recognition of conspecifics during adolescence. Some of the earliest empirical studies on cognitive development during adolescence investigated the effect of puberty on face recognition in girls and produced a surprising result. Performance on face-recognition tasks improved steadily during the first decade of life, but this was followed by a decline at approximately age 12 (REF. 50). Puberty (rather than age *per se)* was implicated in this decline, as a later study showed that mid-pubertal girls performed worse than prepubertal or postpubertal girls matched for age[51]. A more recent study also found evidence of a pubertal 'dip' on a match-to-sample task in which participants ranging from 10 to 17 years of age had to match emotional faces to emotion words[52]. A 10–20% increase in reaction time on the match-to-sample task was found in children of pubertal age (10–11-year-old girls and 11–12-year-old boys) compared with younger children. Performance then improved, regaining its earlier level at approximately 16–17 years of age. Whether this dip can be replicated, whether it is specific to face processing and what causes it are questions that remain to be answered.

A number of functional neuroimaging studies have investigated the neural correlates of facial-expression recognition from childhood to adulthood. An fMRI study reported increased activity in a number of lateral and superior prefrontal regions (bilaterally for girls, right sided for boys) in response to fearful faces in individuals between the ages of 8 and 15 years (REF. 53). Thus, frontal activity increased between childhood and adolescence in this study. In a different study, adolescents (aged 9–17 years) showed activation of the ACC and left OFC during passive viewing of fearful faces (relative to neutral faces), whereas adults (aged 25–36) did not[54]. When attention was directed to a non-emotional aspect of fearful faces, activity in the ACC was higher in adolescents than in adults (FIG. 3). Therefore, in this study, frontal activity tended to decrease between adolescence and adulthood. In addition the findings indicate that, whereas adults modulate brain activity based on attention demands, adolescents modulate activity based on the emotional nature of a stimulus. This suggests that the neural basis of the ability to pay attention to a non-salient stimulus (in this case, the nose of a fearful face) in the presence of emotionally evocative, attention-grabbing stimuli (the eyes of a fearful face) is still undergoing maturation between adolescence and adulthood.

To summarize, there is some indication that, notwithstanding potential sex differences (BOX 2), activity in parts of the frontal cortex during face-processing tasks increases between childhood and adolescence and then decreases between adolescence and adulthood.

So far, few studies have investigated the development of the neural substrates of biological-motion processing. However, a recent study indicated that activity in the STS, which is associated with biological-motion perception, increased with age in children aged 7–10 years (REF. 55).

Development of mentalizing ability during adolescence. Although there is no strong evidence that performance in mentalizing tasks changes during adolescence, fMRI studies of mental-state attribution have shown that frontal-cortex activity decreases between adolescence and adulthood. A recent fMRI study investigated the development of our ability to perceive communicative intent, using a task in which participants had to decide whether a speaker was being sincere or ironic[56]. Understanding irony requires the ability to separate the literal meaning of a comment from its intended meaning. In children/young adolescents (aged 9–14 years), the mPFC and left inferior frontal gyrus were more active during this task than they were in adults (aged 23–33). The authors interpreted the increased mPFC activity in young adolescents as a reflection of the need to resolve the discrepancy between the literal and the intended meaning of an ironic remark. The region of the mPFC that was more active in young adolescents than in adults (Montreal Neurological Institute (MNI) coordinates –8, 58, 20), as well as the region in which activity was significantly negatively correlated with age over the whole group of participants (MNI coordinates –2, 44, 32), lies in the dorsal mPFC, an area that is consistently activated by mentalizing tasks in adults[32,33] (FIG. 2; green dots).

A similar region of the dorsal mPFC was found to be more active in adolescents than in adults in an fMRI study that involved thinking about one's own intentions[57]. Adolescents (aged 12–18 years) and adults (aged

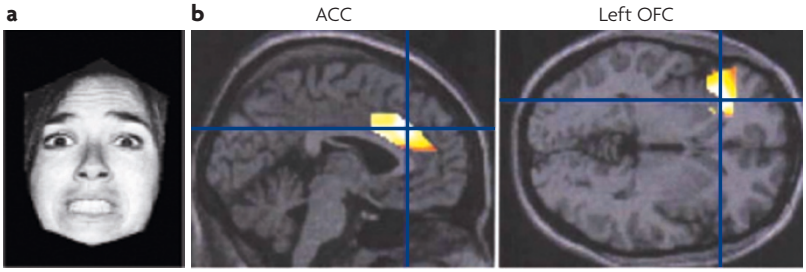


Figure 3 | **Developmental changes in brain activation elicited by looking at fearful faces.** In a study by Monk and colleagues[54], a group of adolescents aged 9 to 17 and a group of adults aged 25 to 36 viewed fearful (an example of which is shown in **a**) and neutral faces and attended to either the emotional facial feature (the eyes) or a non-emotional facial feature (the nose). **b** | Adolescents showed higher activation of the anterior cingulate cortex (ACC) and left orbitofrontal cortex (OFC) than adults when passively viewing fearful faces (relative to neutral faces). When attending to a non-emotional physical feature of a fearful face (the nose), adolescents showed greater activation than adults in the ACC. Part **a** reproduced, with permission, from REF. 101 © (1976) CPP. Part **b** reproduced, with permission, from REF. 54 © (2003) Elsevier Science.

22–38 years) were presented with scenarios about intentional causality (involving intentions and consequential actions) or physical causality (involving natural events and their consequences). In both groups, intentional causality (relative to physical causality) activated the classic mentalizing network that includes the mPFC, the temporal poles and the pSTS/TPJ. However, intentional causality activated the dorsal mPFC (MNI coordinates 12, 42, 21) more in adolescents than in adults, relative to physical causality (FIG. 2; blue dots). A different activity cluster in the same region (MNI coordinates 15, 45, 18) was negatively correlated with age over the whole group of participants. Conversely, a region in the right STS was more activated by intentional causality in adults than in adolescents, relative to physical causality. These results suggest that the neural strategy for thinking about intentions changes from adolescence to adulthood. Although the same neural network is active, the relative roles of the different areas change with age, with activity moving from anterior (mPFC) regions to posterior (STS) regions.

In the intentional-causality study described above, the scenarios pertained to the self insomuch as they asked about participants' own hypothetical intentions[57]. In another developmental study that focused on the processing of self-related sentences[58], children (aged 9.5–10.8 years) and adults (aged 23–31.7 years) read phrases about academic skills and social competence. In the 'self' condition, participants were asked to indicate whether the phrases accurately described themselves. In the 'other' condition, they were asked to indicate whether the phrases accurately described a fictional, familiar other person (Harry Potter). The mPFC (MNI coordinates –16, 54, 24 and –10, 54, 14) and the ACC (MNI coordinates –12, 42, 2) were more active in children than in adults during self-knowledge retrieval relative to other-knowledge retrieval (FIG. 2; yellow dots). The authors suggested that, compared with adults, adolescents might rely more on 'on-line' self-reflective processing that is performed by the mPFC.

In another study of mentalizing, participants aged 9 to 16 years were scanned during participation in an animation-based mentalizing task[59] (BOX 1). Age correlated positively with activity in the dorsal mPFC (Talairach coordinates –6, 57, 14) and negatively with activity in the ventral mPFC (Talairach coordinates 10, 43, 0) (FIG. 2; red dots). The researchers suggested that this might reflect a change in strategy, from simulation in childhood (based on the self, and involving the ventral mPFC) to a more objective strategy in adults (involving the dorsal mPFC). The developmental change in dorsal mPFC activation reported in this study seems to contradict those of the mentalizing studies described above. However, this task is different from other mentalizing tasks in that it is non-verbal, and the attribution of mental states to the shapes in the animations is illusory and subjective. In addition, the oldest participants in this study were 16 years of age, and it is unknown how activity in the dorsal mPFC during participation in the animations task changes after this age. Because no adult group was included for comparison, it cannot be ruled out that activity in this region decreases between 16 years of age and adulthood.

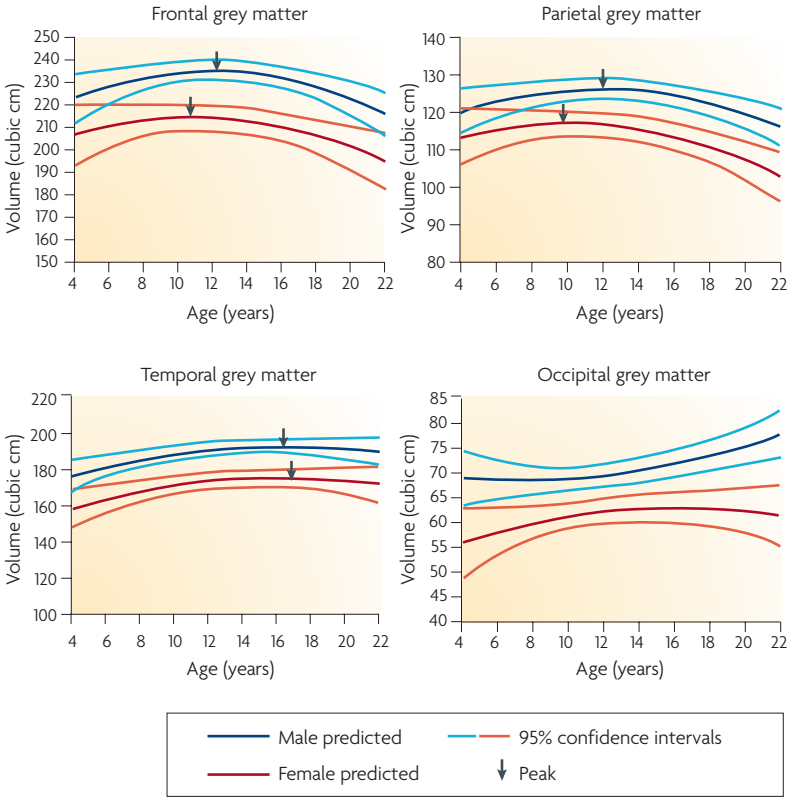
To summarize, as of yet there have been only a handful of developmental-neuroimaging studies of social cognition, but there does seem to be some consistency with respect to the direction of change in frontal activity. Overall, the studies reviewed here have found that activity in various frontal regions decreases between adolescence and adulthood, despite performance being equated across groups. Equating performance between groups is critical for the interpretation of the functional neuroimaging data: if performance between groups were significantly different, it would be impossible to know whether a group difference in neural activity was the cause, or simply a consequence of, the difference in performance. On the other hand, matching performance between groups negates important differences between adolescents and adults in terms of social cognition, as has been reported in a large number of social psychology studies. If the neural substrates of social cognition change during adolescence, what are the consequences for social cognitive behaviour? Most developmental studies of social cognition focus on early childhood, possibly because children perform adequately in even quite complex mentalizing tasks by five years of age (BOX 1). It is a challenge therefore to design a task on which older children and adolescents do not perform at ceiling level (note that there is one recently developed ingenious mentalizing task on which even healthy adults make mistakes[60]).

One possible explanation for the decrease in prefrontal activity on social-cognition tasks is that adolescence represents a time of synaptic reorganization in the PFC. This is discussed in the following section.

Structural brain development during adolescence

Cellular development. Research in the 1970s and 1980s carried out on post-mortem brain tissue revealed that the human PFC undergoes a protracted period of synaptic development that continues well into adolescence[61,62].

Box 2 | **Sex differences and the role of hormones in brain development**



How adolescent brain development differs between the sexes, how it is affected by hormonal changes and how this interaction affects social cognition are still empirical questions. Anecdotal evidence suggests that relationships with peers, other social behaviours, and the way in which these develop during puberty and adolescence differ between males and females. An early MRI study demonstrated significant sex differences in age-related grey-matter changes in a range of cortical regions[67]. Specifically, there was a delay of approximately two years in the peak total brain grey-matter volume in males relative to females. The figure illustrates the predicted volume, with 95% confidence intervals, of cortical grey matter in frontal, parietal, temporal and occipital lobes for males and females aged 4 to 22 years. The arrows indicate the age at which grey-matter volume was maximal. Note that grey-matter volume in the frontal cortex peaks at approximately the age of puberty onset: 11 years in girls and 12 years in boys. In the temporal cortex the peak is not reached until approximately 16 years. Although no measure of puberty was taken in this study, the study does suggest that puberty, rather than age, might be the trigger for neuroanatomical changes, at least in frontal and parietal regions[77].

Sex hormones influence a range of neurodevelopmental processes in animals, including neuronal survival, neurogenesis, synaptogenesis, receptor expression, neurotransmitter synthesis and neuronal excitability[77]. Research in animals[88] and humans has shown that sex hormones also influence social behaviour. In humans, affective responses to male faces vary across the menstrual cycle in women[89]. In men and women, sex-hormone levels are associated with differential emotional responses to infants. For example, changes in female sex hormones during pregnancy predict post-partum attachment feelings to infants[90], and lower testosterone levels in men are associated with higher levels of sympathy and a greater need to respond to infant cries[91]. In addition, sex hormones affect sexual behaviour, by binding to receptors in limbic areas, including the hypothalamus and the amygdala. In monkeys the amygdala has a predominance of androgen receptors[92] whereas the hippocampus has a predominance of oestrogen receptors[93]. This difference might account for the finding that, in humans, amygdala volume increased between the ages of 4 and 18 years in males only, whereas hippocampal volume increased only in females[94]. Figure reproduced, with permission, from REF. 67 © (1999) Macmillan Publishers Ltd.

Huttenlocher's research contrasted with earlier studies on the development of sensory and motor regions in animal brains (in particular those of cats and monkeys), which demonstrated that synaptogenesis and synaptic pruning occur early in an animal's life[63]. In the primary motor cortex of macaque monkeys, for example, synaptogenesis starts early in fetal development and results in a greater synaptic density in early infancy than in adulthood. The excess synapses (that is, synapses that are not included in functional neuronal circuits) are then pruned back, and synaptic density declines to adult levels by approximately three years of age (the age of sexual maturity in monkeys)[64]. Huttenlocher's research, by comparison, demonstrated that in the human brain synaptic density reaches a maximum before one year of age in the primary auditory and visual cortices and at approximately three and a half years of age in the PFC (middle frontal gyrus; see FIG. 4)[61,62,65]. Interestingly, whereas in the human auditory cortex synaptic elimination is complete by 12 years of age, pruning continues until mid-adolescence in the PFC[65].

Developmental MRI studies of the human brain. Huttenlocher's research relied on post-mortem human brains. In the past decade or so, structural MRI has enabled researchers to investigate the development of the living human brain. Since the first developmental MRI studies (for examples see REFS 66,67) there have been numerous large-scale studies. Some were longitudinal, and scanned the same children more than once over time to see how brain regions change with age; others were cross-sectional, and scanned participants of different ages to see how their neuroanatomy compared. MRI studies have mostly focused on developmental changes in grey matter (which corresponds to cell bodies, synapses and neuropil) and white matter (which corresponds to myelinated axons). The results of these studies are remarkably consistent: several cortical regions, in particular parts of the PFC, the temporal cortex and the parietal cortex, as well as a number of subcortical structures, undergo substantial changes in white- and grey-matter volume during the first two (and in some studies even three) decades of life. White-matter volume seems to increase linearly during the first two decades[68,69]. This increase in white-matter volume has been suggested to reflect protracted axonal myelination in some cortical regions throughout the first two decades of life[70].

By contrast, grey-matter volume in several cortical areas decreases between childhood and adulthood. A recent longitudinal study of anatomical brain development in participants aged between 4 and 21 years showed that grey-matter loss occurs initially in the primary sensorimotor areas and then spreads over the PFC, the parietal and occipital cortices and finally the temporal cortex[71] (FIG. 4). This finding has been replicated a number of times, with other studies showing that decreases in grey-matter volume continue throughout adolescence, in particular in the lateral and superior PFC[72,73]. The decrease in grey-matter volume in the PFC during adolescence is proposed to reflect, at least in part, synaptic elimination[61,62,65].

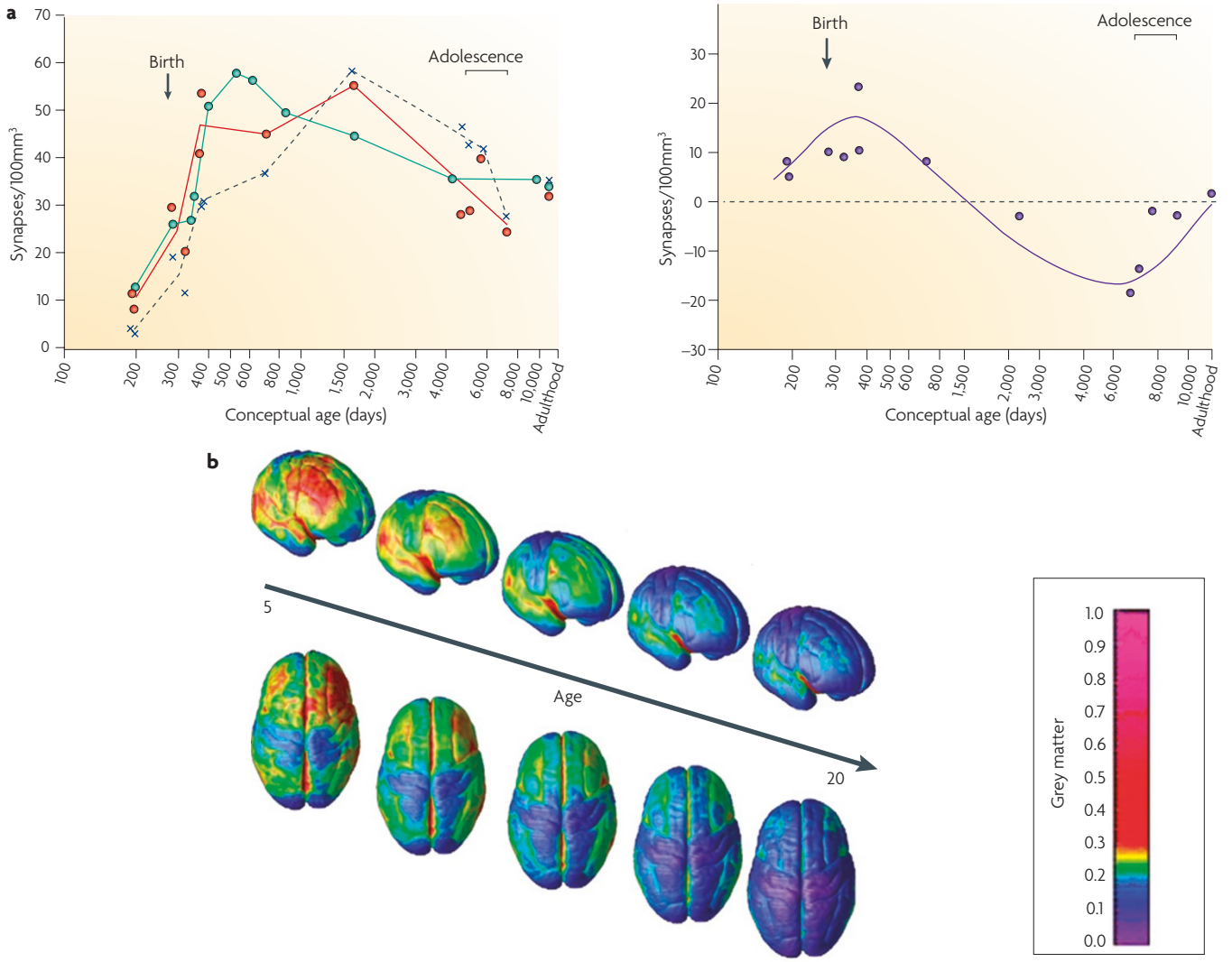


Figure 4 | **Development of synaptic density and grey-matter volume in sensory and frontal regions. a** | The left-hand graph shows the mean synaptic density in the primary auditory cortex (red circles), the primary visual cortex (green circles) and the prefrontal cortex (PFC) (specifically the middle frontal gyrus; crosses) in post-mortem human brains at different ages. The x axes show conceptual age in days from 200 days post-conception to 10,000 days post-conception (approximately 27 years). Synaptic density increases in all three regions in early childhood, but synaptogenesis is most prolonged in the prefrontal cortex. This is further demonstrated in the right-hand graph, which shows the difference in synaptic density between the auditory cortex and the middle frontal gyrus (purple circles) plotted against conceptual age. The line represents a curve of best fit for the data. Thus, although the peak synaptic density in the auditory cortex occurs early (at approximately three months after birth), the peak synaptic density in the PFC occurs significantly later. **b** | Right lateral and top views of the dynamic sequence of grey-matter maturation over the cortical surface between 4 and 21 years, as viewed in a longitudinal MRI study in which 13 children were scanned every 2 years for 8–10 years. The side bar shows a colour representation in units of grey-matter volume, with shades of blue corresponding to grey-matter loss. The images show that grey-matter loss occurs initially in the primary sensorimotor areas and then spreads over the PFC, the parietal and occipital cortices and finally the temporal cortex. This sequence can be viewed in movie form online — see REF. 71. Part **a** reproduced, with permission, from REF. 65 © (1997) Wiley-Liss. Part **b** reproduced, with permission, from REF. 71 © (2004) National Academy of Sciences.

Synaptogenesis
The generation of new synapses in the brain.

Synaptic density
The number of synapses per unit brain tissue.

Other studies report a nonlinear, 'inverted-U'-shaped pattern of grey-matter change with age in frontal, parietal and temporal regions[67] (see BOX 2 figure). In an early study by Giedd and colleagues, the region in which grey-matter volume peaked latest (at approximately 16 years of age) was the temporal cortex, and this was followed by a decline during late adolescence and the early twenties[67]. Sowell and colleagues observed a similar inverted-U-shaped pattern of grey-matter volume in the STS[72,74]. It is unknown why some studies report an inverted-U-shaped pattern whereas others report a steady decline in grey-matter volume between childhood and adulthood. However, it is possible that the increase in grey-matter volume during childhood that is reported in some studies reflects prolonged synaptogenesis.

Box 3 | **Mental illness and the influence of the environment on neural development in adolescence**

Although adolescence represents a period of cognitive improvement, it also marks a period of increased rates of antisocial and risky behaviours and mental illness[95]. After puberty and throughout adolescence there is a marked increase in the incidence of depression, anxiety and mood disorders, eating disorders and substance abuse. It is possible that this arises owing to asynchronous trajectories of neural development, an idea that has been developed by Nelson and colleagues in their Social Information Processing Network model[96]. This model posits that social-information processing occurs by way of three interacting neural 'nodes'. The 'detection node', comprising the intraparietal sulcus, the superior temporal sulcus, the fusiform face area and temporal and occipital regions, deciphers the social properties of a stimulus such as biological motion. The 'affective node', including limbic areas of the brain such as the amygdala, the ventral striatum, the hypothalamus and the orbitofrontal cortex, is thought to process the emotional significance of a social stimulus. The 'cognitive-regulatory node', consisting of much of the prefrontal cortex, is responsible for mentalizing, impulse inhibition and goal-directed behaviour. Nelson and colleagues propose that there is a mismatch in the maturation of the different nodes — namely that the development of the cognitive-regulatory node lags behind the development of the other nodes — and that this contributes to the onset of mood and anxiety disorders in adolescence.

Schizophrenia is a condition that often has its onset at approximately the end of adolescence, perhaps as a consequence of abnormal brain development during adolescence[97]. This abnormal development is probably genetically determined to a significant extent, but there is evidence that it might also be influenced by environmental factors, such as cannabis use: adolescents who regularly smoke cannabis have a significantly greater chance of developing schizophrenia than adolescents who do not smoke cannabis[98]. Adolescents with a genetic risk of schizophrenia might be more likely to use cannabis, and these longitudinal studies attempted to control for this by excluding participants who reported any psychotic symptoms or feelings that preceeded cannabis use. Therefore, the results suggest that cannabis use might affect brain development during adolescence and have a causal role in the onset of schizophrenia[99].

Relationship between neuroanatomical, cognitive and functional brain development. One possible consequence of the relatively late elimination of excess synapses in the human PFC and other cortical regions is that it renders information processing in the relevant brain regions less efficient. The excess, 'untuned' synapses are thought to result in a low signal-to-noise ratio. Input-dependent synaptic pruning eliminates those excess synapses, thereby effectively fine-tuning the remaining connections into specialized functional networks. After pruning, it is possible that it takes fewer synapses to do same amount of work, because the remaining synapses are more efficient. This would engender a system with a higher signal-to-noise ratio, which might result in more efficient cognitive processing and improved performance with age. The dip in performance at puberty on face-processing tasks[50–52] might be related to the increase in grey-matter volume at approximately this age in frontal[67] and temporal regions[67,72,74]. On the other hand, there are other potential causes of a pubertal dip in performance, including changes in hormones (BOX 2) and changes in the social environment — puberty is the age at which most children enter new schools and are exposed to many new faces. Rendering the picture even more complex, hormonal and environmental changes might trigger, or at least influence, alterations in grey- and white-matter volume in the social brain, which might then influence social cognition and behaviour. It is currently difficult to disentangle genetically pre-programmed developmental changes from those that are triggered by changes in the environment.

The developmental neuroimaging studies of social cognition reviewed above tend to show a decrease in frontal activity between adolescence and adulthood. In face-processing tasks, activity in the lateral and superior PFC seems to increase between childhood and adolescence and then decrease between adolescence and adulthood. This nonlinear pattern of activity might be related to synaptic reorganization. Excess synaptogenesis during childhood might result in increasing levels of activity in the relevant brain region, owing to a low signal-to-noise ratio for the neuronal networks involved. Synaptic pruning during adolescence could then lead to a higher signal-to-noise ratio for the neuronal networks, possibly resulting in decreased levels of activity. This might account for the decrease in activity in the lateral and superior PFC in face-processing tasks and in the mPFC in mentalizing tasks between late childhood/early adolescence and adulthood.

This is a purely speculative idea that makes several assumptions that are yet to be tested. First, it assumes that a larger number of synapses in a given unit of brain tissue results in an increased blood-oxygen-level-dependent (BOLD) signal if those synapses are active. This notion assumes that there is a more-or-less linear relationship between synaptic density and the BOLD signal. Exactly how linear the coupling between synaptogenesis and the BOLD response is remains to be determined. It is likely that the coupling is different in different brain regions and that there is at least some degree of nonlinearity[75]. Second, it makes the assumption that vascular changes correlate with synaptic changes; whether this is the case is as yet unknown. Furthermore, it would be useful to know whether there are correlations between structural changes (in grey matter) and functional changes (to the BOLD signal) in the same individuals. Although this has been investigated in one neuroimaging study on executive control[76], none has yet attempted to correlate structural and functional development of the social brain.

Conclusion and questions for further research

Here I have reviewed evidence that certain areas of the social brain, namely the pSTS and the mPFC, undergo substantial functional and structural development during adolescence. Recent functional neuroimaging studies of social cognitive development suggest that activity in

a number of prefrontal areas increases between childhood and adolescence and then decreases between early adolescence and adulthood. The decrease in prefrontal activity during adolescence might be related to structural development in this area, namely the elimination of unused synapses.

There are many outstanding questions. A fundamental question is how synaptic reorganization affects neural activity and cognitive function and what triggers its reorganization at puberty. Virtually nothing is known about this relationship, but it seems likely that hormonal changes at puberty trigger neuroanatomical changes[77] (BOX 2).

How the environment influences brain development during adolescence is another empirical question. It has been proposed that synaptic pruning in early development fine-tunes neuronal circuitry in an input-dependent manner. Rats that are brought up in an enriched environment — that is, together with other rats in a cage with toys and exercise wheels — have higher synaptic density in the visual cortex than rats that are brought up individually with little stimulation[78]. The 'enriched' rats also show better performance on spatial-navigation tasks, but at present the relationship between enrichment, synaptic density and memory is purely correlational and no inference about causality can be drawn. In humans, synaptic pruning in early childhood has been proposed to underlie sound categorization. The ability to distinguish certain speech sounds depends on being exposed to those sounds in early development. For example, before approximately 12 months of age, babies that have been brought up in the United States can detect the difference between certain sounds that are common in the Hindi language; after 12 months they can no longer distinguish these sounds because the English language does not contain them[79]. Although there is no direct evidence, this fine-tuning of sound categorization is thought to rely on the pruning of synapses in sensory areas that are involved in processing sound. It is unknown whether the pruning of synapses in the PFC during adolescence might be similarly influenced by environmental input. It has recently been suggested that cannabis use might influence the development of the brain during adolescence, although the precise mechanisms by which cannabis might affect synaptogenesis or synaptic pruning are not known (BOX 3).

A number of neuroimaging studies have reported lower levels of activity during face-processing, emotion-recognition and mentalizing tasks in the PFC in adults than in adolescents. This difference implies that damage to the PFC during adolescence might be more detrimental to associated cognitive functions than damage that is suffered during adulthood. There is evidence that damage to the PFC (including the mPFC) in adulthood does not impair mentalizing[30]. A comparison between people who have suffered mPFC damage at different ages would be interesting. Perhaps the mPFC is important for the early development of mentalizing, but becomes less important with age. On the other hand, as discussed above, this region is consistently activated when adults think about mental states. The question, then, is what is the role of the mPFC in social cognition in adulthood? Also, how and why does its role in social cognition change between adolescence and adulthood?

Adolescence is a period in which individuals undergo changes in their social behaviour, yet few empirical behavioural studies have reported significant behavioural development that is specific to social cognition and that cannot be explained by general improvements in attention, concentration, memory and so on. One possibility is that adolescents are more adept at completing complicated social cognition tasks in the laboratory than they are at dealing with situations that arise in everyday life. More naturalistic paradigms might be useful in addressing this question. Another possibility is that it is not mentalizing *per se* that changes, but rather the modulation of mentalizing by executive functions. An example of this kind of relationship was reported by Monk and colleagues in their study of face processing[54]. In this study, whether participants directed their attention to emotional facial features (the eyes) or non-emotional facial features (the nose) affected neural activity associated with face processing differentially in adolescents and adults (FIG. 3). However, it is important not to try to explain all of adolescent behaviour in terms of neuroanatomical changes, as this neglects other important factors such as hormonal and social changes (although these could in turn trigger neuroanatomical changes). There are presumably large differences between individuals in the development of the social brain, but these have so far been neglected in the literature. Furthermore, synaptic plasticity is a baseline property of the brain even in adulthood, and it occurs whenever something is learned[80]. An unanswered question is whether and how plasticity that takes place during adolescence differs from plasticity in adulthood.

These are just some of the many questions that remain to be investigated in this new and rapidly expanding field. The study of neural development during adolescence is likely to have important implications for society in relation to education and the legal treatment of teenagers, as well as for various mental illnesses that often have their onset in adolescence (BOX 3).

1. Brothers, L. The social brain: a project for integrating primate behavior and neurophysiology in a new domain. *Concepts Neurosci.* **1**, 27–51 (1990).
2. Steinberg, L. & Morris, A. S. Adolescent development. *Annu. Rev. Psychol.* **52**, 83–110 (2001).
3. Frith, C. D. & Frith, U. Social cognition in humans. *Curr. Biol.* **17**, 724–732 (2007).
4. Farroni, T. *et al.* Newborns' preference for face-relevant stimuli: effects of contrast polarity. *Proc. Natl Acad. Sci. USA* **102**, 17245–17250 (2005). **This elegant study on newborn babies replicated the finding that faces are recognised from birth and demonstrated that contrast polarity has a role in this ability: newborns preferentially looked at photographs and schematics of upright faces only when the pattern of contrast polarity was also face-like.**
5. Johnson, M. H. Subcortical face processing. *Nature Rev. Neurosci.* **6**, 766–774 (2005).
6. Perrett, D. I., Hietanen, J. K., Oram, M. W. & Benson, P. J. Organization and functions of cells responsive to faces in the temporal cortex. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **335**, 23–30 (1992).
7. Allison, T., Puce, A. & McCarthy, G. Social perception from visual cues: role of the STS region. *Trends Cogn. Sci.* **4**, 267–278 (2000).
8. Puce, A., Allison, T., Bentin, S., Gore, J. C. & McCarthy, G. Temporal cortex activation in humans viewing eye and mouth movements. *J. Neurosci.* **18**, 2188–2199 (1998).
9. Johansson, G. Visual perception of biological motion and a model for its analysis. *Percept. Psychophys.* **14**, 201–211 (1973).
10. Bertenthal, B. I., Proffit, D. R. & Cutting, J. E. Infant sensitivity to figural coherence in biomechanical motions. *J. Exp. Child. Psychol.* **37**, 213–230 (1984).
11. Oram, M. W. & Perrett, D. I. Responses of anterior superior temporal polysensory (STPa) neurons to biological motion stimuli. *J. Cogn. Neurosci.* **6**, 99–116 (1994).

12. Grossman, E. *et al.* Brain areas involved in perception of biological motion. *J. Cogn. Neurosci.* **12**, 711–720 (2000).
13. Puce, A. & Perrett, D. Electrophysiology and brain imaging of biological motion. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **358**, 435–445 (2003).
14. Saygin, A. P. Superior temporal and premotor brain areas necessary for biological motion perception. *Brain* **130**, 2452–2461 (2007).
15. Dolan, R. J. Emotion, cognition, and behavior. *Science* **298**, 1191–1194 (2002).
16. Winston, J. S., Strange, B. A., O'Doherty, J. & Dolan, R. J. Automatic and intentional brain responses during evaluation of trustworthiness of faces. *Nature Neurosci.* **5**, 277–283 (2002).
17. Moll, J. & de Oliveira-Souza, R. Moral judgments, emotions and the utilitarian brain. *Trends Cogn. Sci.* **11**, 319–321 (2007).
18. Nakamura, K. *et al.* Activation of the right inferior frontal cortex during assessment of facial emotion. *J. Neurophys.* **82**, 1610–1614 (1999).
19. Fletcher, P. C. *et al.* Other minds in the brain: a functional imaging study of "theory of mind" in story comprehension. *Cognition* **57**, 109–128 (1995).
The first neuroimaging study to investigate the neural correlates of theory-of-mind. This PET study made use of stories that elicited mental-state attribution and showed activation in the social-brain network for the theory-of-mind stimuli.
20. Gallagher, H. L. *et al.* Reading the mind in cartoons and stories: an fMRI study of 'theory of mind' in verbal and nonverbal tasks. *Neuropsychologia* **38**, 11–21 (2000).
21. Saxe, R. & Kanwisher, N. People thinking about thinking people. The role of the temporo-parietal junction in "theory of mind". *Neuroimage* **19**, 1835–1842 (2003).
22. den Ouden, H. E., Frith, U., Frith, C. & Blakemore, S. J. Thinking about intentions. *Neuroimage* **28**, 787–796 (2005).
23. Mitchell, J. P., Heatherton, T. F. & Macrae, C. N. Distinct neural systems subserve person and object knowledge. *Proc. Natl Acad. Sci. USA* **99**, 15238–15243 (2002).
24. Brunet, E., Sarfati, Y., Hardy-Bayle, M. C. & Decety, J. A PET investigation of the attribution of intentions with a nonverbal task. *Neuroimage* **11**, 157–166 (2000).
25. Castelli, F., Happé, F., Frith, U. & Frith, C. D. Movement and mind: a functional imaging study of perception and interpretation of complex intentional movement pattern. *Neuroimage* **12**, 314–325 (2000).
26. Samson, D., Apperly, I. A., Chiavarino, C. & Humphreys, G. W. Left temporoparietal junction is necessary for representing someone else's belief. *Nature Neurosci.* **7**, 499–500 (2004).
This study of patients with brain damage showed that the left temporoparietal junction is necessary for reasoning about the beliefs of others.
27. Happe, F., Malhi, G. S. & Checkley, S. Acquired mind-blindness following frontal lobe surgery? A single case study of impaired 'theory of mind' in a patient treated with stereotactic anterior capsulotomy. *Neuropsychologia* **39**, 83–90 (2001).
28. Rowe, A. D., Bullock, P. R., Polkey, C. E. & Morris, R. G. "Theory of mind" impairments and their relationship to executive functioning following frontal lobe excisions. *Brain* **124**, 600–616 (2001).
29. Stuss, D. T., Gallup, G. G. Jr & Alexander, M. P. The frontal lobes are necessary for 'theory of mind'. *Brain* **124**, 279–286 (2001).
30. Bird, C. M., Castelli, F., Malik, O., Frith, U. & Husain, M. The impact of extensive medial frontal lobe damage on 'Theory of Mind' and cognition. *Brain* **127**, 914–928 (2004).
This study reported the surprising finding that theory-of-mind function was not impaired in an adult who had suffered recent damage to the frontal lobes, including the bilateral mPFC.
31. Anderson, S. W., Bechara, A., Damasio, H., Tranel, D. & Damasio, A. R. Impairment of social and moral behavior related to early damage in human prefrontal cortex. *Nature Neurosci.* **2**, 1032–1037 (1999).
Unlike patients with adult-onset prefrontal damage, who tend to show normal social and moral reasoning in laboratory tests, the two patients reported here had suffered early-onset prefrontal damage and showed impairments on socio–moral reasoning tasks. This suggests that the age at which prefrontal damage occurs determines outcome in terms of socio–moral functioning.
32. Amodio, D. M. & Frith, C. D. Meeting of minds: the medial frontal cortex and social cognition. *Nature Rev. Neurosci.* **7**, 268–277 (2006).
33. Gilbert, S. J. *et al.* Functional specialization within rostral prefrontal cortex (area 10): a meta-analysis. *J. Cogn. Neurosci.* **18**, 932–948 (2006).
This meta-analysis of 104 functional neuroimaging studies provided strong evidence for the existence of distinct subregions of rostral PFC. Activations in the most rostral part of the PFC were particularly associated with multi-tasking, whereas more caudal activations were associated with mentalizing if they were medial and episodic-memory retrieval if they were lateral.
34. Vogeley, K. *et al.* Mind reading: neural mechanisms of theory of mind and self-perspective. *Neuroimage* **14**, 170–181 (2001).
35. Johnson, S. C. *et al.* Neural correlates of self-reflection. *Brain* **125**, 1808–1814 (2002).
36. Lou, H. C. *et al.* Parietal cortex and representation of the mental self. *Proc. Natl Acad. Sci. USA* **101**, 6827–6832 (2004).
37. Ochsner, K. N. *et al.* Reflecting upon feelings: an fMRI study of neural systems supporting the attribution of emotion to self and other. *J. Cogn. Neurosci.* **16**, 1746–1772 (2004).
38. Ruby, P. & Decety, J. How would you feel versus how do you think she would feel? A neuroimaging study of perspective-taking with social emotions. *J. Cogn. Neurosci.* **16**, 988–999 (2004).
39. Goel, V., Grafman, J., Sadato, N. & Hallett, M. Modeling other minds. *Neuroreport* **6**, 1741–1746 (1995).
40. Mitchell, J. P., Banaji, M. R. & Macrae, C. N. General and specific contributions of the medial prefrontal cortex to knowledge about mental states. *Neuroimage* **28**, 757–762 (2005).
41. McCabe, K., Houser, D., Ryan, L., Smith, V. & Trouard, T. A functional imaging study of cooperation in two-person reciprocal exchange. *Proc. Natl Acad. Sci. USA* **98**, 11832–11835 (2001).
42. Gallagher, H. L., Jack, A. I., Roepstorff, A. & Frith, C. D. Imaging the intentional stance in a competitive game. *Neuroimage* **16**, 814–821 (2002).
43. Frith, C. D. The social brain? *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **362**, 671–678 (2007).
44. Gusnard, D. A. & Raichle, M. E. Searching for a baseline: functional imaging and the resting human brain. *Nature Rev. Neurosci.* **2**, 685–694 (2001).
45. Saxe, R. Uniquely human social cognition. *Curr. Opin. Neurobiol.* **16**, 235–239 (2006).
46. Mitchell, J. P. Activity in right temporo-parietal junction is not selective for theory-of-mind. *Cereb. Cortex* **18**, 262–271 (2008).
This fMRI study examined the extent to which the right TPJ, identified by a theory-of-mind task, also distinguished between trials on a target-detection task that required reorienting attention. Results were incompatible with claims that this region is selective for mental-state attribution, as the same region was also modulated by the non-social attentional task.
47. Friston, K. J., Rotshtein, P., Geng, J. J., Sterzer, P. & Henson, R. N. A critique of functional localisers. *Neuroimage* **30**, 1077–1087 (2006).
48. Damon, W. in *Handbook of Adolescent Psychology* 2nd edn (eds Lerner, R. M. & Steinberg, L.) vii–viii (Wiley, New Jersey, 2003).
49. Brown, B. B. in *Handbook of Adolescent Psychology* 2nd edn (eds Lerner, R. M. & Steinberg, L.) 363–394 (Wiley, New Jersey, 2004).
50. Carey, S., Diamond, R. & Woods, B. The development of face recognition – a maturational component. *Dev. Psychol.* **16**, 257–269 (1980).
51. Diamond, R., Carey, S. & Back, K. Genetic influences on the development of spatial skills during early adolescence. *Cognition* **13**, 167–185 (1983).
52. McGivern, R. F., Andersen, J., Byrd, D., Mutter, K. L. & Reilly, J. Cognitive efficiency on a match to sample task decreases at the onset of puberty in children. *Brain Cogn.* **50**, 73–89 (2002).
53. Yurgelun-Todd, D. A. & Killgore, W. D. Fear-related activity in the prefrontal cortex increases with age during adolescence: a preliminary fMRI study. *Neurosci. Lett.* **406**, 194–199 (2006).
54. Monk, C. S. *et al.* Adolescent immaturity in attention-related brain engagement to emotional facial expressions. *Neuroimage* **20**, 420–428 (2003).
55. Carter, E. J. & Pelphrey, K. A. School-aged children exhibit domain-specific responses to biological motion. *Soc. Neurosci.* **1**, 396–411 (2006).
56. Wang, A. T., Lee, S. S., Sigman, M. & Dapretto, M. Developmental changes in the neural basis of interpreting communicative intent. *Soc. Cogn. Affect. Neurosci.* **1**, 107–121 (2006).
57. Blakemore, S. J., den Ouden, H., Choudhury, S. & Frith, C. Adolescent development of the neural circuitry for thinking about intentions. *Soc. Cogn. Affect. Neurosci.* **2**, 130–139 (2007).
58. Pfeifer, J. H., Lieberman, M. D. & Dapretto, M. "I know you are but what am I?!": neural bases of self- and social knowledge retrieval in children and adults. *J. Cogn. Neurosci.* **19**, 1323–1337 (2007).
59. Moriguchi, Y., Ohnishi, T., Mori, T., Matsuda, H. & Komaki, G. Changes of brain activity in the neural substrates for theory of mind during childhood and adolescence. *Psychiatry Clin. Neurosci.* **61**, 355–363 (2007).
60. Keysar, B., Lin, S. & Barr, D. J. Limits on theory of mind use in adults. *Cognition* **89**, 25–41 (2003).
The ingenious paradigm used in this study required participants to take into account a speaker's false belief when following their instructions. It was the first paradigm to show that a mentalizing ability that adults clearly possess might not always be used reliably.
61. Huttenlocher, P. R. Synaptic density in human frontal cortex - developmental changes and effects of aging. *Brain Res.* **163**, 195–205 (1979).
62. Huttenlocher, P. R., De Courten, C., Garey, L. J. & Van der Loos, H. Synaptic development in human cerebral cortex. *Int. J. Neurol.* **16–17**, 144–154 (1983).
63. Cragg, B. G. The development of synapses in the visual system of the cat. *J. Comp. Neurol.* **160**, 147–166 (1975).
64. Zecevic, N., Bourgeois, J. P. & Rakic, P. Changes in synaptic density in motor cortex of rhesus monkey during fetal and postnatal life. *Brain Res. Dev. Brain Res.* **50**, 11–32 (1989).
65. Huttenlocher, P. R. & Dabholkar, A. S. Regional differences in synaptogenesis in human cerebral cortex. *J. Comp. Neurol.* **387**, 167–178 (1997).
66. Giedd, J. N. *et al.* Quantitative magnetic resonance imaging of human brain development: ages 4–18. *Cereb. Cortex* **6**, 551–560 (1996).
67. Giedd, J. N. *et al.* Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neurosci.* **2**, 861–863 (1999).
68. Paus, T. *et al.* Structural maturation of neural pathways in children and adolescents: *in vivo* study. *Science* **283**, 1908–1911 (1999).
69. Giedd, J. N. *et al.* Brain development during childhood and adolescence: a longitudinal MRI study. *Nature Neurosci.* **2**, 861–863 (1999).
70. Yakovlev, P. A. & Lecours, I. R. in *Regional Development of the Brain in Early Life* (ed. Minkowski, A.) 3–70 (Blackwell, Oxford, 1967).
71. Gogtay, N. *et al.* Dynamic mapping of human cortical development during childhood through early adulthood. *Proc. Natl Acad. Sci. USA* **101**, 8174–8179 (2004).
72. Sowell, E. R., Thompson, P. M., Holmes, C. J., Jernigan, T. L. & Toga, A. W. *In vivo* evidence for post-adolescent brain maturation in frontal and striatal regions. *Nature Neurosci.* **2**, 859–861(1999).
73. Sowell, E. R. *et al.* Mapping cortical change across the life span. *Nature Neurosci.* **6**, 309–3150 (2003).
74. Sowell, E. R. *et al.* Longitudinal mapping of cortical thickness and brain growth in normal children. *J. Neurosci.* **24**, 8223–8231 (2004).
75. Lauritzen, M. Reading vascular changes in brain imaging: is dendritic calcium the key? *Nature Rev. Neurosci.* **6**, 77–85 (2005).
76. Konrad, K. *et al.* Development of attentional networks: an fMRI study with children and adults. *Neuroimage* **28**, 429–439 (2005).
77. Romeo, R. D. Puberty: a period of both organizational and activational effects of steroid hormones on neurobehavioural development. *J. Neuroendocrinol.* **15**, 1185–1192 (2003).
78. Turner, A. M & Greenough, W. T. Differential rearing effects on rat visual cortex synapses. I. Synaptic and neuronal density and synapses per neuron. *Brain Res.* **329**, 195–203 (1985).
79. Werker, J. F., Gilbert, J. H., Humphrey, K. & Tees, R. C. Developmental aspects of cross-language speech perception. *Child Dev.* **52**, 349–355 (1981).
80. Buonomano, D. V. & Merzenich, M. M. Cortical plasticity: from synapses to maps. *Annu. Rev. Neurosci.* **21**, 149–186 (1998).

81. Johnson, S. C. Detecting agents. *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **358**, 549–559 (2003).
82. Carpenter, M., Nagell, K. & Tomasello, M. Social cognition, joint attention, and communicative competence from 9 to 15 months of age. *Monogr. Soc. Res. Child Dev.* **63**, 1–143 (1998).
83. Leslie, A. Pretence and representation. The origin of "theory of mind". *Psychol. Rev.* **94**, 412–426 (1987).
84. Barresi, J. & Moore, C. Intentional relations and social understanding. *Behav. Brain Sci.* **19**, 107–154 (1996).
85. Onishi, K. H. & Baillargeon, R. Do 15-month-old infants understand false beliefs? *Science* **308**, 255–258 (2005).
86. Baron-Cohen, S., Leslie, A. M. & Frith, U. Does the autistic child have a "theory of mind"? *Cognition* **21**, 37–46 (1985).
87. Abell, F., Happe, F. & Frith, U. Do triangles play tricks? Attribution of mental states to animated shapes in normal and abnormal development. *J. Cogn. Dev.* **15**, 1–20 (2000).
88. Schulz, K. M. *et al.* Gonadal hormones masculinize and defeminize reproductive behaviors during puberty in the male Syrian hamster. *Horm. Behav.* **45**, 242–249 (2004).
89. Penton-Voak, I. S. *et al.* Menstrual cycle alters face preference. *Nature* **399**, 741–742 (1999).
90. Fleming, A. S., Ruble, D., Krieger, H. & Wong, P. Y. Hormonal and experiential correlates of maternal responsiveness during pregnancy and the puerperium in human mothers. *Horm. Behav.* **31**, 145–158 (1997).
91. Fleming, A. S., Corter, C., Stallings, J. & Steiner, M. Testosterone and prolactin are associated with emotional responses to infant cries in new fathers. *Horm. Behav.* **42**, 399–413 (2002).
92. Clark, A. S., MacLusky, N. J. & Goldman-Rakic, P. S. Androgen binding and metabolism in the cerebral cortex of the developing rhesus monkey. *Endocrinology* **123**, 932–940 (1988).
93. Morse, J. K., Scheff, S. W. & DeKosky, S. T. Gonadal steroids influence axonal sprouting in the hippocampal dentate gyrus: a sexually dimorphic response. *Exp. Neurol.* **94**, 649–658 (1986).
94. Giedd, J. N. *et al.* Quantitative MRI of the temporal lobe, amygdala, and hippocampus in normal human development: ages 4–18 years. *J. Comp. Neurol.* **366**, 223–230 (1996).
95. Green, H., McGinnity, A., Meltzer, H., Ford, T. & Goodman, R. *Mental Health of children and Young People in Great Britain, 2004* (Palgrave Macmillan, London, 2005).
96. Nelson, E. E., Leibenluft, E., McClure, E. B. & Pine, D. S. The social re-orientation of adolescence: a neuroscience perspective on the process and its relation to psychopathology. *Psychol. Med.* **35**, 163–174 (2005).
97. McGlashan, T. H. & Hoffman R. E. Schizophrenia as a disorder of developmentally reduced synaptic connectivity. *Arch. Gen. Psychiatry* **57**, 637–648 (2000).
98. Arseneault, L. *et al.* Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. *BMJ* **325**, 1212–1213 (2002).
99. Murray, R. M., Morrison, P. D., Henquet, C. & Di Forti, M. Cannabis, the mind and society: the hash realities. *Nature Rev. Neurosci.* **8**, 885–895 (2007).
100 Martin, J. H. *Neuroanatomy: Text & Atlas* 2nd edn (Appleton and Lange, Stamford, Connecticut, 1996).
101. Ekman, P. & Friesen, W. V. *Pictures of Facial Affect* (Consulting Psychologists Press, California, 1976).

Acknowledgements

The author is funded by a Royal Society University Research Fellowship. I am grateful to C. Frith, U. Frith, C. Sebastian, S. Burnett and I. Dumontheil for reading previous versions of the manuscript.

FURTHER INFORMATION

Sarah-Jayne Blakemore's homepage:
http://www.icn.ucl.ac.uk/sblakemore/

ALL LINKS ARE ACTIVE IN THE ONLINE PDF