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Social cognition in schizophrenia

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Abstract | Individuals with schizophrenia exhibit impaired social cognition, which manifests as difficulties in identifying emotions, feeing connected to others, inferring people's thoughts and reacting emotionally to others. These social cognitive impairments interfere with social connections and are strong determinants of the degree of impaired daily functioning in such individuals. Here, we review recent findings from the fields of social cognition and social neuroscience and identify the social processes that are impaired in schizophrenia. We also consider empathy as an example of a complex social cognitive function that integrates several social processes and is impaired in schizophrenia. This information may guide interventions to improve social cognition in patients with this disorder.

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Schizophrenia is a serious and debilitating psychiatric disorder that affects nearly 1% of the world's population[1] and is diagnosed by characteristic psychotic and non-psychotic symptoms (BOX 1). Schizophrenia is one of the most-disabling conditions among all diseases, in both developing and developed countries, and is associated with a reduction in social connections, reduced rates of employment and impaired ability to live independently[2]. Two perplexing questions are why the functional disability of schizophrenia is so severe and why levels of disability among patients has changed little over the past century, despite the availability of medications that reduce psychotic symptoms in most patients. Although they are not considered in the diagnosis, deficits in perception, non-social cognition and social cognition are also features of schizophrenia[3–5]. Deficits in these perceptual and cognitive areas are consistently correlated with the functional disability of patients[6,7].

Social cognition refers to the psychological processes that are involved in the perception, encoding, storage, retrieval and regulation of information about other people and ourselves. These processes include social cue perception, experience sharing, inferring other people's thoughts and emotions, and managing emotional reactions to others. Although social and non-social cognition share some overlapping cognitive processes, some brain regions are specifically involved in the former (BOX 2).

Individuals with schizophrenia often display marked impairments in processing social information, which can result in misinterpretations of the social intent of others, social withdrawal and impaired daily social functioning[8,9]. Indeed, in such individuals, social cognitive impairment has a more-negative effect on daily functioning than does non-social cognitive impairment[8,9]. A greater understanding of social cognitive impairments may therefore provide opportunities for targeted recovery-focused interventions. Furthermore, social cognitive impairments have trait-like qualities that precede the onset of illness and are candidate endophenotypes for schizophrenia (BOX 3). Thus, studies of social cognition in schizophrenia may also provide more general insight into the mechanisms underlying the disorder[10,11].

In this Review, we discuss studies of social cognition and social neuroscience in schizophrenia, fields that have recently benefited from a dramatic surge of knowledge in social neuroscience[12,13]. We focus on the four general social cognitive processes — perception of social cues, experience sharing, mentalizing, and experiencing and regulating emotion — that have received the most attention in the schizophrenia literature and are consistent with recent organizational models of neural systems in social neuroscience[14,15]. For each social cognitive process, we provide a brief description of the underlying psychological processes and a summary of the brain structures involved, and discuss studies that have investigated that social process in schizophrenia. Finally, we summarize what has been learned from studies of social cognition in schizophrenia and consider the example of empathy as a complex social cognitive function that relies on the integration of these separate social processes and that is often impaired in people with schizophrenia.

Perception of social cues

In everyday life, individuals encounter a diverse array of social cues from others' faces, voices and body movements, including gait, posture and gestures. Individuals

Box 1 | **Symptoms of schizophrenia**

Diagnosing schizophrenia is a complex process that involves carefully examining symptoms and ruling out other potential explanations for them. A diagnosis of schizophrenia requires that at least two of the following characteristic symptoms of schizophrenia be present during a 1-month period: delusions (that is, a firmly held belief despite it being contradicted by what is generally accepted as reality, often persecutory or grandiose in nature); hallucinations (that is, perception of something not present, most frequently hearing voices that no one else hears); speech that is difficult to follow because it is tangential or has loose associations; odd, eccentric or agitated behaviour that would attract attention if observed by others; and negative symptoms (such as lack of drive, reduced motivation for social and productive activities, or reduced expression of emotion)[175].

The two systems for diagnosing psychiatric conditions are the Diagnostic and Statistical Manual, 5th edition (DSM-5), published by the American Psychiatric Association, and the International Classification of Diseases (ICD), published by the World Health Organization[2,175]. Aside from the characteristic symptoms, both systems include guidelines that list other considerations needed for diagnosis, including the duration of the symptoms, and exclusions for other causes of the symptoms, such as drug use and neurological disorders. They also list diagnostic boundaries with other neuropsychiatric disorders (for example, mood disorders and developmental disorders).

Notably, non-social and social cognitive impairments are not part of the diagnosis of schizophrenia for DSM-5, despite their clear relevance for the prognosis, outcome and daily functioning of the patient. Instead, ratings of the severity of cognitive impairment appear in an appendix (Section III) of DSM-5 (REF. 176). Cognitive impairment (both social and non-social) is listed as a specifier (that is, a coded rating of cognitive impairment) for schizophrenia in the current draft of the guidelines for the next revision of the ICD.

must perceive the social information in these cues to make appropriate responses to others, thereby facilitating social interactions. To date, studies of social cue perception in schizophrenia have focused largely on the perception of faces and voices.

Face perception. Face perception is the most-extensively studied aspect of social cue perception in schizophrenia. Non-affective face perception involves the processing of non-emotional information from the faces of others (for example, determining the identity, sex or age of a person) and is associated with increased activation in the bilateral fusiform face area (FFA; also known as lateral fusiform gyrus), visual extrastriate cortex, lateral occipital gyri, anterior temporal pole and posterior superior temporal gyrus (pSTG)[16,17]. Affective face perception involves processing the emotional expressions on the faces of others, and it uses many of the same brain regions activated during non-affective face perception. In addition, affective face perception is associated with increased activation in limbic regions (amygdala, parahippocampal gyrus and posterior cingulate cortex), inferior frontal gyrus (IFG), medial prefrontal gyrus and putamen[17–19] (FIG. 1).

Behavioural studies of non-affective face perception have shown that patients with schizophrenia and healthy controls show comparable performance in age- and sex-discrimination tasks, but the former have difficulty in matching and discriminating the identity of individuals[20,21]. Thus, patients with schizophrenia have less difficulty with coarse judgments of facial features (such as those used in determining the sex of an individual) but have more difficulty with finer-grained judgments (such as those used to determine an individual's identity). Several studies have shown that individuals with and without schizophrenia have similar levels of neural activation in the FFA[22,23] during non-affective face perception. However, patterns of neural activation across FFA voxels during a non-affective face-perception task were less cohesive in patients with schizophrenia[24], which could lead to poor performance on a relatively demanding non-affective face-perception task.

By contrast, affective face perception has consistently been found to be impaired in patients with schizophrenia. Behaviourally, individuals with schizophrenia perform poorly when explicitly asked to identify facial expressions[25,26]. Four meta-analyses of functional magnetic resonance imaging (fMRI) studies and one meta-analysis of studies using event-related potentials (ERPs) demonstrate that there is aberrant neural activity associated with affective face perception in individuals with schizophrenia compared with healthy individuals[27–31]. Although the fMRI meta-analyses also included some studies using other types of emotional stimuli, the majority of studies in the meta-analyses used face stimuli. One meta-analysis focused on the amygdala and showed that individuals with schizophrenia showed decreased amygdala activation compared with healthy controls when aversive emotional stimuli were contrasted with neutral stimuli, but not when aversive stimuli were presented alone[31]. This finding suggests that the blunted response in the amygdala seen in individuals with schizophrenia during contrasts of emotional versus neutral conditions might be due to increased activation in response to neutral stimuli. The other three meta-analyses focused on areas beyond the amygdala[27–29]. Despite differences in the meta-analytic approaches used, these studies indicate that, for affective face perception, individuals with schizophrenia show less activation in the right inferior occipital gyrus, right fusiform gyrus, left amygdala and hippocampal regions, anterior cingulate cortex (ACC), medial prefrontal cortex (mPFC) and thalamus, but they show greater activation in the insula, cuneus, parietal lobule and STG during affective face perception[27–29]. Studies using ERP to assess neural activation during face perception have focused on two components: N170 at occipitotemporal sites, which is associated with structural information of faces[32], and N250 at frontocentral sites, which is associated with facial emotional information[33]. A meta-analysis of various schizophrenia studies revealed robust deficits in N170 and N250 components during affective face perception[30].

To summarize, studies of non-affective face processing in schizophrenia have yielded conflicting results, whereas studies of affective face processing in schizophrenia are more consistent and have shown that patients with schizophrenia demonstrate hypoactivation in brain regions associated with affective face perception and hyperactivation in regions not typically associated with face perception. Thus, patients may recruit other areas to compensate for dysfunction in the key face-processing regions.

Event-related potentials
(ERPs). A way of analysing electroencephalography (EEG) data during cognitive tasks by time-locking EEG activity to specific events (for example, stimulus onset or responses) and extracting neural activity that can be represented as waveforms that reflect certain sensory or cognitive processes.

N170
An event-related potential component that has a negative peak around 170 ms after stimulus presentation at occipitotemporal sites and is associated with processing the structural information of faces.

N250
An event-related potential component that has a negative peak around 250 ms after stimulus presentation at frontocentral sites and is associated with processing facial emotional information.

Box 2 | **Social and non-social cognition**

Non-social and social cognitive tasks use very different types of stimuli; for example, a list of numbers is a non-social stimulus and an expressive face is a social stimulus. However, non-social and social cognition use overlapping cognitive processes, such as working memory and perception, and performance in both types of cognitive task is often correlated in healthy individuals. Despite them using overlapping cognitive processes, several lines of evidence suggest that social and non-social cognition are largely distinct at behavioural and neural levels[177,178].

Human neuroimaging studies indicate that processing social and non-social stimuli uses semi-independent neural systems[179,180]. Brain regions (FIG. 1) such as the medial prefrontal cortex (mPFC), fusiform gyrus, superior temporal sulcus (STS), temporoparietal junction (TPJ) and amygdala are preferentially active during processing of social information[178,181]. In addition, certain neuropeptides, such as oxytocin, seem to have relatively specific effects on social cognition[171,182]. The separation of the neural substrates for social and non-social cognition is also supported by neurophysiological and morphological studies in animals, including non-human primates[183,184]. However, it is important to note that neuroimaging studies of social processes typically apply a subtraction method and include a condition designed to control for non-social processing (for example, reading or memory demands). Thus, this design does not capture the overlapping neural regions between social and non-social cognitive tasks[185].

One of the strongest lines of evidence from neuroimaging of a distinction between social and non-social tasks comes from the default mode network, which shows an inverse correlation described as a 'neural seesaw' (REF. 78). The default mode network, which heavily overlaps with brain regions associated with mentalizing, becomes more active during rest and after a non-social task is completed[186]. If the default mode network remains active when a task is over, it disrupts non-social processing[187,188].

Finally, the distinction between social and non-social cognition is also supported by the schizophrenia literature. Statistical models using exploratory and confirmatory factor analyses of performance-based social cognitive studies in schizophrenia indicate that the models fit better when tasks from the two dimensions of cognition (social and non-social) are separated versus when they are grouped together[189–191].

Voice perception. The acoustic properties of speech (for example, pitch, intonation and rhythm; also called prosody), including emphasis and emotional tone, provide critical information beyond the meaning of words. The limited evidence on non-affective prosody indicates that individuals with schizophrenia may have difficulty only with certain acoustic properties of speech. For example, patients did not differ from controls when discriminating intonation of sentences[34] but showed deficits in discriminating pitch and rhythm of voice stimuli[35,36].

Most studies of voice perception in individuals with schizophrenia have investigated affective prosody, in which emotional quality is conveyed. Notably, impaired pitch discrimination is associated with, and may contribute to, poor affective prosody perception[35,36]. Affective prosody perception has typically been examined using tasks of implicit and explicit processing. Tasks of implicit affective prosody perception involve asking participants to listen to sentences read with and without emotional intonation, but the participants are not asked to make any judgments of the emotion involved. By contrast, in tasks of explicit processing, participants are asked to make emotional judgments about a sentence read with and without emotional intonation. A meta-analysis[37] of fMRI studies in which healthy individuals performed these tasks revealed that implicit processing is associated with activation in the bilateral mid-STG and the bilateral IFG, whereas explicit processing is associated with activation in the right pSTG and the right IFG (FIG. 1).

Although individuals with schizophrenia demonstrate impairments in perceiving affective prosody using explicit behavioural paradigms[38,39], few studies have examined neural correlates. In one fMRI study, patients with schizophrenia showed greater activation in the left middle temporal gyrus and less activation in the left STG than did controls while performing an implicit processing task[40]; during an explicit task, the patients showed greater activation in the left insula. In another fMRI study with an explicit task, patients showed reduced activation in the bilateral IFG compared with healthy controls; furthermore, controls showed increased activation in the mid-STG as affective prosody became more expressive but patients did not show such modulation[41].

To summarize, findings of non-affective prosody in schizophrenia are mixed, in that patients correctly perceive certain features of non-affective prosody (for example, intonation) but have difficulties with perceiving pitch and rhythm. Studies on affective prosody perception have shown consistent behavioural impairment, and the few neuroimaging studies carried out to date suggest hypoactivation in key regions, for example, the STG and IFG.

Experience sharing

Observation of another person's behaviour triggers neural activity in the brain region that becomes activated when engaging in that behaviour oneself[42]. This common neural coding between first-hand and second-hand experiences is referred to as experience sharing. Vicarious neural activation during experience sharing occurs rapidly and without effort[14,42–45], and is thought to directly facilitate understanding of the mental states of others. Experience sharing can be separated into two processes with different functions and partly distinct neural substrates: motor resonance and affect sharing[14,43]. Whereas previous behavioural studies of spontaneous mimicry and imitation indirectly suggested that experience sharing might be diminished in patients with schizophrenia[46–48], the findings that have recently emerged on these processes are conflicting.

Prosody
The acoustic properties of speech that provide critical information beyond the meaning of words or grammatical structure, such as emotional state, emphasis, contrast and focus.

Box 3 | **A candidate endophenotype for schizophrenia**

The endophenotype approach has become an important strategy in genetic studies of complex neuropsychiatric disorders, such as schizophrenia. Endophenotypes are quantitative, trait-like deficits that are typically assessed by laboratory-based methods rather than by clinical observation. It is thought that these markers can provide clues about the genetic basis of disease because they are likely to have a simpler genetic architecture than the disease syndrome itself[192,193]. The four primary criteria for an endophenotype are that it is present in probands with the disorder, that it is not state-related (that is, it does not occur only during clinical episodes) but instead is present early in the disease course and during periods of remission, that it is observed in unaffected family members at a higher rate than in the general population and that it is heritable.

Growing evidence indicates that social cognitive impairments, assessed by performance-based measures, are strong candidate endophenotypes for schizophrenia. Several social cognitive impairments are present in probands, with large deficits in social cue perception and mentalizing tasks being the most-extensively documented[25,26,79]. These impairments are longitudinally stable and persist both during periods of acute symptom exacerbation and during clinical remission of symptoms[79,194]. Furthermore, these impairments are present during chronic and recent-onset phases of schizophrenia, with research increasingly identifying social cognitive impairments in prodromal individuals who have not yet experienced the onset of frank psychotic symptoms[195].

Several studies have also documented more-subtle social cognitive impairments in unaffected relatives of individuals with schizophrenia, including moderate impairments in social cue perception[196,197] and mentalizing[198]. The level of impairment in relatives of these tasks falls between that seen in probands and that seen in healthy non-relatives. Notably, the presence of social cognitive impairment in unaffected relatives and unmedicated prodromal subjects suggest that the impairments seen in schizophrenia are not side effects of antipsychotic medications. Finally, a few studies indicate that social cognitive impairments are heritable in the general population[199,200]. Thus, investigations of social cognition in healthy individuals could provide important insights into neurobiological and genetic factors that contribute to vulnerability to schizophrenia.

Motor resonance. Motor resonance refers to a functional correspondence between the state in the motor system of an observer and that in the motor system of the person making the action[49]. The first evidence for motor resonance in primates was the demonstration that neurons in ventral premotor and intraparietal cortices of the macaque monkey fire both when producing and when observing goal-directed actions[50]. This discovery led to an emerging literature on the mirror neuron system, which has been identified in several species. Studies of the human mirror neuron system have primarily used fMRI to identify brain regions that are active as individuals observe others performing motor actions (such as simple finger or hand movements) or as they themselves execute the motor action[42]. These studies have found that the human mirror neuron system includes the anterior parietal sulcus, which specifies the context of the action and the objects that are being acted on, the premotor cortex, in which the input is compared with stored motor representations, and the IFG, which facilitates the comparison of the observed actions with actions previously performed by the observer[51] (FIG. 1).

Electroencephalography (EEG) recordings have also been used to study the mirror neuron system in humans. The mu rhythm is an EEG oscillation in the 8–13 Hz frequency band that is recorded primarily over sensorimotor cortex in resting states. Suppression of mu during observation and execution of actions has been found and is thought to be a physiological index of mirror neuron system activity[52]. In patients with schizophrenia, mu suppression during observation and execution of finger or hand movements is reported to be normal; three studies found no differences in mu suppression between individuals with schizophrenia and healthy subjects[53–55], although a fourth study found diminished mu suppression in patients compared with healthy controls[56]. However, studies using magnetoencephalography (MEG) and transcranial magnetic stimulation (TMS) to assess neural activity during motor resonance in schizophrenia provide a more complex picture. Two small MEG studies yielded results that were interpreted to reflect diminished mirror neuron system activity in individuals with schizophrenia compared with healthy controls[57] and with healthy co-twins[58]. Two TMS studies yielded mixed findings, showing evidence of either diminished or intact mirror neuron system activation[59,60].

Similarly, two fMRI studies of motor resonance in schizophrenia have provided conflicting results. The first study involved presenting videos of finger-movement sequences or still images of cues corresponding to finger positions to participants and instructing them to either imitate or execute the associated sequential finger movements or to simply observe them[61]. Patients with schizophrenia showed decreased activation in the right inferior parietal lobule (IPL) and posterior superior temporal sulcus (STS) during action observation, but increased activation in these regions during imitation of finger movements, a pattern collectively interpreted to indicate less-fine-tuned motor resonance. The second study involved asking patients to observe, imitate or execute simple finger movements[62]. Patients and controls showed similar activation in the expected brain regions across conditions, including inferior frontal, premotor and inferior parietal cortices, suggesting intact motor resonance in schizophrenia.

Overall, the findings from motor resonance studies of schizophrenia are mixed. However, it should be noted that this area of research is still relatively new and the scientific approaches used are highly diverse, which may account for some of the discrepancies in the findings.

Magnetoencephalography (MEG). A functional neuroimaging method that records magnetic fields produced by electrical currents in the brain to assess brain activity during rest or cognitive tasks; it generally has better temporal resolution than functional magnetic resonance imaging and better spatial resolution than electroencephalography.

Transcranial magnetic stimulation (TMS). A non-invasive procedure that uses magnetic fields to stimulate small regions of the brain and can be used to probe the functional activity of specific brain regions.

Affect sharing. Affect sharing, the functional correspondence between the observation of a person who is displaying an emotional expression and the activation of emotion-related brain regions of the observer, is also a component of experience sharing. In healthy subjects, neural activation in certain limbic regions, particularly the amygdala, insula and cingulate gyrus, occurs when an individual executes facial expressions of emotion and when an individual observes another person making such expressions[51]. Studies of affect sharing have also focused on the perception of others when they display physical pain. Studies in healthy people demonstrate that the anterior insula and dorsal ACC, which are involved in the affective and motivational processing of pain, are also activated by the observation of others' pain[63] (FIG. 1).

Although the findings regarding motor resonance in patients with schizophrenia are mixed, the findings for affect sharing in this group suggest that this subprocess is intact. In self-report studies, patients score similarly to healthy controls for personal traits associated with affect sharing[64,65], and some individuals with schizophrenia even indicate a tendency to be overly sensitive and reactive to the feelings of others compared with healthy controls[65]. In healthy individuals, EEG mu suppression is greater when viewing stimuli that depict individuals engaged in social interaction than when viewing stimuli that depict individuals not involved in social interaction. In agreement with self-report studies, one such study found that patients and controls showed a similar pattern of mu suppression in response to stimuli depicting various social interactions[55]. In another study, individuals with recent-onset schizophrenia showed normal mu suppression for stimuli depicting social interaction stimuli, although they displayed diminished mu suppression while viewing stimuli depicting human biological motion[54]. One study examined early ERP-processing components (that is, N110, P180 and N240) during an affect-sharing task in which subjects observed images of hands that are shown in painful versus non-painful situations[66]. Both patients and healthy controls showed similar levels of sensitivity to pain-relevant stimuli.

To date, only one study of affect sharing in individuals with schizophrenia has used fMRI. In this study, participants observed, imitated or executed facial expressions of emotion[62]. Although imitation and execution of emotional expressions were impaired in patients, both groups showed similar levels of activation in regions associated with affect sharing, including inferior prefrontal, premotor, and inferior and superior parietal cortices.

In summary, several studies using various methods report normal, or even enhanced, affect sharing in schizophrenia. Thus, affect sharing may reflect a relatively preserved aspect of social cognition in schizophrenia.

Mentalizing

To understand the behaviour of others in a social environment, it is often necessary to take other people's viewpoints into account and to make inferences about the mental states of others based on available social cues and social context. This ability to infer the mental states of other people (including their intentions, beliefs and emotions) is called mentalizing (also known as theory of mind or mental state attribution)[67,68].

Brain regions associated with mentalizing have been studied using a wide range of paradigms that vary by stimulus modality (verbal or visual) and the mental states being inferred. These tasks typically involve presenting the participants with simple written stories about people interacting, cartoon panels depicting people interacting, or pictures showing only the eye region of the face, and asking the participants to infer the beliefs, intentions or emotions of the people depicted in these stories, cartoons or pictures. Even simpler tasks can also be used to assess mentalizing; for example, people sometimes attribute intentions or emotions to interacting geometric shapes in short videos[69]. Several brain regions, including the mPFC, bilateral temporoparietal junction (TPJ) and precuneus, have been consistently found to be activated in various mentalizing tasks in healthy individuals[70,71] (FIG. 1). These brain regions are considered the core components of the mentalizing system, but the specific role that each region has in mentalizing processes is not clear[72–75]. In addition to these core mentalizing regions, several additional brain regions seem to be activated in a task-dependent manner; for example, the STS is activated while watching animated geometric shapes, and the IFG is active when participants infer emotions from pictures of eyes. The brain regions associated with mentalizing, such as the mPFC and precuneus, partly overlap with the default mode network[76,77] (BOX 2). This overlap has led to speculation that humans may be predisposed to engaging the mentalizing system when not working on non-social tasks[78].

Impaired mentalizing in schizophrenia is well documented. Meta-analyses indicate that patients with schizophrenia have difficulty understanding the intentions of others from a cartoon panel and inferring the beliefs of others from simple written stories[25,79,80]. Neuroimaging studies have also shown a complex pattern of aberrant neural activation in individuals with schizophrenia during mentalizing in various activation tasks. Several studies found that patients had decreased activity in some core regions of the mentalizing system. For instance, when inferring emotions from pictures of eyes, patients showed reduced activation of the left IFG compared with controls[81]. During a task that required participants to use the perspectives of others to correctly identify objects, patients showed reduced activation of the ventromedial PFC (vmPFC) and orbitofrontal cortex[82]. Patients also showed decreased activation of the mPFC and TPJ while making inferences about the beliefs of others[83,84]. Furthermore, controls showed less activation in the mentalizing system when inferring the intentions of a person in isolation compared with inferring the intentions of a person who is participating in a social interaction, and patients failed to show this modulation[85]. Patients also showed reduced activation of the bilateral TPJ and IFG while viewing interacting geometric shapes[86].

However, some studies have reported that individuals with schizophrenia exhibit hyperactivation or delayed activation of certain brain regions during mentalizing tasks. For instance, patients showed

Default mode network
A set of brain regions that are activated (as identified using functional magnetic resonance imaging) when individuals are in a resting state, not focusing on the outside world, and are deactivated when individuals direct attention to the outside world.

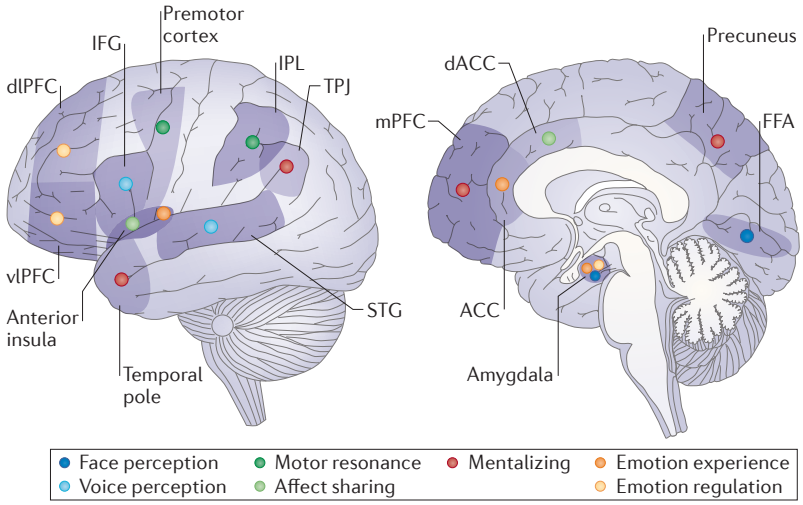

Figure 1 | **Brain regions associated with social processes.** Social cognition can be divided into several distinct processes, which involve many different brain regions, some of which show overlap between processes. Perceiving social cues incorporates face perception, which is associated with activation of the amygdala and fusiform face area (FFA), and voice perception, which activates the superior temporal gyrus (STG) and inferior frontal gyrus (IFG). Experience sharing includes the processes of motor resonance, which activates the inferior parietal lobule (IPL) and premotor cortex, and affect sharing, which activates the dorsal anterior cingulate cortex (dACC) and anterior insula. Mentalizing activates various regions, including the temporoparietal junction (TPJ), temporal pole, precuneus and medial prefrontal cortex (mPFC). Emotion experience activates the amygdala, anterior hippocampus (not shown), ACC and anterior insula, and emotion regulation activates brain regions including the dorsolateral PFC (dlPFC), ventrolateral PFC (vlPFC) and amygdala. These brain regions and associated social processes are not entirely separate; for example, the anterior insula is involved in both affect sharing and emotion experience, and the amygdala is involved in face perception, emotion experience and emotion regulation. Note that these regions are a representative, but not comprehensive, listing of relevant brain regions for each social cognitive process.

increased activity in the pSTG and mPFC when tasked with inferring emotions from pictures of eyes, compared with healthy controls[87]. Another study found that, compared with controls, people with schizophrenia exhibited increased activity in the STG, dorsomedial PFC (dmPFC) and precuneus when inferring the intentions of others[88]. In both of these studies, the individuals with schizophrenia showed intact performance, suggesting that they required greater levels of neural activity to achieve the same levels of performance on mentalizing tasks as controls. In addition, these findings of increased neural activity in mentalizing regions fit with the tendency of some individuals with schizophrenia to over-attribute intention to others. This tendency, called hypermentalizing, has been linked to paranoid symptoms of schizophrenia[89,90]. Finally, a study using animated geometric shapes found that patients showed decreased activation in the TPJ during the first half of the task, compared with controls, but increased activation in the same brain region during the second half of the task[91]. This finding may suggest that individuals with schizophrenia infer the mental states of others more slowly than healthy individuals, rather than that they have an overall impairment in mentalizing ability.

To summarize, individuals with schizophrenia show aberrant neural activation in brain regions associated with mentalizing when inferring the mental states of others. The patterns of aberrant activation on mentalizing tasks are not consistent across studies. Most studies report hypoactivation of the core mentalizing system and impaired mentalizing ability in behavioural tasks. However, a few studies found hyperactivation of brain regions associated with mentalizing, and patients in these studies showed normal metalizing capacity. Individuals with schizophrenia may need greater activation in these regions to achieve the same level of mentalizing proficiency, suggesting neural inefficiency. Inefficient mentalizing in schizophrenia could also result in delayed activation of this network.

Emotion experience and regulation

Social interactions are often saturated with emotion. The emotional reactions to others that an individual experiences, and the manner in which they deal with these reactions, determines the adaptive response to the complexities of social life. Two aspects of emotion processing, emotion experience and emotion regulation, have received the most attention in schizophrenia, and research into emotion experience has revealed that, surprisingly, this function is intact in people with schizophrenia.

Emotion experience. Emotion experience refers to the immediate emotional responses induced by pleasant or unpleasant stimuli. These responses are composed of the subjective experience of the individual (which can be self-reported), observable facial or gestural expressions and neurophysiological responses. An extensive set of brain regions has been associated with emotion experience, such as the limbic system (including the amygdala, anterior hippocampus, anterior insula and cingulate gyrus), brain stem nuclei, thalamus, ventral striatum, medial prefrontal cortex, posterior cingulate cortex, precuneus, lateral temporal cortex and temporal poles[92,93] (FIG. 1). The precise functions of these regions in emotion experience, and how they interact with each other, are active areas of research[94,95].

Historically, the negative symptoms of schizophrenia (such as anhedonia and affective flattening) were thought to reflect impairment in experiencing pleasure. However, dozens of studies now indicate that, despite showing diminished emotional expressions, individuals with schizophrenia report normal levels of pleasure in response to stimuli in the laboratory and during their daily lives[96,97]. These findings of intact self-reported pleasure are largely supported by fMRI and EEG studies. For example, individuals with schizophrenia consistently show normal striatal responses to monetary rewards, and a recent meta-analysis found no differences between individuals with schizophrenia and controls in activation in brain regions typically associated with emotion experience[29,97]. ERP studies have focused on the late positive potential (LPP), a midline centroparietal ERP component that begins approximately 300 ms after stimulus onset and is sustained for up to several-hundred milliseconds.

In healthy individuals, the LPP is increased while viewing pleasant and unpleasant images, compared with viewing neutral images, and is considered an index of motivated attention to emotionally arousing stimuli[98]. Individuals with schizophrenia show the typical pattern of enhanced LPP to pleasant versus neutral images[99–101]. Thus, the neural response to pleasant stimuli seems to be intact in schizophrenia.

Studies of negative emotion experience in schizophrenia provide a more nuanced picture. Individuals with schizophrenia report normal levels of negative emotion to unpleasant stimuli, but they also report elevated levels of negative emotion in response to neutral and pleasant stimuli, compared with healthy controls[96,97]. Similarly, in fMRI studies, patients show normal activation of the amygdala and other relevant regions during exposure to unpleasant stimuli[29,97]. Although some studies find amygdala hypoactivity during contrasts of unpleasant versus neutral stimuli, this pattern may reflect amygdala hyperactivity to neutral conditions in patients rather than hypoactivity to negative stimuli[102,103]. ERP studies using tasks involving the viewing of emotional pictures indicate that individuals with schizophrenia show the typical pattern of LPP enhancement in response to unpleasant versus neutral stimuli that is seen in healthy subjects[99–101,104].

Overall, these findings indicate that emotion experience in schizophrenia is largely intact during exposure to pleasant stimuli and that emotion experience is also normal (or in some contexts, heightened) in response to unpleasant stimuli. The capacity to effectively regulate negative emotions would therefore be critical for normal adaptive functioning in schizophrenia.

Emotion regulation. According to an influential model[105], control over emotion is conceptualized in terms of a dynamic interplay between two processes: emotion generation and emotion regulation. At any stage of emotion generation, an individual can apply strategies to regulate their emotions, which influences how emotion is experienced, when it is experienced and how it is expressed. In healthy individuals, the most extensively studied emotion regulation strategy is cognitive reappraisal, which involves changing one's interpretations or appraisals of stimuli before an emotional response is fully generated.

The neural systems involved in cognitive reappraisal in healthy subjects have been established in dozens of fMRI studies, most of which examined areas involved in decreasing negative emotion[106–108]. Prevailing models of cognitive reappraisal indicate that adaptive emotion regulation occurs through an interaction between regions involved in implementing cognitive control strategies and those involved in emotion generation[106]. The cognitive control regions include the dorsolateral PFC, which is thought to support the maintenance of appraisals in working memory, the ventrolateral PFC (vlPFC), which supports selection and inhibition of appraisals, and the dmPFC, which supports semantic and self-reflective processes for elaborating the meaning of affective stimuli (FIG. 1). These control regions modulate activity in key regions involved in generating emotions, particularly the amygdala, which is involved in detecting and triggering responses to arousing stimuli[109]. Depending on the task involved, studies have reported that other brain regions — including the ventral striatum, insula and vmPFC — may also be involved in regulating emotion[106].

Most studies using self-reporting have shown that individuals with schizophrenia use cognitive reappraisal less frequently than do healthy individuals, and that lower use of this process is associated with poor outcomes in community functioning and more severe clinical symptoms[110–114]. One psychophysiological study measured subtle emotional expressions through facial electromyography (EMG) and self-reported emotion experience while participants watched sad films. The participants were instructed either to just watch the films or to emotionally distance themselves while watching the films by pretending they were a film reviewer (an example of cognitive reappraisal)[115]. Although individuals with schizophrenia and controls reported comparable decreases in sadness during the cognitive-reappraisal task, patients had greater expression of negative emotions across sad and neutral control films.

Two electrophysiological studies of individuals with schizophrenia[110,116] have examined the effectiveness of a cognitive-reappraisal strategy at reducing the LPP neural response to unpleasant pictures. In these studies, neutral control images were always preceded by a neutral audio description of the image, whereas unpleasant images were preceded by descriptions of the image that were either negative or neutral. Thus, the preceding descriptions served to change the meaning and emotional intensity of the image. In terms of self-reported emotions, both patients and controls indicated that their negative reactions to unpleasant stimuli were reduced when those stimuli were preceded by a neutral description. Regarding ERPs, healthy subjects showed the typical pattern[117], in which LPP was suppressed when unpleasant images were preceded by neutral descriptions compared with when unpleasant images were preceded by negative descriptions. By contrast, individuals with schizophrenia did not show a decrease in LPP when images were preceded with negative descriptions compared with when images were preceded by neutral descriptions. Thus, reappraisal did not decrease neural responses to unpleasant stimuli in individuals with schizophrenia, suggesting they have impaired emotion regulation.

Two fMRI studies investigated neural activation during cognitive-reappraisal tasks in schizophrenia. The first study involved instructing participants to maintain, increase or decrease their emotional responses to unpleasant images via reappraisal[118]. Across all conditions, patients self-reported higher levels of negative emotion than controls, and they showed vlPFC hypoactivation while emotional responses were decreased and vlPFC hyperactivation while emotional responses were increased. Furthermore, neural activity in the amygdala was inversely coupled with PFC activation in controls, but not in those with schizophrenia. The second fMRI study yielded similar results using a task that involved

Cognitive reappraisal
A method of regulating emotion by construing an emotion-eliciting situation in a way that changes its meaning and emotional impact.

Electromyography
(EMG). A non-invasive procedure that measures the electrical activity produced by skeletal muscles and has been used to assess the activity of facial muscles related to social interaction.

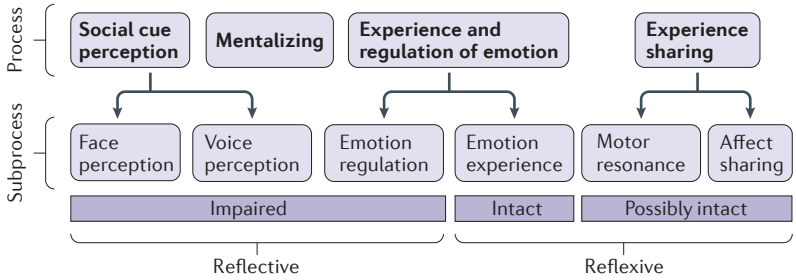

Figure 2 | **Social cognitive processes in schizophrenia.** The figure includes several broad domains of social processing that have been investigated in people with schizophrenia: perception of social cues (including perception of faces and of voices), experience sharing (including motor resonance and affect sharing), mentalizing, and emotion experience and regulation. These processes can be divided according to the degree to which they are likely to be impaired or relatively intact in schizophrenia. Four of these processes are consistently impaired: face perception, voice perception, mentalizing and emotion regulation. One, emotion experience, is consistently found to be intact in schizophrenia. The findings are inconsistent for two subprocesses, motor resonance and affect sharing, and these may be largely intact or only subtly impaired. The relatively intact processes are considered reflexive social process, whereas the impaired processes are considered reflective social processes.

two conditions that maintained or decreased (via reappraisal) emotional responses to unpleasant images in patients, unaffected siblings and healthy controls[119]. Patients and siblings both self-reported higher overall levels of negative emotion than healthy controls across both conditions, although all three groups self-reported significantly lower levels of negative emotion during the decrease condition compared to during the maintain condition. At the neural level, patients showed less activation than controls in the vlPFC (among other areas) when instructed to decrease their emotional responses, although no regulation-related changes in the amygdala were seen in any group. In addition, non-affected siblings showed vlPFC hypoactivation when asked to decrease their emotional responses[120].

To summarize, converging evidence suggests that the use of cognitive-reappraisal strategies is disrupted in schizophrenia, a conclusion that is consistent with the neural impairments in cognitive control processes in this disorder[121,122]. The interface between cognitive control and emotional processes is an active area of translational research in schizophrenia[123–125].

Pattern of social cognitive impairment

From the behavioural and neuroscientific studies discussed above, we conclude that there is strong evidence to suggest that people with schizophrenia have impairments in some, but not all, social processes. We find consistent evidence to suggest schizophrenia is associated with impairments in face and prosody perception, mentalizing and emotion regulation (FIG. 2). By contrast, the findings regarding emotion experience in schizophrenia suggest that this process is largely intact[96,126]. In addition, some evidence suggests that motor resonance and affect sharing are intact in schizophrenia. However, it is important to note that there are relatively few studies on experience sharing to date and that some of the findings of these studies are inconsistent; hence, it is difficult to make firm conclusions. Nonetheless, the available data suggest that any impairment in experience sharing may be subtle. Furthermore, when assessing these findings on social cognitive impairment in schizophrenia, most of the studies discussed in this Review included samples in which the vast majority of patients were receiving psychoactive medication, and the individuals involved were predominantly male. The potential implications of these factors need to be evaluated in future studies because there are known sex differences in social cognition in healthy people[127–129] and it is not known whether antipsychotic medications have any effects (either beneficial or detrimental) on these tasks.

The four social cognitive processes discussed in this Review can also be grouped into interpersonal processes (perception of social cues, experience sharing and mentalizing) and intrapersonal processes (emotion experience and regulation)[15]. Using this classification system, the social cognitive impairments in schizophrenia occur in both the interpersonal and the intrapersonal dimensions. Alternatively, social cognition can be divided into reflective and reflexive social processes[15]. The social processes that are clearly impaired in schizophrenia (perception of social cues, mentalizing and emotion regulation) are all considered reflective, meaning that they require effortful controlled processing. By contrast, experience sharing and emotion experience are considered reflexive processes, which require less mental effort than the other social processes[130].

A challenging question that remains is how, and where in the brain, the processing of social information goes awry in people with schizophrenia. The seven social processes discussed in this Review are associated with brain regions that are largely distinct but also show some degree of overlap (FIG. 1). Furthermore, the brain regions involved in social processing do not operate in isolation but rather are nodes in a network. Impairments in social processing may thus emerge either within a network, when components of the network need to interact with each other, or between networks, when higher-level integration is needed. For example, emotion regulation requires interaction between lower-level regions associated with emotion experience and higher-level cognitive control systems. Similarly, mentalizing requires the higher-level ability of taking another person's perspective into account, but it also depends on perception of social cues. An important example of integration among social processing systems is empathy.

Empathy impairment in schizophrenia

Empathy refers to sharing, understanding and responding to the unique emotional experiences of another person, and is viewed as an emergent phenomenon that depends on multiple components of social cognition[131–133]. Both experience sharing and mentalizing are included in most models of empathy[43,133,134], and some models also emphasize the role of emotion regulation as a way to modulate an empathic response when it becomes maladaptive[135]. Prosocial motivation (that is,

the motivation to affiliate with and care for other people) is also incorporated into some models of empathy as a basis for empathic responding and helping others[136].

In studies of empathy, there is an increasing focus on whether people are accurate when they want to be empathic[137]. Empathic accuracy refers to the degree to which one can track the momentary changes in mood of another person[137]. All of the social cognition systems discussed in this Review are relevant to empathic accuracy[138], and individuals with schizophrenia show problems in monitoring the emotions of others, suggesting that they do exhibit impairments in empathic accuracy[139–141]. These empathic accuracy deficits in schizophrenia are likely to begin with impaired perception of social information; that is, the impairment in schizophrenia seems to arise from a reduced ability to capitalize on the social cues being emitted by people that normally facilitate accurate interpretation of their moods[139]. Thus, the construct of empathy illustrates how integration among social processing systems is essential for adaptive social interactions, and how higher-level integrative processes can become disrupted in schizophrenia.

As increasingly sophisticated methods, such as graph theory[142,143], are used to examine brain connectivity, it will be possible to better determine whether there are deficits among nodes and between systems that produce complex social behaviours. Fittingly, one of the most-influential theories of the pathophysiology of schizophrenia is one of neural disconnection[144,145]. According to this theory, several features of schizophrenia, including problems in social functioning, arise from an underlying problem in neural connectivity emerging during adolescence or early adulthood. Studies of synaptic connections (for example, dendritic spine density)[146,147], white-matter changes[148,149] and EEG recordings of synchronized oscillations in schizophrenia[150,151] support this theory of disrupted connectivity. A close evaluation of structural and functional connectivity in social processing brain networks might identify specific points of vulnerability (within a node, within a social processing system or across systems) in schizophrenia. In that way, we might understand how specific disruptions in connectivity lead to the impaired social functioning observed in people with this disorder.

Conclusions and implications

Much of our discussion has categorically described social cognitive processes as either impaired or largely intact. However, each social process can also be measured as a continuous dimension that reflects the degree of impairment on relevant performance-based or neuroscientific tasks. Such a dimensional approach is consistent with current efforts by the US National Institute of Mental Health to understand psychiatric disorders through underlying brain-based dimensions[152,153]. Dimensional analysis of social brain systems may also help to explain variation in social processing and social integration in the general community, in individuals without clinically defined disorders. Furthermore, social disconnectedness (defined objectively as a low level of social contact) and perceived social isolation (usually defined as feeling lonely, independent of the actual level of social contact) are remarkably common in the general population and are associated with a markedly elevated risk for physical and mental health morbidity[154–157].

Our focus here has been on schizophrenia, but social cognitive impairments are also important in other disorders. Autism is associated with abnormalities in social cue identification and mentalizing, similar to schizophrenia, but these impairments start earlier in development and tend to be more clinically prominent[158,159]. The behavioural variant of frontotemporal dementia, which has an onset later in life, is also characterized by impairment in mentalizing[160]. Borderline personality disorder and bipolar disorder are partly defined by abnormalities in emotion regulation, and the roles of other social processing systems in these conditions are being explored[161,162]. Finally, psychopathy (a disorder characterized by antisocial behaviour, diminished empathy and remorse, and disinhibited behaviour) is associated with abnormalities in experience sharing, but mentalizing is thought to be intact[163,164]. Hence, various neuropsychiatric disorders demonstrate social cognitive impairments, and they differ in terms of the patterns of social deficits observed and their developmental courses.

Finally, these findings regarding social cognition in schizophrenia have treatment implications. The social processes that are aberrant in schizophrenia may each require their own specific therapeutic intervention. Training programmes that target facial emotion perception and mentalizing deficits have been validated in individuals with schizophrenia[165,166]. These programmes show positive effects that are large in magnitude on some of the targeted social processes, and there are also more limited data showing the effects generalize to social functioning[165]. Social cognitive training programmes for people with autism are also under development[167,168]. Emotion regulation is a central feature of borderline personality disorder and bipolar disorder, and there are existing intervention approaches specifically designed to enhance emotion regulation, such as dialectical behaviour therapy[169] as well as mindfulness training, which is now starting to be applied to schizophrenia[170]. Psychopharmacological interventions may also be beneficial. Oxytocin has been examined as a possible pharmacological tool to enhance social cognition in healthy individuals and in several clinical conditions[171,172]; however, despite considerable attention in schizophrenia, its effects on social cognition are not consistent across studies[172–174]. Given our growing understanding of the neural systems that are involved in social processes, it is entirely possible that future pharmacological treatments or neural-stimulation approaches (such as transcranial direct current stimulation) could be used in a targeted manner to affect a particular social processing system. Ultimately, it is hoped that a better understanding of social cognition and the related neural mechanisms in schizophrenia will enable us to decrease social disability in this complex condition.

Oxytocin
A neuropeptide that acts both as a hormone and a neurotransmitter and is known to play an important part in regulating mammalian social behaviours.

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Competing interests statement
The authors declare competing interests: see Web version for details.