

# Neural basis for social cognitive impairment in schizophrenia

*Bases neurais do comprometimento da cognição social na esquizofrenia*

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## SOCIAL COGNITION AND ITS NEURAL BASIS

Social cognition is defined as “the mental operations underlying social interactions, which include the human ability to perceive the intentions and dispositions of others”<sup>1</sup>. This ability would be required in situations in which plural individual humans as well as primates are present, therefore, having good or superior social cognitive abilities would be advantageous for an individual’s survival from an evolutionary perspective.

In recent years, insight into the neural basis of this ability has rapidly been growing with the use of functional and structural neuroimaging techniques and neuropsychological measures. Such evidence suggests that several different brain regions across the frontal, temporal, and parietal regions and limbic system, would play a role in social cognitive processing, with the construction of neural networks among each region. Among such widely ranged putative neural underpinnings of social cognition, the orbitofrontal cortex (OFC), amygdala (Amy), medial prefrontal cortex (MPFC), anterior cingulate cortex (ACC), insular cortex (IS), inferior parietal cortex, temporo-parietal junction (TPJ), superior temporal sulcus (STS) and fusiform gyrus (FG) have been consistently reported. For example, FG, STS, and Amy (which plays a critical role in recognizing emotions) would underlie emotional face processing. With respect to Theory of mind (ToM), the ability to infer the other’s mental status, the TPJ, MPFC, ACC, and STS are the representative regions that have been repeatedly demonstrated as the neural underpinnings. In Empathic ability, ACC, Amy, OFC and IS are considered to be critical for this processing.

Taken together, the neural basis of the various different facets of social cognition overlap to some extent, however, these different facets of social cognition are considered to be processed by different neural networks among plural brain regions, and such variety of the network would make these complex cognitive processing, including complex social judgments, possible.

## SOCIAL COGNITIVE IMPAIRMENT IN SCHIZOPHRENIA

A deficit in social functioning is one of the most disabling clinical features of schizophrenia (SCZ) and a significant factor in the resulting social isolation experienced by many patients. Several cognitive deficits, for example, memory, attention and working memory, would have an influence on the patient’s social functioning, however, one factor leading to social dysfunction is miscommunication with others, which is, at least partially, the result of impaired social cognition<sup>2</sup>. In daily clinical psychiatric practice, it is sometimes necessary to provide patients with rehabilitation therapy, such as social skills training, in addition to anti-psychotic medication therapy, which might imply the presence of social cognitive impairment in the disorder.

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Meanwhile, cumulative evidence of neuroimaging studies suggest that the neural basis of SCZ involves several brain regions, for example, MPFC, Amy, MPFC, ACC and temporal regions. These regions, as the neural basis of the disorder, remarkably overlap with those of social cognitive functions. This highlights the need to investigate social cognitive disabilities in SCZ and their associations with neuroimaging findings, which would lead to further understanding of the pathophysiology of schizophrenia. Below, neuroimaging studies are presented and discussed in terms of the neural underpinnings of different social cognitive domains.

## EMOTIONAL FACIAL RECOGNITION

Although speech is the most straightforward tool for communications with others, it is also critical for social interactions to recognize non-verbal messages including eye gaze, gestures and facial expressions. Emotional (especially basic emotions including fear, happy, anger, sad, disgust, surprise) facial recognition is one of the most widely researched social cognitive processes. The neural system implicated in facial emotion recognition has been proposed to include the Amy, the FG and the STS<sup>3</sup>. In particular, Amy is suggested to be closely involved in the recognition of negative facial emotions, and this theory has been supported by both lesion studies and imaging studies. Human lesion studies have consistently found impaired recognition of facial emotion following bilateral Amy damage. This impaired recognition is often disproportionately prominent for recognizing the emotion fear. Moreover, recent functional (PET, SPECT and fMRI) imaging studies also supports the consensus that Amy and its related network is the neural underpinning of the processing of emotion recognition. Such deficits are repeatedly reported in SCZ, however, it is still possible that social cognitive impairments might be related to other general cognitive deficits, for example, dysexecutive function or memory dysfunction (although it is not always restricted to emotional facial recognition). In other words, it is very important to adequately control for confounding factors in the experimental design, in order to investigate whether such deficits are specific to the domain of social cognition.

## ToM

To engage in successful social interaction, one must recognize that others have independent experiences and intentions, and perhaps even ulterior motives. The ability to represent another person's psychological perspective is referred to as ToM<sup>4</sup> or mentalizing<sup>5</sup>. ToM allows us to predict the behavior of others. Various ToM tasks have been studied, including story and cartoon comprehension in social situations.

Several brain regions have consistently been suggested as the neural basis of ToM, included the TPJ, STS, the temporal poles, and the MPFC (for convenience, including ACC)<sup>6</sup>. ToM deficits have been reported early in the course of pervasive developmental disorders (PDD), and such impairment has also been suggested in SCZ. However, it is still obscure whether the deficits are unique or whether they are related to the symptomatology of the disorder, like affective flattening or impairment in other cognitive domains. Thus, further investigation would be needed to clarify the issue with strictly controlled conditions.

## EMPATHY

The term "empathy" refers to the process of inferring and sharing the emotional experiences of others, in addition to representing what others are thinking (i.e. ToM). In this sense, empathy refers to affective facets of the ToM ability for example, imagining joy and sadness in others' minds, rather than ToM alone (i.e. only thinking about other's intentions without an emotional component). From this point of view, the neural bases of empathy and ToM would be hypothesized to be, at least partially, independent. Indeed, several functional imaging studies provide evidence that supports this hypothesis.

In an fMRI study that used a cartoon task (in which each story represented either ToM or empathy), brain activations during the ToM condition were relatively greater in the OFC, middle frontal and superior temporal regions than during the empathy condition. Conversely, greater activations in the anterior/posterior cingulate and Amy were observed during the empathy condition compared to the ToM condition<sup>7</sup>. As well, Hynes *et al.*<sup>8</sup> applied several written sentences, in which affective and cognitive components of perspective taking (PT) are represented, as a paradigm to investigate the differences between the neural bases of these two facets of PT. As a result, differential subregions in OFC were suggested to be specifically responsible for each cognitive and emotional PT. Thus, although the overlap of the activations is present in different facets of empathy, differential processes should still be considered.

In respect to empathic disability in SCZ, such deficits have been repeatedly suggested with self-rating questionnaires, for example the Interpersonal Reactivity Index<sup>9,10</sup>.

## NEUROIMAGING AND SOCIAL COGNITION IN SCHIZOPHRENIA

The number of imaging studies showing neural underpinnings of social cognitive impairments in SCZ is getting larger in recent years. Particularly, lines of evidence in functional ima-

ging studies suggest that social cognitive impairments are present in SCZ and their neural basis is widely spread across different brain regions, such as the Amy, IFG, IS and MPFC.

Several structural imaging studies have also provided knowledge of the relationship between social cognitive impairments and brain abnormalities in SCZ. Namiki *et al.*<sup>11</sup>, by using an MRI manual tracing method, suggested that a deficit of emotional facial recognition (particularly "fear" face recognition) was associated with volume reductions in Amy. Yamada *et al.*<sup>12</sup>, investigated the relationship between brain changes (assessed by voxel-based morphometry: VBM) and social cognitive disability of SCZ by using PAT (Perception of Affect Tasks)<sup>13</sup>, which are designed to assess the ability to infer others' emotions in situations which are closely related to actual daily life. As a result, the association of MPFC volume reduction with lower task performance was found in SCZ<sup>12</sup>. Additionally, using the same paradigm, Fujiwara *et al.*<sup>14</sup> also demonstrated that lower PAT scores were associated with ACC volume reductions, as well as abnormal sulcal variation in SCZ. This indicates that ToM deficits could be both state- and trait- related because brain sulcal variation is generally stable after birth, while ACC volume change often occurs before as well as after the onset of SCZ.

In summary, the neural basis of social cognitive impairment in SCZ is gradually gaining some clarification as mentioned above, however, it is still unknown whether such deficits are related to other characteristics of SCZ pathology including basic cognitive dysfunction and symptomatology of the disorder. Furthermore, it is also still unclear whether social cognitive dysfunction is state-related or trait-related or both. In this sense, a small number of fMRI studies attempted to address these issues with longitudinal designs. Similarly, studies involving individuals at high-risk for psychosis have demonstrated differences in brain activity before and after the psychotic episode<sup>15</sup>, as well as differences between high-risk individuals who later developed psychosis and those who did not<sup>16</sup>. Further studies in these areas are needed to clarify above-mentioned questions in the future.

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