## REVIEW

# Social Cognition, Negative Symptoms and Psychosocial Functioning in Schizophrenia

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## Abstract

Although functional recovery could be advocated as an achievable treatment goal, many effective interventions for the treatment of psychotic symptoms, such as antipsychotic drugs, may not improve functioning. The last two decades of cognitive and clinical research on schizophrenia were a turning point for the firm acknowledgment of how relevant social cognitive deficits and negative symptoms could be in predicting psychosocial functioning. The relevance of social cognition dysfunction in schizophrenia patients' daily living is now unabated. In fact, social cognition deficits could be the most significant predictor of functionality in patients with schizophrenia, non-redundantly with neurocognition. Emerging evidence suggests that negative symptoms appear to play an indirect role, mediating the relationship between neurocognition and social cognition with functional outcomes. Further explorations of this mediating role of negative symptoms have revealed that motivational deficits appear to be particularly important in explaining the relationship between both neurocognitive and social cognitive dysfunction and functional outcomes in schizophrenia. In this paper we will address the relative contribution of two key constructs—social cognitive deficits and negative symptoms, namely how intertwined they could be in daily life functioning of patients with schizophrenia.

**Keywords:** Schizophrenia, Social Cognition, Negative Symptoms, Functioning.

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## Introduction

In Eugene Bleuler's seminal works on schizophrenia, nearly a century ago, it was clear that he had a perceptive understanding of cognitive impairment as a core part of this psychotic disorder; that was consubstantiated in the definition of his fundamental symptoms—substantially cognitive in their essence, yet distinguished from what was observed in organic dementias [1,2]. Nonetheless, modern diagnostic criteria on schizophrenia have relied heavily on positive symptoms, based on the prescient contributions of other authors such as Emil Kraeplin and Kurt Schneider. Despite the appearance, in the 1950s, of the first antipsychotics, followed by subsequent and more effective pharmacological therapies, a considerable number of patients with schizophrenia still face substantial difficulties in fulfilling normative social and occupational roles. The last two decades of cognitive and clinical research on schizophrenia were a turning point for the firm acknowledgment of how relevant social cognitive deficits and negative symptoms could be in predicting psychosocial functioning.

Given that the 5th Edition of the Diagnostic and Statistical Manual of Mental Disorders—DSM-5—requires deterioration of psychosocial functioning (including social activities, personal and social relationships, and self-care) to make a diagnosis of schizophrenia, it came as no surprise that functional outcomes have somehow surpassed clinical remission goals in measuring success of interventions and mental health care in patients with psychosis [3]. Nonetheless, although functional recovery could be advocated as an achievable treatment goal, many effective interventions for the treatment of psychotic symptoms, such as antipsychotic drugs, may not improve functioning [4]. In this paper we will address the relative contribution of two key constructs—social cognitive deficits and negative symptoms, namely how intertwined they could be in daily life functioning of patients with schizophrenia.

## Social cognition

Social cognition refers to the psychological processes involved in the perception, encoding, storage, retrieval, and regulation of information about others and ourselves: social cue perception, experience sharing, inferring other people's thoughts and emotions, and managing emotional reactions to others [5]. Social cognition became one of the major areas of research interest in schizophrenia because it has been identified as one of the most important predictors of functional outcome [6,7]. Individuals with schizophrenia often present marked impairments in processing social information, which results in misinterpretations of the social intent of others, social withdrawal, and impaired daily social functioning [8,9]. Over the past few years we have seen an increased research interest concerning the relationships between social cognition and functioning due to three major reasons. First, research has indicated that these deficits are separable from those of neurocognition [10]. On the other hand, these deficits have strong and independent relationships to functional outcomes [8]. Lastly, emerging research suggests that these deficits may be more proximal to some dimensions of functional outcomes than deficits in neurocognition. In this regard, Schmidt et al. demonstrated that social cognition served in many cases as a robust mediator of the relationship between neurocognition and functional outcome [11]. Thus, social cognition has been identified as a crucially important area of research in schizophrenia; as a means of exploring both the interpersonal difficulties experienced by individuals with this illness, as well as the consequences of these difficulties, such as poorer vocational outcomes, a lack of community participation and independence, and limitations in the formation and maintenance of close emotional relationships [6]. Deficits in social cognition are well evidenced in schizophrenia, both in the established illness [12] and prior to illness onset [9,13], suggesting that they are relatively stable [14]. Thus, an understanding of social cognitive impairments in schizophrenia may provide opportunities for targeted recovery-focused interventions [15]. Studies of social cognition in schizophrenia may also provide more general insight into the mechanisms underlying the disorder, as these impairments have trait-like qualities that precede the onset of illness and are candidate endophenotypes [16,17].

## Dimensions of social cognition: impairments in schizophrenia

From a conceptual point of view, taking into account organizational models of neural systems in social neurosciences, we can identify four general social cognitive processes: perception of social cues, experience sharing, mentalizing, and experiencing and emotion regulation [5].

### Perception of social cues

In interpersonal contexts, individuals encounter a diverse array of social cues from other's faces, voices, and body movements (gait, posture, gestures). In schizophrenia, studies of social cue perception have focused on the perception of faces and voices.

Studies of non-affective face processing have shown that patients with schizophrenia and healthy controls show comparable performance in age and sex discriminations tasks, but patients have difficulty in matching and discriminating the identity of individuals [18]. Studies concerning affective face processing are more consistent and have shown that patients demonstrate lower activation in brain regions associated with affective face perception but they show increased activation in areas not associated with face perception [19]. Patients may, therefore, recruit alternative areas to compensate for dysfunction in the key face emotion processing regions.

Vocal perception of social relevant cues refers to the acoustic properties of speech (pitch, intonation and rhythm;

also called prosody), including emphasis and emotional tone, that provides critical information beyond the meaning of words. Most studies of voice perception in individuals with schizophrenia have investigated affective prosody. Affective prosody perception has been examined using tasks of implicit and explicit processing: listening to sentences read with and without emotional intonation or making emotional judgments about a sentence read with and without emotional intonation. Findings of non-affective prosody in schizophrenia are mixed: patients did not differ from controls when discriminating intonation of sentences [20], but showed deficits in discriminating pitch and rhythm of voice stimuli [21]. Regarding affective prosody perception, studies have shown consistent behavioral impairment and lower activation in key regions, for example, the superior temporal gyrus and the inferior frontal gyrus [22].

### Experience sharing

Observation of another person's behavior triggers neural activity in the brain regions that become activated when engaging in that behavior oneself. It is thought that vicarious neural activation during experience sharing directly facilitates understanding of the mental states of others [23]. Experience sharing could be separated into two processes with different functions and partly distinct neural substrates: motor resonance and affect sharing [24].

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 [25]. Studies of motor resonance using fMRI in schizophrenia have provided mixed results [26]. However, it should be noted that this area of research is still new and the scientific approaches used are diverse, which may account for some of the discrepancies in available evidence [6].

Affect sharing refers to 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. The available evidence suggests that this subprocess is intact. In self-report studies, patients score similarly to healthy controls for personal traits associated with affect sharing and some of them suggest a tendency to be overly sensitive and reactive to the feelings of others compared with healthy controls [27]. To date, only one study has used fMRI to study affect sharing in these patients: 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 [28].

### Mentalizing

To understand the behavior 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 [29].

Brain regions associated with mentalizing have been studied using a wide range of paradigms: 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 [30]. 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 [31,32]. These patients show aberrant neural activation in brain regions associated with mentalizing when they are asked to infer the mental states of others. However, the reported changes are not consistent across studies. Most studies describe lower activation of the core mentalizing system and impaired mentalizing ability in behavioral tasks [33-35]. A few studies found increased activation of brain regions associated with mentalizing [36,37] leading to the hypothesis that individuals with schizophrenia may need greater activation in these regions to achieve the same level of mentalizing proficiency, suggesting neural inefficiency. It was proposed that positive symptoms are linked to hypermentalizing and negative symptoms to hypomentalizing; positive symptoms should result in a pattern of additional emotion and intention attributions to other people, while negative symptoms should result in a lack of emotion and intention attributions [38].

The findings of increased neural activity in mentalizing regions and results of behavioural studies fit with the tendency of some individuals with schizophrenia to over-attribute intention to others and to perceive (negative) emotions in stimuli that are emotionally neutral. This tendency, called hypermentalizing, has been linked to paranoid symptoms of schizophrenia [39].

### Emotion experience and regulation

The emotional reactions to others and how an individual deals with these reactions determines the adaptive response to the complexities of social environment. Two aspects of emotion processing, emotion experience and emotion regulation, have received the most attention in schizophrenia [5].

Emotion experience refers to the immediate emotional responses induced by pleasant or unpleasant stimuli. It has been demonstrated that in schizophrenia emotion experience 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 [40,41].

Control over emotion is thought in terms of a dynamic interplay between two processes: emotion generation and emotion regulation [42]. Most studies using self-report measures 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 [43]. Evidence suggests that the use of cognitive-reappraisal strategies is disrupted in schizophrenia [44,45], which is consistent with the neural impairments in cognitive control processes in this disorder [46].

We can summarize these findings by stating that there is strong evidence to suggest that people with schizophrenia have impairments in some, but not all, social cognitive processes. There is consistent evidence suggesting schizophrenia is associated with impairments in facial and prosody perception, mentalizing, and emotion regulation. Conversely, the findings regarding emotion experience in schizophrenia suggest that this process is largely intact [40]. Furthermore, some evidence shows that motor resonance and affect sharing are intact in schizophrenia. However, it is important to note that a few studies on experience sharing and some of the findings are contradictory. To date, the available data suggest that any impairment in experience sharing may be subtle. Lastly, it is important to underline some of the limitations of the findings on social cognitive impairment in schizophrenia: most of the studies included samples in which the majority of patients were medicated and the individuals involved were predominantly male [5].

### Measuring social cognition in schizophrenia

From an empirical point of view, an National Institute of Mental Health's (NIMH) consensus statement, generated from a convention of leading social cognitive researchers, recognized theory of mind, emotion perception/processing, attributional style, social perception, and social knowledge as representing the major domains of social cognition [17]. Penn and colleagues [12] similarly identified theory of mind, emotion perception, and attributional style as being particularly salient for individuals with schizophrenia, who consistently demonstrate impaired social cognitive abilities in each of these areas [31,47,48]. The Social Cognition Psychometric Evaluation (SCOPE) study [7], designed to achieve a consensus on the key domains of social cognition schizophrenia, identified four major domains: 1) theory of mind (ToM) or the ability to attribute beliefs and intentions; 2) emotion processing (prosodic and facial) or the ability to recognize other people's feelings from either facial expressions or vocal inflections and use them to guide behaviors; 3) social perception and knowledge or the ability to judge and be aware of cues and rules that occur is social situations; and 4) attributional style or bias, which refers to an individual's tendency to attribute the cause of an event to either oneself, others or the environment.

ToM is defined as the ability to represent the mental states of others including the inference of intentions, dispositions, and/or beliefs [49,50]. This ability is also referred to as mentalizing, mental state attribution, or cognitive empathy [51]. Research in this field has used tasks like: Adult Faux Pas [52], Brune Picture Sequencing Task [53], Happe's Stories [54], Reading the Mind in the Eyes

Test [29], Silent Animations [55], The Awareness of Social Inference Test (TASIT) [56], The Hinting Task [57], Visual Perspective Tasking Task [58]. The final measures integrating the SCOPE study were Reading the Mind in the Eyes Test, The Awareness of Social Inferences Test—part III and The Hinting Task [7].

Emotion processing is broadly defined as perceiving and using emotions [17]. It subsumes three domains that represent both lower level and higher level processes. At a lower perceptual level is the first subdomain emotion perception/recognition (identifying and recognizing emotional displays from facial expressions and/or nonface cues such as voice). At a higher level we have the two subdomains of understanding emotions and managing emotions. Some of the instruments studied in this field are: Bell Lysaker Emotion Recognition Task (BLERT) [59], Diagnostic Analysis of Nonverbal Accuracy 2 (DANVA2) [60], Face Emotion Discrimination Test (FEDT) [61], Penn Emotion Recognition Task (ER-40) [62]. The Bell Lysaker Emotion Recognition Task and the Penn Emotion Recognition Test were the chosen measures in SCOPE study [7].

Social perception refers to decoding and interpreting social cues in others [63,65]. It includes social context processing and social knowledge, which can be defined as knowing social rules, roles, and goals (RRGs), utilizing those RRGs, and understanding how such RRGs may influence others' behaviors [66,67]. Assessing this domain of social cognition has used diverse measures such as: Half Profile of Nonverbal Sensitivity (Half PONS) [68], Interpersonal Perception Task (IPT-15) [69], and Relationships Across Domains (RAD) [70], which was the test chosen to integrate the final SCOPE battery [7].

Attributional style or bias describes the way in which individuals explain the causes, or make sense, of social events or interactions [17,49]. The Ambiguous Intentions and Hostility Questionnaire (AIHQ) [71] and the Internal, Personal, and Situational Attributions Questionnaire (IPSAQ) [72] are the most used tasks assessing attributional style. The Ambiguous Intentions and Hostility Questionnaire is the final task considered in the SCOPE study [7].

As part of the Social Cognition Psychometric Evaluation (SCOPE) study, the psychometric properties of 8 tasks were assessed in a sample of one hundred and seventy-nine stable outpatients with schizophrenia and 104 healthy controls, who completed the battery at baseline and a retest 2–4-weeks later, at 2 sites. Tasks included the AIHQ, BLERT, ER-40, RAD, Reading the Mind in the Eyes Test, TASIT, Hinting Task, and Trustworthiness Task. Tasks were evaluated on: (i) test-retest reliability, (ii) utility as a repeated measure, (iii) relationship to functional outcome, (iv) practicality and tolerability, (v) sensitivity to group differences, and (vi) internal consistency. The BLERT and Hinting task showed the strongest psychometric properties across all evaluation criteria and are recommended for use in clinical trials. The ER-40, Eyes Task, and TASIT showed somewhat weaker psychometric properties and require

further study. The AIHQ, RAD, and Trustworthiness Task showed poorer psychometric properties [48].

## Empathy impairment in schizophrenia—an integrated model of social cognition

Impairments in social processing may emerge within a network, when components of the network need to interact with each other, or between networks, when higher-level integration is needed [5]. Empathy refers to sharing, understanding and responding to the emotional experiences of another person, depending on multiple components of social cognition and is viewed as an example of integration among social processing systems [51,73]. Both experience sharing and mentalizing are included in most models of empathy [24,51], and some models also emphasize the role of emotion regulation as a way to modulate an empathic response when it becomes maladaptive [74]. It was shown that patients with schizophrenia have impairments in monitoring the emotions of others, suggesting that they do exhibit problems in complex social-cognitive abilities such as empathy [75,76]. Studies on empathy reveal that patients with schizophrenia are impaired in this cognitive domain, but unaffected with regard to the affective domain [76], a pattern comparable to recent findings in autism [77]. These empathic accuracy deficits in schizophrenia are likely to begin with impaired perception of social information and illustrate how integration among social cognitive processing systems is essential for adaptive social interactions [5].

## Negative symptoms: evolution of the concept

Negative symptoms have been regarded as a core feature of Schizophrenia since the seminal descriptions of Emil Kraepelin and Eugen Bleuler, whose observations underlined the key role of volitional and affective disturbances in the course of the disorder [78]. However, the term "Negative Symptoms" was only introduced in psychiatry when John Hughlings Jackson conceptualized these symptoms as the core lesion of the disease, reflecting a loss of normal function and "dissolution of neural arrangements". In turn, Jackson attributed the emergence of positive symptoms to a loss of top-down inhibitory activity [79,80].

The discovery of antipsychotic drugs and their efficacy on positive symptoms posed excessive attention on this latter symptom domain. Nonetheless, the importance of negative symptoms continued to be recognized. Thus, in the

1980s, Andreasen [81] introduced a new conceptualization, emphasizing affective flattening and alogia, among other symptoms like avolition, apathy, anhedonia and asociality, also included in the construct [78]. Moreover, Crow's proposal of "Type I and Type II Schizophrenia" [82] was based on the preponderance of negative symptoms over positive symptoms. Importantly, Carpenter et al. [83] distinguished between primary negative symptoms, inherent to the disease process itself and secondary negative

symptoms that could be a medication side-effect, a reaction to the illness or its associated deprivations, or responses to other symptoms, such as withdrawal secondary to paranoia [79]. It has been suggested that a "deficit syndrome" associated with a particularly poor outcome and predominately entailing primary and persistent negative symptoms can be found in 15% of first-episode patients and in approximately a third of cases of chronic schizophrenia [84,85].

The impact of negative symptoms on outcomes in Schizophrenia, and the lack of effective treatments, has driven the NIMH to develop a consensus definition of negative symptoms in Schizophrenia which has included symptoms of affective flattening, alogia, avolition, asociality, and anhedonia [86]. Although a considerable overlap exists between the NIMH consensus definition and Andreasen's historical definition [81], factor analysis studies have shown that symptoms of inattention, poverty of content in speech and inappropriate affect are more in line with the disorganization than with the negative symptoms domain [87,88].

Moving beyond the definition itself, studies investigating the factor structure of the construct [87-90] have revealed that negative symptoms usually cohere into two distinct, yet related, subdomains: diminished expression, consisting of affective flattening and poverty of speech; and amotivation, consisting of avolition, apathy, asociality, and hedonic deficits. In addition, recent research has been focusing in further refining the negative symptom construct, with the majority of studies exploring the anhedonia and amotivation symptom domain. In short, the available evidence demonstrates that people with schizophrenia report levels of in-the-moment positive emotion and subjective arousal similar to healthy controls when exposed to pleasant stimuli but present an anticipatory pleasure deficit, or alternatively "reduced pleasure-seeking behavior" and "beliefs of low pleasure" [79,91]. In what concerns to motivation, research has identified underlying deficits in reward learning, reward prediction, update of internal value representations, and impairments using this information to guide motivated behavior [91-93].

## Negative symptoms and psychosocial functioning

Negative symptoms are well established predictors of poor functional outcome in schizophrenia [84,94,95], this being true whether we consider impairments in socially useful activities, personal and social relationships, activities related to one's self-care [4] or decreased quality of life [96].

Negative symptoms are common and long lasting: their prevalence in short-term follow-up studies (up to 2.5 years) is about 45%, and in longer term studies (7.5–10 years) 20–30% [97]. The deleterious impact of negative symptoms on functional performance has been shown to be present throughout the lifespan of schizophrenia and not only in medicated, chronic, remitting-relapsing subjects [85]. Accordingly, in the early stages of the disease, at the first-ep-

isode [89] and during the proceeding years [98,99], the presence of this symptom cluster is one of the greatest barriers to the achievement of functional recovery. Moreover, before full blown psychosis occurs, during the so-called high-risk (HR) or prodromal state, negative symptoms and impaired social cognition have been associated with marked impairment in psychosocial function [100,101] which appears to be a core feature of the HR state and tends to be resistant to all types of treatment [102]. The presence of negative symptoms of "avolition" and "poor emotional expression" in the prodrome is in agreement with the notion of their primary nature and suggests that negative symptoms and their neural substrates may even be a driver (like impaired social cognition) of transition to psychosis [85]. In fact, there is evidence that negative symptoms rather than positive symptoms can significantly impact the transition from a HR state to frank psychosis and its long-term outcomes [103,104].

Research has yielded insights on the impact of each of the two independent subdomains ("amotivation" and "poor emotional expression") of negative symptoms on functional outcomes in schizophrenia [94]. Accordingly, the amotivation subdomain of negative symptoms has demonstrated significant relationship to functional outcomes in schizophrenia, including instrumental role performance, household adjustment, extended family functioning, and social/leisure functioning [105]. In line with this, several studies examined the prevalence of motivational deficits in patients throughout the different stages of the illness, and the impact these deficits have on psychosocial functioning, both cross-sectionally and longitudinally. Current research into the determinants of social functioning impairments in HR individuals suggests that motivational impairment is more important in determining level of social functioning relative to expression symptoms of affective flattening and alogia [101]. Correspondingly, it may be hypothesized that treatments alleviating negative symptoms in HR young subjects would both alleviate suffering and reduce the risk of transition to schizophrenia [85,102].

Motivational deficits are common in first episode psychosis (FEP) and have been shown to persist significantly in long-term. In the TIPS (Early Treatment and Intervention in Psychosis) FEP cohort, 30% of patients showed clinical levels of apathy when assessed ten years after the first psychotic episode and its presence was related to impaired functioning and poorer subjective quality of life [106].

The prevalence of motivational deficits in patients early in the illness (within 5 years of initiating antipsychotic treatment) and the impact these deficits have on community functioning have been also examined. Fervaha et al. [98] found that motivational impairments were present in more than 75% of patients. These deficits served as the most robust and reliable predictor of functional outcome in early-course patients even after selected demographic and clinical characteristics (e.g., positive symptoms) were accounted for. Finally, in studies designed to identify predic-

tors of real-life functioning in people with chronic schizophrenia, avolition had both a direct [94,107] and an indirect relationship real-life functioning [94,105]. In those studies, avolition was an independent domain with respect to both neurocognition and social cognition suggesting that the search for treatments with an impact on this domain should be a priority of mental health research strategies.

Within the motivational domain of negative symptoms, the relationship between anhedonia and functional outcomes has also received considerable attention with conflicting results: anhedonia has correlated with functional outcomes in some studies but not in other [79].

Findings regarding a relationship between the diminished expression subdomain of negative symptoms and functional outcomes in schizophrenia have been mixed, with a relationship found in one study [108] but not in others, particularly after accounting for the predictive role of amotivation [105,109].

It was recently been suggested that different negative symptoms correlate with different functional outcomes: expression-related symptoms predicted social competence while symptoms reflecting social amotivation were directly correlated with everyday social outcomes [107]. In addition, motivational deficits also appear to play an indirect role, partially mediating the relationship between neurocognition and social cognition with functional outcomes [79].

Overall, the available evidence indicates that motivational deficits are a key predictor of functional impairment beyond the impact of other negative symptoms not only in individuals with chronic schizophrenia but also at the early stages of the disease. This underscores the need to better understand the underlying mechanisms of motivational deficits [92,93] in order to provide the opportunity to personalize treatment and therefore establish effective interventions that will curb longer-term poor functioning [98]. In agreement, such interventions may benefit from focusing on strategies to enhance engagement in one's life, increasing goal-directed behavior, supporting greater effort expenditure, and harnessing intact consummatory pleasure to improve quality of life [101].

## The interplay of negative symptoms with deficits in social cognition

The interplay between negative symptoms and social cognition in terms of phenotype, underlying neurobiological substrates and potential treatment strategies is a complex and unresolved matter since, while distinct, these two constructs interact. As described in the previous sections, both negative symptoms and impaired social cognition exert a deleterious impact on functional outcomes. The emerging evidence suggests that social cognition drives negative symptoms which, in turn, may play an indirect role, mediating the relationship between social cognition with functional outcomes [9,110,111]. Further explorations of this mediating role of negative symptoms have revealed that

motivational deficits appear to be particularly important in explaining the relationship between both neurocognitive and social cognitive dysfunction with functional outcomes in schizophrenia [9, 79, 98]. This cross-talk between social cognition impairment and negative symptoms is unsurprising since they share several underlying neurobiological substrates, namely the temporal cortex (including the superior temporal gyrus) and the prefrontal cortex (PFC) [112]. Another example of this interrelationship is that social withdrawal is both a feature of negative symptoms and a consequence of faulty social cognition. On the other hand, a lack of motivation to engage in social contact reinforces deficits in social cognition [85]. The key issue is that deficits in social cognition not only worsen positive symptoms, but also contribute to and drive negative symptoms. Therefore, improving social outcomes seems to require a multi-faceted approach which considers social cognition and negative symptoms.

## Concluding remarks

Despite earlier formulations that established poor prognosis as a key criterion in the definition of schizophrenia, long-term follow-up studies have demonstrated a diversity of patterns in terms of course and prognosis, including good outcome, as in Manfred Bleuler's (Eugene's son) enduring follow-up of more than 200 patients with schizophrenia at the Burghölzli Hospital [113,114]. Nonetheless, individuals with schizophrenia frequently have significant difficulties in life functioning; as many as two-thirds of schizophrenia patients are unable to accomplish psychosocial roles, even when psychotic symptoms are in remission [115,116].

The relevance of social cognition dysfunction in schizophrenia patients' daily living is now unabated. Extensive research on this subject has brought some light to aspects such as its neural basis, but most of all focusing on this domain as a potential therapeutic target [117]. In fact, social cognition deficits could be the most significant predictor of functionality in patients with schizophrenia, non-redundantly with neurocognition [6].

The emerging evidence suggests that negative symptoms appear to play an indirect role, mediating the relationship between neurocognition and social cognition with functional outcomes [79,98] Further explorations of this mediating role of negative symptoms have revealed that motivational deficits appear to be particularly important in explaining the relationship between both neurocognitive and social cognitive dysfunction and functional outcomes in schizophrenia [9].

A recent investigation (the North American Prodrome Longitudinal Study) on clinically high-risk (CHR) patients for psychosis reported that negative symptoms mediated the relationship between composite neurocognition and social and role functioning; such findings replicate what a previous meta-analysis of schizophrenia studies had reported [118,119]. Nonetheless, the modest overlap among neurocognition, negative symptoms, and social functioning suggests that these domains make substantially separate contributions to the outcome in CHR patients [118].

### Abbreviations

AIHQ: Ambiguous Intentions and Hostility Questionnaire; BLERT: Bell Lysaker Emotion Recognition Task; CHR: Clinically high-risk; DAN-VA2: Diagnostic Analysis of Nonverbal Accuracy 2; ER-40: Penn Emotion Recognition Task; FEDT: Face Emotion Discrimination Test; FEP: Episode psychosis; Half PONS: Half Profile of Nonverbal Sensitivity; HR: High-risk; IPSAQ: Internal, Personal, and Situational Attributions Questionnaire; IPT-15: Interpersonal Perception Task; PFC: Prefrontal cortex; RAD: Relationships Across Domains; RRG: Rules, roles, and goals; SCOPE: Social Cognition Psychometric Evaluation; TASIT: The Awareness of Social Inference Test; TIPS: Early Treatment and Intervention in Psychosis; ToM: Theory of mind

### Competing interests

The authors declare no conflict of interest.

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