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Exploring functioning in schizophrenia: Predictors of functional capacity and real-world behaviour

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ABSTRACT

Impairment in daily functioning still represents a major treatment issue in schizophrenia and a more in-depth knowledge of underlying constructs is crucial for interventions to translate into better outcomes. This study aims to model factors influencing both functional capacity and real-life behaviour in a sample of outpatients with chronic schizophrenia, through a comprehensive assessment including evaluations of psychopathology, cognitive and social cognitive abilities, premorbid adjustment, family environment and early childhood experiences. No significant correlation was observed between functional capacity and real-life behaviour. Functional capacity was significantly predicted by IQ, while real-life behaviour was significantly predicted by empathy, affect recognition and symptoms. Functional capacity seems mainly related to neurocognition, whereas real-life behaviour appears more complex, requiring the integration of different factors including symptoms, with a major role of empathy. Results thus support a divergence between the two constructs of functioning and their underlying components and highlight the need to target both dimensions through individualized sequential rehabilitation programs in order to optimize functional outcome.

1. Introduction

Schizophrenia is a severe chronic mental disorder, listed into the top ten medical disorders causing disability by the World Health Organization (WHO, 2004). The major burden depends on the chronic disability associated to the illness, even when a good antipsychotic response is achieved. Restoring the patient ability to function independently in the community thus represents the ultimate treatment goal (Fett et al., 2011; Green, 2016).

In line with the consensus that functional recovery is a treatment priority, there has been a growing interest toward factors underlying functioning, as a more in-depth knowledge is crucial for treatments to achieve better outcomes, not only in schizophrenia but also across the psychosis spectrum (Bowie et al., 2008; Cotter et al., 2014; Lin et al., 2013).

According to the literature, two different constructs of functioning can be distinguished: functional capacity (i.e. the ability to perform a skill under optimal conditions) and real-world behaviour (i.e. what the patient actually does in real life, also called real-world functioning) (Best et al., 2014; Brune et al., 2011; Harvey et al., 2007). Functional capacity can be assessed using performance-based measures in which the participant demonstrates the ability to perform every-day real-world tasks in a neutral environment, for instance a laboratory or an hospital setting. Real-world behaviour can instead be evaluated through ratings of actual performance of activities in the real-world, verified by a third party (Gupta et al., 2012). Although functional capacity has been showed to predict world functioning (Bowie et al., 2006), many other factors influence behaviour in everyday life and thus account for the discrepancy between functional capacity and the actual performance (Gupta et al., 2012; Harvey and Strassnig, 2012). For instance, impairments in functional capacity have been reported to be largely independent of positive symptoms and only slightly correlated to negative symptoms. Nevertheless, psychopathological assessments are often found to be associated with poorer everyday real world activities even after other factors are considered (Bowie et al., 2006, 2008, 2010; Leifker et al., 2009; Sabbag et al., 2011). Indeed, several domains, spanning from symptoms to cognitive and social cognitive abilities, have been investigated with respect to their relation with global functioning. Clinical variables associated to poorer levels of every-day life adjustments include positive and negative symptoms

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(Smith et al., 2002), depressed mood (Bowie et al., 2006, 2010) and course of illness (Stefanopoulou et al., 2010), however their predictive value is relatively low. Cognitive abilities, encompassing linking and appraising information, verbal and visual learning and memory, working memory, speed of processing and attention as well as reasoning and problem solving, showed a stronger relationship with functioning (Kurtz et al., 2015) and are currently considered the most significant predictors of functional status (Best et al., 2014; Bowie et al., 2008; Green, 1996). Still, despite the significant association between cognitive and functional impairment, correlations are generally moderate with composite measures of cognition accounting only for 20–30% of the variance in functional outcome (Best et al., 2014). This has prompted the search for other factors that may act as mediators of the relationship between neurocognition and functional impairments. Among these, a key role seems to be played by social cognition, a multifactorial construct that includes the ability of individuals to understand themselves and others in the context of social interactions, especially others' thoughts, feelings and intentions (Adolphs, 2009; Fiske et al., 1991). Social cognitive abilities have been directly linked to quality of life, frequency and significance of interpersonal relationships, work attainments and personal achievements (Fett and Maat, 2013; Green, 2016). So far, studies have mainly focused on Theory of Mind (ToM), defined as the ability to infer other people mental states, as well as emotions recognition, i.e. the capacity to discern emotions and capitalize on them for social interaction, showing a correlation with several functional domains and with quality of life (Brune et al., 2007; Irani et al., 2012; Ventura et al., 2015). Also empathic processes, including “affective” and “cognitive” subcomponents, respectively referring to sharing the emotions and understanding the emotional perspective of others (Dodell-Feder et al., 2015; Lee et al., 2011), have been suggested to affect functioning in schizophrenia (Decety, 2004; Dodell-Feder et al., 2015; Michaels et al., 2014; Smith et al., 2012), although less explored.

Studies taking into account both cognitive and social cognitive abilities showed that the two domains are related (Fanning et al., 2012; Ventura et al., 2013), although not overlapping (Horan et al., 2015; Sergi et al., 2006), suggesting that they each could make unique contributions to predicting functional outcomes. Hoe and colleagues proposed a model in which social cognition acts indirectly as a mediator between neurocognition and functional outcome (Hoe et al., 2012). Overall, social cognition showed a stronger association with functioning, accounting for up to 16% of variance in functional outcome, compared to the 6% by neurocognition (Schmidt et al., 2011). Still, the variance explained by models including both domains is around 20–30% (Hoe et al., 2012; Kalin et al., 2015; Tas et al., 2013), suggesting that other factors significantly contribute to functional impairment in schizophrenia.

Recent evidence outlined a possible role of premorbid characteristics. Indeed, premorbid functioning, intended as the maximum level achieved prior to the disease onset in several domains (including relationships, work and personal autonomy), seems to have a prognostic value in terms of symptoms severity, illness course and outcome, as well as social capacity (Ayesa-Arriola et al., 2016; Bucci et al., 2016; Fett et al., 2015). Moreover, premorbid adjustment has been associated to educational level, age of onset and both cognitive and social cognitive performance (Chang et al., 2013; Faber et al., 2011; Galderisi et al., 2013). Finally, a role has also been claimed for family environment and early childhood experiences. Several studies reported a higher exposure to adverse events during childhood among patients with schizophrenia, compared to healthy controls (Grau et al., 2016) and suggested a strong link between these experiences and premorbid adjustment with impact on functional outcome and illness course (Benedetti et al., 2011; Schiffman et al., 2002). The severity of adverse childhood experiences was also reported to influence neural responses and gray matter volumes in structures implicated in emotional processing. These data are of extreme relevance, consistent with recent evidence indicating that environmental risk factors contribute to crucial determinants of symptom severity and age of onset of schizophrenia, even more strongly than genetic variability, as observed among genome-wide association studies (Rosenberg et al., 2007).

In sum, functional outcome represents a rather multifaceted variable relying on different constructs and depending on several clinical neuropsychological and environmental factors.

Taking into account this complex background, this study aims to explore, through a comprehensive assessment, the interplay of clinical, neurocognitive and social cognitive domains, including empathy, as well as premorbid factors and their relative contribute in determining both functional capacity and real-life behaviour in a sample of outpatients with chronic schizophrenia.

2. Methods

2.1. Participants

79 outpatients were recruited from September 2014 to May 2016 at the referral center of IRCCS San Raffaele Hospital, Dept. of Clinical Neurosciences, Milan, Italy. They all met DSM IV-TR criteria for schizophrenia, as determined by trained psychiatrists through clinical interview. Patients were clinically stabilized and treated with a stable dose of the same antipsychotic for at least 3 months. Exclusion criteria were the following: substance dependence or abuse, co-morbid diagnosis on Axis I or II, major neurological illness, perinatal trauma and mental retardation. All subjects provided informed consent to a protocol approved by the local Ethical Committee, following the principles of the Declaration of Helsinki.

2.2. Assessments

Psychopathology was assessed by means of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987).

Intellectual level was assessed by means of the Wechsler Adult Intelligence Scale–Revised (WAIS-R) Italian Version (Wechsler, 1997).

Cognition was evaluated with the Italian version of the Brief Assessment of Cognition in Schizophrenia (BACS, (Anselmetti et al., 2008), including the following tasks: word recall (verbal memory), digit sequencing (working memory), token motor task (psychomotor speed and coordination), symbol coding (processing speed), semantic and phonemic fluency (verbal fluency) and Tower of London (executive functions). Raw scores were converted into z-scores, based on normative data.

ToM was assessed using the Reading the mind in the eyes Test (RMET) revised for adult (Baron-Cohen et al., 2001), consisting in 36 black-and-white photographs of the area of the face including and surrounding the eyes. Participants were asked to choose one of four words (three distractors and one correct word) describing the mental state of the depicted person.

Emotion recognition was assessed with FEIT (Facial Emotion Identification Test), a computerized version of the Ekman-Friesen Pictures of Facial Affect Test (Ekman and Friesen, 1976), consisting of 55 static full-face images on a white background. Participants were required to choose the emotion label (happy, sad, angry, fearful, disgusted, surprised and neutral– presented in this standardized order) that best described what the individual was feeling, faces remained on the screen for 10 s and the next face appears until a response was made.

Empathy was assessed using the Interpersonal Reactivity Index (IRI) (Davis, 1983), a validated multi- dimensional self-report questionnaire assessing cognitive and affective empathy through the following subscales: Perspective Taking, Empathic Concern, Personal Distress and Fantasy.

The level of functioning prior to onset was assessed with the Premorbid Adjustment Scale (PAS) (Cannon-Spoor et al., 1982), a