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## Influence of social cognition on daily functioning in schizophrenia: Study of incremental validity and mediational effects

Sara Martínez-Domínguez<sup>a,b</sup>, Rafael Penadés<sup>a,b,c,d,\*</sup>, Bàrbara Segura<sup>a</sup>,  
Alexandre González-Rodríguez<sup>d</sup>, Rosa Catalán<sup>a,b,c,d</sup>

<sup>a</sup> Department of Psychiatry and Clinical Psychobiology, Faculty of Medicine, University of Barcelona, C/ Casanova 143, 08036 Barcelona, Spain

<sup>b</sup> Institute of Biomedical Research August Pi i Sunyer (IDIBAPS), C/ Villarroel 170, 08036 Barcelona, Spain

<sup>c</sup> Centre for Biomedical Research on Mental Health (CIBERSAM), Instituto de Salud Carlos III, Barcelona, Spain

<sup>d</sup> Department of Psychiatry and Psychology, Clinical Institute of Neurosciences (ICN), Hospital Clinic, C/ Villarroel 170, 08036 Barcelona, Spain

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### ABSTRACT

While the role of impaired neurocognition in accounting for functional outcome in schizophrenia is generally established, the influence of social cognition on this relationship is far from clear. This study aims to explore in depth the nature of the relationship between neurocognition, social cognition and daily functioning in people with schizophrenia. Twenty-one individuals diagnosed with schizophrenia and 15 controls completed the assessment of symptom severity, neuropsychological status, social cognition (Theory of Mind and affect processing) and other functional measures. A statistical mediation model based on hierarchical regression analyses was used to establish the mediation path with significant variables. Social cognition played a mediating role between neurocognition and functioning, accounting for significant trends in incremental variance in specific functional indexes (interpersonal behavior and employment/occupation). Consequently, this study adds to the evidence underlining the importance of targeting not only social cognitive or neurocognitive functions but to combine both interventions to reveal the best daily functioning results in schizophrenia patients.

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### 1. Introduction

Existing research shows that individuals with schizophrenia show substantial deficits in social cognitive domains, including emotion processing, social perception, social knowledge, and Theory of Mind (Bora et al., 2009; Kohler et al., 2010; Savla et al., 2013). Growing evidence indicates that impairments in social cognition may precede onset of the disorder, remain stable throughout the course of illness (Comparelli et al., 2013) and are present in first-degree relatives of people with schizophrenia (Lavoie et al., 2013), suggesting that social cognitive impairments in schizophrenia are likely core features of the illness and not simply a result of medication side-effects or clinical episodes.

In addition to these findings, interest in social cognition in schizophrenia has increased because it appears to be a key determinant of daily functioning. Consensus exists that social cognition is related to, though distinct from, (nonsocial) neurocognition (such as attention, memory, and problem solving) (Allen et al., 2007). Several

studies suggest that social cognition may contribute unique variance in functional outcomes above and beyond that provided by neurocognition, and may have a greater impact than cognition on social outcomes (Fett et al., 2011). This has stimulated a NIMH-sponsored workshop report to specifically recommend that researchers further examine the relationships between social cognitive domains and functional outcomes, as well as exploring the stability and correlates of social cognitive impairments (Green et al., 2008).

Despite evidence of social cognition being a determinant of daily functioning in schizophrenia, many of the relevant studies are mainly based on correlational analysis (Couture et al., 2006). Unfortunately, results from such studies do not provide information about the directionality of relationships, and explanatory models of associations remain heterogeneous. A methodological approach that has gained attention more recently considers social cognitive processes as a potential mediator between neurocognition and functional outcome. Nevertheless, there is substantial variability in the type of statistical analysis employed, with studies using Structural Equation Modeling (SEM) (Sergi et al., 2006; Rassovsky et al., 2011), path analysis (Brekke et al., 2005; Gard et al., 2009) or regression analysis (Addington et al., 2006). In addition, research diverged in the statistical procedure used to test mediation effects. While some studies estimated the parameters of the mediation model controlling the direct effect of

\* Corresponding author at: Clinical Institute of Neurosciences (ICN), Hospital Clinic, C/ Villarroel 170, 08036 Barcelona, Spain.  
Tel.: +34 93 227 54 00; fax: +34 93 403 52 94.

E-mail address: [rpenades@clinic.ub.es](mailto:rpenades@clinic.ub.es) (R. Penadés).

neurocognition on functional outcome (Sergi et al., 2006), others did not (Gard et al., 2009). Finally, when social cognition is measured in studies by means of correlational analyses (including regression analysis, path analysis and SEM), to have adequate range properties is crucial. However, most of these studies have employed measures with unknown or questionable psychometric properties and, in numerous cases, have only focused on one specific social cognition domain. Therefore, a statistical mediation approach including a wide range of measures is lacking (Schmidt et al., 2011).

The issue of differential associations between social cognition, neurocognition, and functional outcomes is important for identifying specific cognitive domains as possible targets for treatment intervention (Gold, 2004). Following the indication of the international Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) consensus in which each domain has to be composed by two different tests at least (Nuechterlein et al., 2008), we conduct exploratory analyses of composite scores to elucidate the mediation model of the relationship between a wide range of well-defined neurocognitive and social cognitive measures (Pinkham et al., 2013) and daily functioning (Leifker et al., 2011) in a sample of stable outpatients with schizophrenia. We studied a sample of predominant negative symptoms because they have shown to be more consistently associated with functional outcome than positive symptoms, but have garnered much less attention (Ventura et al., 2009). Specifically, we examined (1) whether the social cognitive performance uniquely accounts for incremental variance in daily functioning, independently of neurocognitive performance and psychiatric symptom severity, and (2) whether social cognitive performance mediates the relationship between neurocognitive performance and daily functioning.

## 2. Methods

### 2.1. Participants

The study included 21 schizophrenic participants recruited from the Schizophrenia Unit at Hospital Clinic (Barcelona), and 15 healthy subjects. The inclusion criteria were (a) age between 20 and 64 years to compose a truly adult schizophrenia sample, (b) diagnosis of schizophrenia confirmed by an experienced clinician following the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 2001), (c) predominance of negative symptoms confirmed by the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987), and (d) no changes in antipsychotic medication in the previous 2 months. Exclusion criteria were (a) a score below 4 (scaled score) on the Vocabulary test from the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) (Wechsler, 1998), (b) organic cerebral disease or primary active diagnosis of substance abuse or dependence, (c) co-occurring DSM-IV Axis I diagnoses, and (d) psychotic symptom exacerbation within the previous month. Healthy control participants were screened for the presence of lifetime Axis I psychotic or mood disorders using the SCID (non-patient version) and matched with patients according to age, gender, and education variables. Exclusion criteria for the control group were the same as for patients, except psychotic symptom exacerbation within the previous month.

The study protocol was approved by the Hospital Clinic Ethics Committee (Barcelona). Following a comprehensive description of the study, all participants gave their written informed consent. Testing of the control group took place in two sessions, usually on the same day. For the schizophrenic patients' group, we completed the assessments in three sessions, all within a 7-day period. Raters for the SCID-I, PANSS and functioning were experienced research clinicians who demonstrated adequate inter-rater reliability at regular intervals. Raters were trained before reaching a reliability on the scales' overall mean equal to 0.80, as calculated by the intra-class correlation coefficient (ICC) (Streiner and Norman, 2003) with confidence interval (CI) of 95%. Neurocognitive and social cognitive tests were administered by trained psychometricians. Schizophrenic participants were clinically stable at the time of the assessment.

### 2.2. Symptom assessment

Severity of psychiatric symptoms was assessed with the Spanish version of the Positive and Negative Syndrome Scale (PANSS) (Peralta and Cuesta, 1994), which has similar psychometric properties to those obtained in the original version (Kay and Sevy, 1990). Symptom severity was assessed at baseline with respect to the previous month.

### 2.3. Neurocognitive assessment

All participants completed a comprehensive battery of neuropsychological subtests that was consistent with batteries generally used in the schizophrenia literature. Assessment of cognitive function included (a) general intelligence: Vocabulary, Similarities and Block Design (WAIS-III), (b) attention/vigilance: Conner's Continuous Performance Test II (CPT-II), (c) working memory: Digit Span and Letter-Number Sequencing (WAIS-III), (d) psychomotor speed: Digit Symbol-Coding (WAIS-III), and Trail Making Test-Part A (TMT-A), (e) verbal memory: Rey Auditory Verbal Learning Test (RAVLT), and Logical Memory I and II (Wechsler Memory Scale-Third Edition; WMS-III), (f) non-verbal learning: Faces I and II (WMS-III), and (g) executive function: Wisconsin Card Sorting Test (WCST) Perseverative errors, Trail Making Test-Part B (TMT-B), and Letter Fluency (Controlled Oral Word Association Test; COWAT). The distinct raw scores were converted into *T*-scores (Mean=50; S.D.=10) and, to make all scores comparable, the norms adapted for age and educational level outlined in the manual covering each test were applied. Where the Spanish validation was available, we used its norms, as in the WAIS-III (Seisdedos et al., 1999) and WMS-III subtests (Pereña et al., 2004). For the remaining subtests we used the standard norms outlined in their respective manuals: RAVLT (Schmidt, 1996), TMT (Tombaugh, 2004), CPT-II (Conners, 2004), WCST (Heaton, 1981) and COWAT (Tombaugh et al., 1999). Composite scores for each cognitive domain were obtained by calculating the mean of the standardized *T*-scores from the respective subtests of each domain as described above. Finally, we used a composite score based on the average *T*-scores from all neurocognitive domains.

### 2.4. Social cognitive assessment

Measures of social cognition included: the Spanish version of the Hinting Task (Gil et al., 2012; Corcoran et al., 1995), the "Reading the Mind in the Eyes Test" (Baron-Cohen et al., 2001) to assess Theory of Mind, and the Penn Emotion Recognition Task (ER-40) (Kohler et al., 2003) to assess affect processing.

The Hinting Task examines the ability to infer the true intent of indirect speech. It consists of 10 short passages presenting an interaction between two characters that are read aloud by the experimenter. Each passage ends with one of the characters dropping a hint, and participants are asked what the character truly meant. If the first response provided is inaccurate, a second hint is delivered, and participants may earn partial credit for that passage. Total scores range from 0 to 20.

The Reading the Mind in the Eyes Test measures the capacity to determine the mental states of others from expressions in the eye region of the face. Participants view 36 photographs of the eye region of different faces and choose the most accurate descriptor word for the thought/feeling that is portrayed. Four possible options are presented with each photo, and a glossary of mental-state terms is provided for reference. The total score is the number of correct responses, and scores range from 0 to 36.

The ER-40 includes 40 color photographs of static faces expressing 4 basic emotions (happiness, sadness, anger or fear) and neutral expressions. Stimuli are balanced according to subjects' gender, age, and ethnicity, and for each emotion category; 4 high-intensity and 4 low-intensity expressions are included. Participants view 1 image at a time and choose the correct emotion label for each face. Accuracy scores, ranging from 0 to 40, serve as the primary dependent variable. We used a composite score by averaging the three raw scores from social cognitive measures.

### 2.5. Daily functioning assessment

Functional outcome was assessed using the self-reported Spanish version of Social Functioning Scale (SFS) (Vázquez and Jiménez, 2000). The SFS (Birchwood et al., 1990) has a total score and 7 sub-scores: (a) Withdrawal/social engagement, (b) interpersonal behavior, (c) independence-performance, (d) independence-competence, (e) recreation, (f) pro-social activities, and (g) employment/occupation. High scores indicate good social functioning and low scores indicate significant dysfunction and disability. Additionally, we used the Global Assessment of Functioning (GAF) (Endicott et al., 1976) to evaluate the functional outcome.

### 2.6. Statistical analyses

#### 2.6.1. Cross-sectional associations of social cognitive measures with psychiatric symptom severity, neurocognition and functioning

Pearson's correlations were computed to investigate the associations between measures of social cognitive ability and psychiatric symptom severity, composite neurocognitive scores, and functional scales. Multiple testing was applied using Bonferroni procedure.

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