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Cognition and the five-factor model of the Positive and Negative Syndrome Scale in schizophrenia

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ABSTRACT

Different exploratory and confirmatory factorial analyses of the Positive and Negative Syndrome Scale (PANSS) have found a number of factors other than the original positive, negative, and general psychopathology. Based on a review of previous studies and using confirmatory factor analyses (CFA), Wallwork et al. (Schizophr Res 2012; 137: 246–250) have recently proposed a consensus five-factor structure of the PANSS. This solution includes a cognitive factor which could be a useful measure of cognition in schizophrenia. Our objectives were 1) to study the psychometric properties (factorial structure and reliability) of this consensus five-factor model of the PANSS, and 2) to study the relationship between executive performance assessed using the Wisconsin Card Sorting Test (WCST) and the proposed PANSS consensus cognitive factor (composed by items P2-N5-G11). This cross-sectional study included a final sample of 201 Spanish outpatients diagnosed with schizophrenia. For our first objective, CFA was performed and Cronbach's alphas of the five factors were calculated; for the second objective, sequential linear regression analyses were used. The results of the CFA showed acceptable fit indices (NNFI = 0.94, CFI = 0.95, RMSEA = 0.08). Cronbach's alphas of the five factors were adequate. Regression analyses showed that this five-factor model of the PANSS explained more of the WCST variance than the classical three-factor model. Moreover, higher cognitive factor scores were associated with worse WCST performance. These results supporting its factorial structure and reliability provide robustness to this consensus PANSS five-factor model, and indicate some usefulness of the cognitive factor in the clinical assessment of schizophrenic patients.

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1. Introduction

Already from the earlier descriptions of schizophrenia, cognitive deficits have been considered to be a core symptom of the disorder

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(Kraepelin, 1919; Bleuler, 1950). Cognitive impairments have been found not only in chronic schizophrenic patients (Reichenberg, 2010), but also in those with a first psychotic episode (Albus et al, 1996; Mohamed et al, 1999; Addington et al., 2003), patients in clinical remission (Asarnow and MacCrimmon, 1978; Nuechterlein et al., 1992), neuroleptic-naïve patients (Saykin et al., 1994; Torrey, 2002), and even in subjects at high risk for developing psychosis (Erlenmeyer-Kimling and Cornblatt, 1978; Nuechterlein, 1983; Cornblatt et al., 1992) and in healthy siblings of schizophrenic patients (Kuha et al., 2007). This cognitive deficit has considerable relevance regarding prognosis, since it has been shown to be an important predictor of functioning in schizophrenia (Green, 1996; Velligan et al., 1997; Harvey et al., 1998; Green et al, 2000; Bowie and Harvey, 2005; Bowie et al., 2006, 2008).

Among the cognitive functions that have been shown to be impaired in schizophrenic patients, executive functions may be of

special relevance (Joyce et al., 2005). Several studies suggest there may be subgroups of patients based on cognitive performance, with some patients exhibiting specific impairments in executive functions but preserved general intellectual function (Heinrichs and Awad, 1993; Goldstein and Shermansky, 1995; Weickert et al., 2000), and others suffering general intellectual impairments from illness onset, including executive dysfunction (Kremen et al., 1998; Weickert et al., 2000; Fuller et al., 2002). It has been proposed that executive impairments may be considered to be a core deficit in schizophrenia, whatever other cognitive deficits may be present (Joyce et al., 2005). The importance of executive functions has also been noted in some studies that have highlighted their relevance regarding functional outcomes (Martínez-Arán et al., 2002; Reed et al., 2002; Rocca et al., 2009; Penadés et al., 2010), and suggested their potential use as a diagnostic criterion for schizophrenia (Keefe and Fenton, 2007; Peña et al., 2011). Thus, the neuropsychological assessment of schizophrenic patients is of great interest for clinicians. In real-life clinical practice, however, resources and time are often insufficient to carry out a complete neuropsychological evaluation.

The Positive and Negative Syndrome Scale (PANSS) is a widely used instrument for the clinical assessment of schizophrenic patients. In its original form, it was divided in three scales: positive, negative and general psychopathology (Kay et al., 1987). Later factorial analyses, however, have pointed to the existence of other components. Five-factor solutions have been the most frequently described (Kay and Sevy, 1990; Lépine, 1991; Lindstrom and von Knorring, 1993; Bell et al., 1994a; Kawasaki et al., 1994; Lindenmayer et al., 1994, 1995; Dollfus and Petit, 1995; Fredrikson et al., 1997; Marder et al., 1997; White et al., 1997; Higashima et al., 1998; Lançon et al., 2000; Lykouras et al., 2000; Mass et al., 2000; Wolthaus et al., 2000; El Yazaji et al., 2002; Drake et al., 2003; Emsley et al., 2003; Lee et al., 2003; Fresán et al., 2005; Tirupati et al., 2006; van den Oord et al., 2006; van der Gaag et al., 2006; Levine and Rabinowitz, 2007; Citrome et al., 2011), with factors commonly labeled as 'positive', 'negative', 'cognitive', 'depression' and 'excitement'.

The cognitive factor (sometimes called 'disorganization') refers to the patient's cognitive functioning, and is composed of several PANSS items that vary partially in the different factorial analyses. If this cognitive factor were proved to be valid, obtaining information on cognitive performance using the PANSS would be very valuable given the wide use of this instrument in clinical practice. In this respect, several studies to date have examined the concurrent validity of the PANSS cognitive factor in schizophrenic patients (Bell et al., 1994b; Bryson et al., 1999; Mass et al., 2000; Harvey et al., 2001; Cameron et al., 2002; Daban et al., 2002; Bozikas et al., 2004; Ehmann et al., 2004; Good et al., 2004; Hofer et al., 2007). A first study by Bell et al. (1994b) studied the validity of the cognitive factor in 147 patients diagnosed with schizophrenic or schizoaffective disorder by examining correlations between this factor and different neuropsychological tests. They found a significant negative correlation between cognitive factor scores and performance in all the neuropsychological tests. Based on their results, the authors concluded that the cognitive component of the PANSS is a valid measure of cognitive deficits in schizophrenia. Since then, other similar studies have been carried out, with some obtaining results comparable to those of Bell et al. (1994b), and other studies having less consistent findings (Hofer et al., 2007). In general correlations between the PANSS cognitive factor and neuropsychological measures have been found to be moderate, ranging between 0.20 and 0.53 (Bryson et al., 1999; Cameron et al., 2002; Daban et al., 2002; Bozikas et al., 2004; Good et al., 2004; Hofer et al., 2007).

This variability may be due to the use of different neuropsychological tasks, to the study of different cognitive functions (sometimes grouped in a general cognitive index), or to the use of general measures of cognition such as those derived from the WAIS (Wallwork et al., 2012). However, grouping different cognitive measures in a single cognitive index may mask significant correlations of specific cognitive domains if the remaining domains are not correlated or only weakly

so. Consequently, it would be desirable to study the concurrent validity of the PANSS cognitive factor with each of the cognitive functions that are impaired in schizophrenia separately. On other hand, the variability in correlations between the PANSS cognitive factor and neuropsychological measures may also be due to the fact that the cognitive factors used in the different studies are not composed of the same items. Despite the general similarity of five-factor models, none of them has achieved broad consensus. In this respect, the different cognitive factors described in the literature include a number of items ranging from 3 (Kay and Sevy, 1990; Lançon et al., 2000; Mass et al., 2000) to 9 (Citrome et al., 2011). Wallwork et al. (2012) have recently proposed a new consensus model, extending previous work by Lehoux et al. (2009). They used a larger collection of PANSS five-factor models reported in the literature, and tested and refined the consensus model with confirmatory factor analysis (CFA) in an American and in a Japanese sample. The consensus cognitive factor proposed by Wallwork et al. (2012) is only made up of three PANSS items: 'Conceptual disorganization' (P2), 'Difficulty in abstract thinking' (N5), and 'Poor attention' (G11). If this proposed consensus five-factor model shows adequate psychometric properties in other samples, it would gain robustness and could encourage a more generalized use. In addition, if this cognitive factor, with only three PANSS items, could provide some information regarding the cognitive function of patients, it could be of some usefulness in clinical settings. To our knowledge, no studies have addressed this issue to date.

The present study had two objectives:

1. To study the psychometric properties (factorial structure and reliability) of the five-factor model of PANSS proposed by Wallwork et al. (2012) in a large sample of clinically stable schizophrenic patients.
2. To study the concurrent validity of the cognitive factor proposed in this five-factor model using a neuropsychological task of executive function.

2. Methods

2.1. Sample

The present cross-sectional study was carried out with 215 clinically stable outpatients aged 18 to 60 years, who were consecutively referred by their treating psychiatrists. The sample was recruited in two of the participating centers (Hospital Universitario 12 de Octubre, Madrid and Hospital Virgen de la Luz, Cuenca). All patients had been diagnosed with schizophrenia according to DSM-IV criteria (APA, 1994), using the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-I) (First et al., 1995). Of the initial sample, 14 patients declined participation, leaving a final sample of 201 (138 male, 63 female). All patients were on antipsychotic treatment and had been clinically stable (no hospital admissions, no changes in treatment, no significant psychopathological changes) for at least 6 months before inclusion. The scales and neuropsychological tests used are part of the usual clinical protocol, and written informed consent was obtained from all participants prior to their inclusion in the study. Two experienced neuropsychologists who were blind to PANSS ratings carried out cognitive assessments. Analysis of interrater reliability indicated an adequate degree of agreement between researchers (weighted kappa for PANSS scores: 0.69–0.78).

2.2. Instruments

2.2.1. The Positive and Negative Syndrome Scale (PANSS)

The Positive and Negative Syndrome Scale (Kay et al., 1987; Spanish validation by Peralta and Cuesta, 1994) is a 30-item scale designed to obtain a measure of positive (items P1 to P7) and negative (items N1 to N7) symptoms in schizophrenic patients, as well as a measure

of general psychopathology (items G1 to G16). Different studies have carried out factorial analyses of the scale, and have found a cognitive factor composed of several items, which partly vary in the different analyses (for a review, see [Lehoux et al., 2009](#)). The five-factor model proposed by [Wallwork et al. \(2012\)](#) comprises a positive factor (items P1, P3, P5, G9) a negative factor (items N1, N2, N3, N4, N6, G7), a disorganized/concrete (cognitive) factor (items P2, N5, G11), an excited factor (items P4, P7, G8, G14) and a depressed factor (items G2, G3, G6), including a total of 20 items.

2.2.2. The Wisconsin Card Sorting Test (WCST)

The Wisconsin Card Sorting Test is a cognitive task that predominantly assesses executive function, and was chosen since this is the most widely applied test of executive performance in schizophrenic patients ([Nieuwenstein et al., 2001](#)). The task consists of 64 cards with figures varying in shape (triangle, circle, square, cross), color (red, blue, green, yellow) and number of figures (one, two, three, four). Subjects have to match each of their cards in turn with one of the 4 stimulus cards presented, on the basis of a rule which the subject does not know and must learn according to the examiner's feedback ('right' or 'wrong'). When 10 consecutive responses are correct, the rule is changed, and the subject must learn the new rule based on the feedback. The test is over when the subject achieves 6 series or categories, or when 128 trials have been completed. The number of categories completed, the percentage of perseverative errors and the percentage of perseverative responses were considered as executive function variables in the present study (similar to [Nieuwenstein et al., 2001](#)). Factor-analytical findings indicate that these variables load on perseveration, one of the three factors of the WCST, which has been reported to differentiate well between schizophrenic patients and normal subjects ([Cuesta et al., 1995](#); [Koren et al., 1998](#)).

2.3. Statistical analysis

The mean and standard deviation (SD) were used to describe continuous variables, while percentages were used for categorical variables.

To perform the CFAs, the data was screened to determine the appropriate model estimation method. The normalized estimate of Mardia's coefficient of multivariate kurtosis ([Mardia, 1970](#)) indicated significant non-normality in the data ([Bentler and Wu, 1995](#)). Accordingly, the heterogeneous kurtosis (HK) estimator was used. The geometric mean approach to HK model estimation was employed ([Bentler et al., 1991](#)). The variance-covariance matrix was the basis of the analyses and the metric of the latent factors was defined by setting factor variances to 1.0.

Models assessed by CFA are considered to have adequate fit when the Comparative Fit Index (CFI) and the Non-Normed Fit Index (NNFI) are greater than 0.90 and the Root Mean Square Errors of Approximation (RMSEA) is less than 0.08 ([Kline, 2010](#)). The Akaike Information Criterion (AIC) is included because it allows for comparison between models, with lower values indicating better relative fit.

Cronbach's alphas of the five factors were calculated in order to explore internal consistency.

Sequential linear regression analyses were performed to study the relationship between the cognitive factor and the executive function task, with WCST scores as dependent variables. In a first step, the influence of age and gender were controlled for. In a second step, the different PANSS factors of both [Wallwork et al.'s \(2012\)](#) five-factor/20-item model and of the original three-factor/30-item model were included.

The CFAs were performed with EQS (version 6.1) software ([Bentler, 1995](#); [Bentler and Wu, 1995](#)). All other analyses were performed using the SPSS version 15.0 for Windows statistical package.

3. Results

3.1. Patient characteristics, PANSS scores, and neuropsychological performance

The mean age of our sample was 38.0 years (SD: 9.7), and the mean age when they suffered their first psychotic episode was 22.8 years (SD: 5.5). On their first psychiatric admission, patients had been 25.9 (SD: 6.8) years old, and the mean number of previous hospitalizations was 2.9 (SD: 3.1). The predominant subtype of schizophrenia in our sample was paranoid (86.3%), and in 89.8% the antipsychotic received was atypical.

Mean scores were 11.9 (SD: 6.1) in the PANSS positive, 18.4 (SD: 8.4) in the PANSS negative, and 27.7 (SD: 9.3) in the PANSS general psychopathology subscale.

The mean WCST scores obtained by the sample of schizophrenic patients were as follows: completed categories 3.5 (SD: 2.2), percentage of perseverative errors 26.1 (SD: 18.0), percentage of perseverative responses 31.3 (SD: 24.5).

3.2. Confirmatory factor analysis

Fit indices showed the five-factor model of 20 items ($X^2 = 425.14$, d.f. = 160; RMSEA = 0.09; CFI = 0.93; NNFI = 0.91; AIC = 105.14) to fit the data better than the three-factor model of 30 items ($X^2 = 2009.17$, d.f. = 402; RMSEA = 0.14; CFI = 0.75; NNFI = 0.73; AIC = 1205.17). The five-factor/20 item model was further improved by adding parameters using the Lagrange Multiplier (LM) test ([Byrne, 2006](#)). The LM test suggested to include correlations between N2 and N4 item errors ($r = 0.36$, $p < 0.001$), and between G7 and N6 item errors ($r = 0.35$, $p < 0.001$) in the model. The final model showed acceptable fit indices ($X^2 = 335.71$, d.f. = 158; RMSEA = 0.08; CFI = 0.95; NNFI = 0.94; AIC = 19.71). Standardized factor loadings and correlations between factors are presented in [Tables 1 and 2](#) respectively. [Fig. 1](#) shows CFA of the five-factor model of the PANSS.

3.3. Internal consistency

Cronbach's alphas of the five factors are presented in [Table 2](#).

Table 1
Five-factor model of the PANSS standardized estimates of regression weights.

	Positive factor	Negative factor	Disorganized/concrete (cognitive) factor	Excited factor	Depressed factor	R ²	t1.1	t1.2
P1	0.88					0.78	t1.4	
G9	0.73					0.53	t1.5	
P3	0.59					0.35	t1.6	
P5	0.39					0.15	t1.7	
N3		0.87				0.76	t1.8	
N1		0.85				0.73	t1.9	
N2		0.78				0.61	t1.10	
N6		0.76				0.57	t1.11	
N4		0.75				0.57	t1.12	
G7		0.58				0.33	t1.13	
N5			0.76			0.57	t1.14	
P2			0.67			0.45	t1.15	
G11			0.64			0.41	t1.16	
P4				0.63		0.40	t1.17	
G14				0.56		0.31	t1.18	
P7				0.54		0.29	t1.19	
G8				0.41		0.17	t1.20	
G3					0.79	0.63	t1.21	
G6					0.77	0.59	t1.22	
G2					0.62	0.38	t1.23	

Table 2
Correlations between the five factors included in the CFA. The last column shows Cronbach's alpha for each factor.

	1.	2.	3.	4.	5.	Cronbach's alpha
1. Positive factor	–	0.36***	0.44***	0.37***	0.38***	0.74
2. Negative factor		–	0.68***	0.28**	0.26**	0.90
3. Disorganized/concrete (cognitive) factor			–	0.78***	0.31**	0.83
4. Excited factor				–	0.34*	0.59
5. Depressed factor					–	0.76

* p<0.05.
** p<0.01.
*** p<0.001.

3.4. Regression analysis

Regression analyses for both the five- and the three-factor models revealed that the greater the age of patients, the poorer the WCST performance, while gender was not found to influence executive performance (see Table 3). Considering the high correlations between independent variables (see Supplementary material) we checked for multicollinearity for each regression analysis and found no multicollinearity in our data (VIF<10, Tolerance>0.02) (Field, 2009).

In the five-factor model, higher cognitive factor scores were significantly associated with fewer WCST completed categories ($\beta = -0.33$, $p < 0.01$) and a greater percentage of perseverative responses ($\beta = 0.21$, $p < 0.05$), and exhibited a trend towards a greater percentage of perseverative errors ($\beta = 0.19$, $p = 0.06$). Significant relationships were also found between the depressed factor and all the WCST variables, so that the higher the depressed factor scores, the better the WCST performance.

In the classic three-factor model higher negative PANSS scores were found to be significantly associated with a poorer WCST performance.

Finally, regression analyses found that the five-factor model explained a greater proportion of the variance of WCST categories (16% vs. 11%), percentage of perseverative errors (10% vs. 6%) and percentage of perseverative responses (10% vs. 6%) than the classic three-factor model.

4. Discussion

In the present study, our first objective was to examine the psychometric properties of the five-factor model of PANSS proposed by Wallwork et al. (2012). Our CFA with a sample from a different socio-cultural milieu found that their proposed five-factor/20-item model fits our data better than the original PANSS three-factor/30-item model. Exclusion of items with low factor saturation or with similar saturation on several factors would account for this better fit of the 20-item

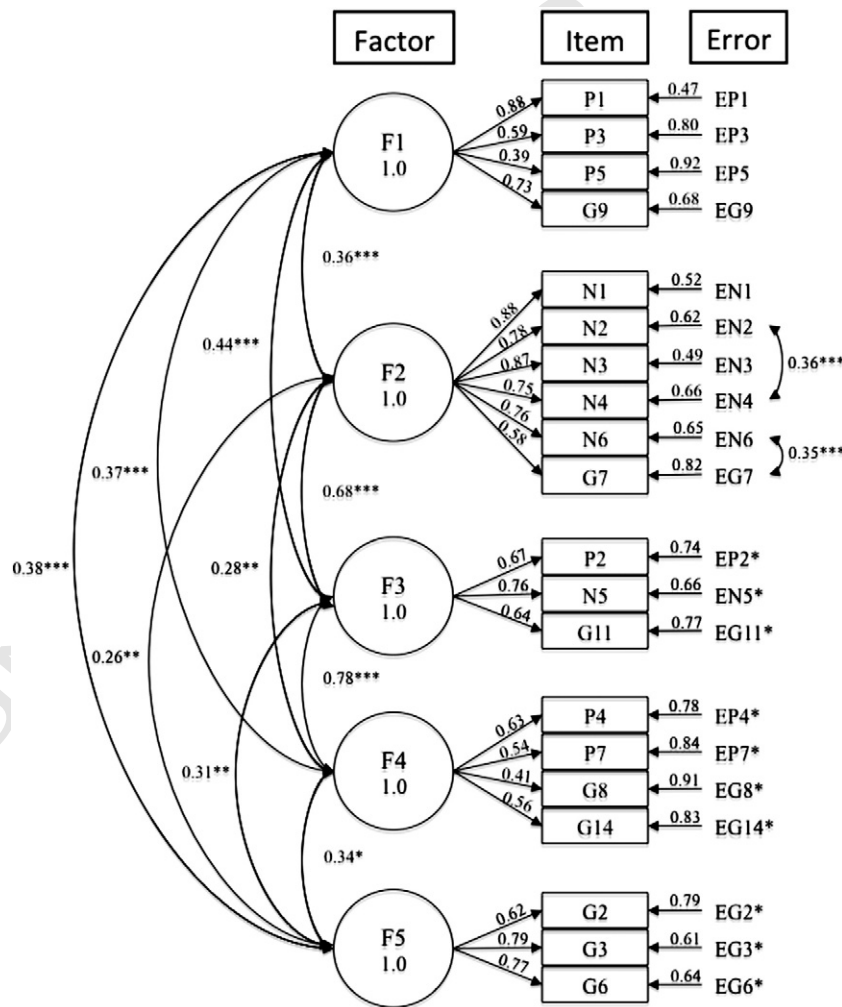


Fig. 1. Diagram showing CFA of the consensus five-factor model of the PANSS. F1: Positive factor, F2: Negative factor, F3: Disorganized/concrete (cognitive) factor, F4: Excited factor, F5: Depressed factor. Standardized Loadings and standard errors are shown over unidirectional lines, while correlations are shown beside bidirectional lines. Significance at *p<0.05, **p<0.01 and ***p<0.001.

Table 3

Stepwise linear regression analyses with WCST scores as dependent variables and PANSS a) five-factor model and b) three-factor model factors as independent variables.

a) Five-factor model		Dependent variables (WCST)					
Independent variables		Categories		Perseverative errors		Perseverative responses	
		β	ΔR^2	β	ΔR^2	β	ΔR^2
Step 1	Age	-0.22**	0.06*	0.16*	0.03	0.17*	0.03*
	Gender	0.10		-0.06		-0.06	
Step 2	Positive factor	-0.04	0.16***	0.02	0.10**	0.02	0.10**
	Negative factor	-0.14		0.11		0.10	
	Disorganized/ concrete (cognitive) factor	-0.33**		0.19		0.21*	
	Excited factor	0.02		0.11		0.09	
	Depressed factor	0.16*		-0.17*		-0.15*	
b) Three-factor model		Dependent variables (WCST)					
Independent variables		Categories		Perseverative errors		Perseverative responses	
		β	ΔR^2	β	ΔR^2	β	ΔR^2
Step 1	Age	-0.22**	0.06**	0.16*	0.03	0.17*	0.03*
	Gender	0.10		-0.06		-0.06	
Step 2	Positive dimension	-0.10	0.11***	0.04	0.06**	0.03	0.06**
	Negative dimension	-0.37***		0.15*		0.26*	
	General psychopathology	0.12		-0.03		-0.09	

* $p < 0.05$.

** $p < 0.01$.

*** $p < 0.001$.

model. In addition, we introduced two post-hoc specifications that were suggested by the LM test in order to improve the model. The inclusion of correlations between the errors of two pairs of items of the negative factor (N2 “emotional withdrawal”–N4 “passive/apathetic social withdrawal”, and N6 “lack of spontaneity”–G7 “motor retardation”) could be related with a possible overlap between the content of the items in each pair (Aish and Joreskog, 1990; Byrne, 2006). Moreover, in a previous study van der Gaag et al. (2006) carried out CFA of the PANSS and found that N2 (emotional withdrawal) and N4 (passive/apathetic social withdrawal) errors were correlated in 10 out of 10 analyses performed. This supports the inclusion in the model of the correlation between N2 and N4 errors. However, to our knowledge, previous studies have not included correlations between N6 and G7 scores, suggesting the need to replicate this result in independent samples. Regarding the comparison of our CFA with that carried out by Wallwork et al. (2012), although some of the standardized loadings of the items differed slightly between our study and Wallwork’s (e.g. P5: 0.39 vs. 0.74; N5: 0.76 vs. 0.41), all of them were salient (i.e., ≥ 0.30 , according to Brown, 2006). The CFA indices obtained in our final model ($X^2 = 335.71$, RMSEA = 0.08; CFI = 0.95; NNFI = 0.94; AIC = 19.71) were similar to those of Wallwork’s study ($X^2 = 290.43$, RMSEA = 0.09; CFI = 0.95; NNFI = 0.96; AIC = 174.43 in the U. S. sample, and $X^2 = 153.81$, RMSEA = 0.13; CFI = 0.94; NNFI = 0.97; AIC = 67.81 in the Japanese sample).

The internal consistencies (Cronbach’s alphas) for the five-factor model ranged from 0.59 (excited factor) to 0.90 (negative factor). Though the excited factor’s internal consistency is below the widely accepted 0.70 cutoff, it is close to 0.60, an acceptable alpha cutoff for brief scales (i.e. those with fewer than 10 items) (Loewenthal, 1996). Moreover, high Cronbach’s alphas could indicate the presence of redundant items in a scale. The fact that the negative factor exhibits a Cronbach’s alpha coefficient of 0.90, includes a greater number of items, and the content of some of them (N2–N4, N6–G7) may partly

overlap suggests that reducing the number of items in this factor may be desirable. Taking into account that the PANSS is a semi-structured interview which is commonly used by clinicians, a briefer scale could facilitate its use in the clinical context, and future research should explore this possibility.

In summary, the psychometric properties found in our study support the five-factor/20-item model proposed by Wallwork et al. (2012), which exhibits acceptable factorial structure indices and reliability in a large sample of patients with schizophrenia from a different socio-cultural context.

The second objective of our study was to examine the relationship between the five-factor model cognitive factor and neuropsychological variables of executive function in a large sample of schizophrenic patients. In order to control for covariation between different PANSS factors, and to find differential associations between the five PANSS factors and WCST scores, regression analyses were performed. Our results show that higher cognitive factor scores were significantly associated with poorer executive function as assessed by the WCST.

When applied to the classical three-factor model, the regression analysis revealed a significant association between higher negative subscale scores and poorer performance on the WCST. Since Crow (1980) proposed his two-syndrome model, in which schizophrenic patients with most cognitive impairment were those with predominantly negative symptoms, different authors have studied the relationship between the negative and cognitive dimensions of schizophrenia. Cross-sectional studies have generally found a correlation between negative and cognitive symptoms, with several studies having specifically investigated the relationship between executive function and symptom dimensions in schizophrenia. A meta-analysis carried out by Nieuwenstein et al. (2001) found a significant relationship between WCST performance and negative symptoms, although the observed association was weak; a more recent meta-analysis by Dibben et al. (2009) found an association between executive dysfunction and negative symptoms, although the effect size was small. It could be hypothesized that part of the association between the negative PANSS subscale of the original three-factor model and executive function found in the literature could be due to the fact that the different PANSS factors (especially the cognitive factor) were not considered. In this respect, our findings indicate that when moving from the three-factor model to the five-factor model, the association between WCST performance and the negative factor disappears, and a relationship with the cognitive factor emerges.

Regarding the relationship observed between the depressed factor in the five-factor model and executive function, it could be speculated that patients with a greater affective component may exhibit better executive performance. However, the fact that no correlations were found between the depressed factor and WCST variables (see Supplementary material) suggests that the relationship observed in the regression analyses could be due to a statistical artifact known as suppression effect. In multiple regression, suppression describes a situation in which a predictor variable that is uncorrelated with the outcome variable nevertheless adds significantly to its prediction when other predictor variables that are correlated with the initial predictor are included in the regression equation. The additional predictor variables essentially suppress outcome-irrelevant variance in the first predictor, allowing it to more efficiently predict the outcome variable (for a detailed discussion of suppression effects, see Paulhus et al., 2004).

In a global comparison between both models, the five-factor model explained a greater proportion of the variance of the cognitive variables than did the three-factor model, even though the five-factor model included 10 items less. In any case, despite the significant relationships between the five-factor model and the WCST, the variance explained by the five factors does not exceed 16%. This is in agreement with previous studies suggesting that although the PANSS cognitive factor may provide information regarding the cognitive status of the patient, it cannot replace formal neuropsychological assessments (Harvey et al., 2001; Hofer et al., 2007).

Our study focused on executive function, which is one of the main cognitive functions that have been found to be impaired in schizophrenic patients (Pantelis et al., 1997; Hutton et al., 1998; Rhinewine et al., 2005). This impairment has been related to structural and functional brain anomalies in regions that are thought to be involved in the pathophysiology of schizophrenia such as the prefrontal cortex (Eisenberg and Berman, 2010), and to alterations in the dopaminergic system (Robbins and Arnsten, 2009). However, despite its relevance, the use of a single cognitive domain could be a limitation of the present study, and it would be interesting to replicate this research including other cognitive functions, such as memory or attention, that are also impaired in schizophrenia.

To conclude, the fact that the data obtained from an independent sample of Spanish schizophrenic patients fits the five-factor/20-item model reasonably well supports the factorial structure of this consensus model proposed by Wallwork et al. (2012). This fact together with the reliability indices and concurrent validity data obtained provides robustness to the model. Nevertheless, although the cognitive factor could provide useful information about patients for whom formal neuropsychological testing is unavailable in the clinical setting, the proportion of the variance that is explained by the five-factor model of the PANSS makes it unadvisable to substitute neuropsychological assessment with the PANSS cognitive factor when studying cognition in schizophrenia.

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Contributors

RR, AB, JS and TP designed the study. AB, ES, JD, IM, NM and MJ managed the literature search and review. IM, MJ, JD, ES and JS selected the sample and evaluated patients. RR, AL, LM, MII and NM undertook the statistical analysis. RR, AB, AL, LM, MII and TP wrote the first draft of the manuscript. The Psychosis and Addictions Research Group (PARG) is a Spanish research group of psychiatrists and psychologists who have contributed to the design of the study and selection of the sample, as well as in the writing and reviewing of the manuscript. All authors contributed to and have approved the final manuscript.

Conflict of interest

The authors report no biomedical financial interests or potential conflicts of interest.

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References

- Addington, J., Brooks, B.L., Addington, D., 2003. Cognitive functioning in first episode psychosis: initial presentation. *Schizophr. Res.* 62, 59–64.
- Aish, A.M., Joreskog, K.G., 1990. A panel model for political efficacy and responsiveness: an application of LISREL 7 with weighted least squares. *Qual. Quant.* 19, 716–723.
- Albus, M., Hubmann, W., Ehrenberg, Ch., Forcht, U., Mohr, F., Sobizack, N., Wahlheim, C., Hecht, S., 1996. Neuropsychological impairment in first-episode and chronic schizophrenic patients. *Eur. Arch. Psychiatry Clin. Neurosci.* 246, 249–255.
- American Psychiatric Association, 1994. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. American Psychiatric Association, Washington, DC.
- Asarnow, R.F., MacCrimmon, D.J., 1978. Residual performance deficit in clinically remitted schizophrenics: a marker of schizophrenia? *J. Abnorm. Psychol.* 87, 597–608.
- Bell, M.D., Lysaker, P.H., Beam-Goulet, J.L., Milstein, R.M., Lindenmayer, J.P., 1994a. Five-component model of schizophrenia: assessing the factorial invariance of the Positive and Negative Syndrome Scale. *Psychiatry Res.* 52, 295–303.
- Bell, M.D., Lysaker, P.H., Milstein, R.M., Beam-Goulet, J.L., 1994b. Concurrent validity of the cognitive component of schizophrenia: relationship of PANSS scores to neuropsychological assessments. *Psychiatry Res.* 54, 51–58.
- Bentler, P.M., 1995. EQS 6 Structural Equations Program Manual. Multivariate Software Inc., Encino.
- Bentler, P.M., Wu, E.J.C., 1995. EQS for Windows User's Guide. Multivariate Software Inc., Encino.

- Bentler, P.M., Berkane, M., Kano, Y., 1991. Covariance structure analysis under a simple kurtosis model. In: Keramidis, E.M. (Ed.), *Computing Science and Statistics*. Interface Foundation of North America, Fairfax Station, pp. 463–465.
- Bleuler, E., 1950. *Dementia Praecox or the Group of Schizophrenias*. International Universities Press, New York.
- Bowie, C.R., Harvey, P.D., 2005. Cognition in schizophrenia: impairments, determinants, and functional importance. *Psychiatr. Clin. North Am.* 28 (613–633), 626.
- Bowie, C.R., Reichenberg, A., Patterson, T.L., Heaton, R.K., Harvey, P.D., 2006. Determinants of real-world functional performance in schizophrenia subjects: correlations with cognition, functional capacity, and symptoms. *Am. J. Psychiatry* 163, 418–425.
- Bowie, C.R., Leung, W.W., Reichenberg, A., McClure, M.M., Patterson, T.L., Heaton, R.K., Harvey, P.D., 2008. Predicting schizophrenia patients' real-world behavior with specific neuropsychological and functional capacity measures. *Biol. Psychiatry* 63, 505–511.
- Bozikas, V.P., Kosmidis, M.H., Kioperlidou, K., Karavatos, A., 2004. Relationship between psychopathology and cognitive functioning in schizophrenia. *Compr. Psychiatry* 45, 392–400.
- Brown, T.A., 2006. *Confirmatory Factor Analysis for Applied Research*. Guilford Press, New York.
- Bryson, G., Bell, M., Greig, T., Kaplan, E., 1999. Internal consistency, temporal stability and neuropsychological correlates of three cognitive components of the Positive and Negative Syndrome Scale (PANSS). *Schizophr. Res.* 38, 27–35.
- Byrne, B.M., 2006. *Structural Equation Modeling With EQS: Basic Concepts, Applications, and Programming*, Second ed. Erlbaum, Mahwah.
- Cameron, A.M., Oram, J., Geffen, G.M., Kavanagh, D.J., McGrath, J.J., Geffen, L.B., 2002. Working memory correlates of three symptom clusters in schizophrenia. *Psychiatry Res.* 110, 49–61.
- Citron, L., Meng, X., Hochfeld, M., 2011. Efficacy of iloperidone in schizophrenia: a PANSS five-factor analysis. *Schizophr. Res.* 131, 75–81.
- Cornblatt, B.A., Lenzenweger, M.F., Dworkin, R.H., Erlenmeyer-Kimling, L., 1992. Childhood attentional dysfunctions predict social deficits in unaffected adults at risk for schizophrenia. *Br. J. Psychiatry Suppl.* 18, 59–64.
- Crow, T.J., 1980. Molecular pathology of schizophrenia: more than one disease process? *Br. Med. J.* 280, 66–68.
- Cuesta, M.J., Peralta, V., Caro, F., De Leon, J., 1995. Schizophrenic syndrome and Wisconsin Card Sorting Test card dimensions. *Psychiatry Res.* 58, 45–51.
- Daban, C., Amado, I., Bayle, F., Gut, A., Willard, D., Bourdel, M.C., Loo, H., Olie, J.P., Millet, B., Krebs, M.O., Poirier, M.F., 2002. Correlation between clinical syndromes and neuropsychological tasks in unmedicated patients with recent onset schizophrenia. *Psychiatry Res.* 113, 83–92.
- Dibben, C.R., Rice, C., Laws, K., McKenna, P.J., 2009. Is executive impairment associated with schizophrenic syndromes? A meta-analysis. *Psychol. Med.* 39, 381–392.
- Dollfus, S., Petit, M., 1995. Principal-component analyses of PANSS and SANS-SAPS in schizophrenia: their stability in an acute phase. *Eur. Psychiatry* 10, 97–106.
- Drake, R.J., Dunn, G., Tarrier, N., Haddock, G., Haley, C., Lewis, S., 2003. The evolution of symptoms in the early course of non-affective psychosis. *Schizophr. Res.* 63, 171–179.
- Ehmann, T.S., Khanbhai, I., Macewan, G.W., Smith, G.N., Honer, W.G., Flynn, S., Altman, S., 2004. Neuropsychological correlates of the PANSS cognitive factor. *Psychopathology* 37, 253–258.
- Eisenberg, D.P., Berman, K.F., 2010. Executive function, neural circuitry, and genetic mechanisms in schizophrenia. *Neuropsychopharmacology* 35, 258–277.
- El Yazaji, M., Battas, O., Agoub, M., Moussaoui, D., Gutknecht, C., Dalery, J., d'Amato, T., Saoud, M., 2002. Validity of the depressive dimension extracted from principal component analysis of the PANSS in drug-free patients with schizophrenia. *Schizophr. Res.* 56, 121–127.
- Emsley, R., Rabinowitz, J., Torremans, M., RIS-INT-35 Early Psychosis Global Working Group, 2003. The factor structure for the Positive and Negative Syndrome Scale (PANSS) in recent-onset psychosis. *Schizophr. Res.* 61, 47–57.
- Erlenmeyer-Kimling, L., Cornblatt, B., 1978. Attentional measures in a study of children at high-risk for schizophrenia. *J. Psychiatr. Res.* 14, 93–98.
- Field, A., 2009. *Discovering Statistics Using SPSS*, 3rd ed. Sage Publications, Thousand Oaks, CA.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1995. *Structured Clinical Interview for DSM-IV Axis I Disorders—Patient Edition (SCID-I/P, Version 2.0)*. Biometrics Research Department, New York State Psychiatric Institute, New York.
- Fredrikson, D., Steiger, J., MacEwan, G., Altman, S., Kopala, L., Flynn, S., Liddle, P., Honer, W., 1997. PANSS symptom factors in schizophrenia. *Schizophr. Res.* 24, 15.
- Fresán, A., De la Fuente-Sandoval, C., Lozaga, C., García-Anaya, M., Meyenberg, N., Nicolini, H., Apiquian, R., 2005. A forced five-dimensional factor analysis and concurrent validity of the Positive and Negative Syndrome Scale in Mexican schizophrenia patients. *Schizophr. Res.* 72, 123–129.
- Fuller, R., Nopoulos, P., Arndt, S., O'Leary, D., Ho, B.C., Andreasen, N.C., 2002. Longitudinal assessment of premorbid cognitive functioning in patients with schizophrenia through examination of standardized scholastic test performance. *Am. J. Psychiatry* 159, 1183–1189.
- Goldstein, G., Shermansky, W.J., 1995. Influences on cognitive heterogeneity in schizophrenia. *Schizophr. Res.* 18, 59–69.
- Good, K.P., Rabinowitz, J., Whitehorn, D., Harvey, P.D., DeSmedt, G., Kopala, L.C., 2004. The relationship of neuropsychological test performance with the PANSS in anti-psychotic naive, first-episode psychosis patients. *Schizophr. Res.* 68, 11–19.
- Green, M.F., 1996. What are the functional consequences of neurocognitive deficits in schizophrenia? *Am. J. Psychiatry* 153, 321–330.
- Green, M.F., Kern, R.S., Braff, D.L., Mintz, J., 2000. Neurocognitive deficits and functional outcome in schizophrenia: are we measuring the "right stuff"? *Schizophr. Bull.* 26, 119–136.
- Harvey, P.D., Howanitz, E., Parrella, M., White, L., Davidson, M., Mohs, R.C., Hoblyn, J., Davis, K.L., 1998. Symptoms, cognitive functioning, and adaptive skills in geriatric patients

- with lifelong schizophrenia: a comparison across treatment sites. *Am. J. Psychiatry* 155, 1080–1086.
- Harvey, P.D., Serper, M.R., White, L., Parrella, M.J., McGurk, S.R., Moriarty, P.J., Bowie, C., Vadhan, N., Friedman, J., Davis, K.L., 2001. The convergence of neuropsychological testing and clinical ratings of cognitive impairment in patients with schizophrenia. *Compr. Psychiatry* 42, 306–313.
- Heinrichs, R.W., Awad, A.G., 1993. Neurocognitive subtypes of chronic schizophrenia. *Schizophr. Res.* 9, 49–58.
- Higashima, M., Urata, K., Kawasaki, Y., Maeda, Y., Sakai, N., Mizukoshi, C., Nagasawa, T., Kamiya, T., Yamaguchi, N., Koshino, Y., 1998. P300 and the thought disorder factor extracted by factor-analytic procedures in schizophrenia. *Biol. Psychiatry* 44, 115–120.
- Hofer, A., Niedermayer, B., Kemmler, G., Rettenbacher, M.A., Trebo, E., Widschwendter, C.G., Fleischhacker, W.W., 2007. Cognitive impairment in schizophrenia: clinical ratings are not a suitable alternative to neuropsychological testing. *Schizophr. Res.* 92, 126–131.
- Hutton, S.B., Puri, B.K., Duncan, L.J., Robbins, T.W., Barnes, T.R., Joyce, E.M., 1998. Executive function in first-episode schizophrenia. *Psychol. Med.* 28, 463–473.
- Joyce, E.M., Hutton, S.B., Mutsatsa, S.H., Barnes, T.R., 2005. Cognitive heterogeneity in first episode schizophrenia. *Br. J. Psychiatry* 187, 516–522.
- Kawasaki, Y., Maeda, Y., Sakai, N., Higashima, M., Urata, K., Yamaguchi, N., Kurachi, M., 1994. Evaluation and interpretation of symptom structures in patients with schizophrenia. *Acta Psychiatr. Scand.* 89, 399–404.
- Kay, S.R., Sevy, S., 1990. Pyramidal model of schizophrenia. *Schizophr. Bull.* 16, 537–545.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261–276.
- Keefe, R.S., Fenton, W.S., 2007. How should DSM-V criteria for schizophrenia include cognitive impairment? *Schizophr. Bull.* 33, 912–920.
- Kline, R.B., 2010. *Principles and Practice of Structural Equation Modeling*. (Guilford, New York).
- Koren, D., Seidman, L.J., Harrison, R.H., Lyons, M.J., Kremen, W.S., Caplan, B., Goldstein, J.M., Faraone, S.V., Tsuang, M.T., 1998. Factor structure of the Wisconsin Card Sorting Test: dimensions of deficit in schizophrenia. *Neuropsychology* 12, 289–302.
- Kraepelin, E., 1919. *Dementia Praecox and Paraphrenia*. E & S Livingstone, Edinburgh.
- Kremen, W.S., Buka, S.L., Seidman, L.J., Goldstein, J.M., Koren, D., Tsuang, M.T., 1998. IQ decline during childhood and adult psychotic symptoms in a community sample: a 19-year longitudinal study. *Am. J. Psychiatry* 155, 672–677.
- Kuha, A., Tuulio-Henriksson, A., Eerola, M., Perälä, J., Suvisaari, J., Partonen, T., Lönnqvist, J., 2007. Impaired executive performance in healthy siblings of schizophrenia patients in a population-based study. *Schizophr. Res.* 92, 142–150.
- Lançon, C., Auquier, P., Nayt, G., Reine, G., 2000. Stability of the five-factor structure of the Positive and Negative Syndrome Scale (PANSS). *Schizophr. Res.* 42, 231–239.
- Lee, K.-H., Harris, A.W., Loughland, C.M., Williams, L.M., 2003. The five symptom dimensions and depression in schizophrenia. *Psychopathology* 36, 226–233.
- Lehoux, C., Gobeil, M.H., Lefebvre, A.A., Maziade, M., Roy, M.A., 2009. The five-factor structure of the PANSS: a critical review of its consistency across studies. *Clin. Schizophr. Relat. Psychoses* 3, 103–110.
- Lépine, J.P., 1991. Dimensions positives et négatives dans les schizophrénies. *Cah. prism* 1, 23–29.
- Levine, S.Z., Rabinowitz, J., 2007. Revisiting the 5 dimensions of the Positive and Negative Syndrome Scale. *J. Clin. Psychopharmacol.* 27, 431–436.
- Lindenmayer, J.P., Bernstein-Hyman, R., Grochowski, S., 1994. Five-factor model of schizophrenia. Initial validation. *J. Nerv. Ment. Dis.* 182, 631–638.
- Lindenmayer, J.P., Grochowski, S., Hyman, R.B., 1995. Five factor model of schizophrenia: replication across samples. *Schizophr. Res.* 14, 229–234.
- Lindstrom, E., von Knorring, L., 1993. Principal component analysis of the Swedish version of the Positive and Negative Syndrome Scale for schizophrenia. *Nord. J. Psychiatry* 47, 257–263.
- Loewenthal, K.M., 1996. *An Introduction to Psychological Tests and Scales*. UCL Press Limited, London.
- Lykouras, L., Oulis, P., Psarros, K., Daskalopoulou, E., Botsis, A., Christodoulou, V.N., Stefanis, C., 2000. Five-factor model of schizophrenic psychopathology: how valid is it? *Eur. Arch. Psychiatry Clin. Neurosci.* 250, 93–100.
- Marder, S.R., Davis, J.M., Chouinard, G., 1997. The effects of risperidone on the five dimensions of schizophrenia derived by factor analysis: combined results of the North American trials. *J. Clin. Psychiatry* 58, 538–546.
- Mardia, K.V., 1970. Measures of multivariate skewness and kurtosis with applications. *Biometrika* 57, 519–530.
- Martínez-Arán, A., Penadés, R., Vieta, E., Colom, F., Reinares, M., Benabarre, A., Salamero, M., Gastó, C., 2002. Executive function in patients with remitted bipolar disorder and schizophrenia and its relationship with functional outcome. *Psychother. Psychosom.* 71, 39–46.
- Mass, R., Schoemig, T., Hitschfeld, K., Wall, E., Haasen, C., 2000. Psychopathological syndromes of schizophrenia: evaluation of the dimensional structure of the Positive and Negative Syndrome Scale. *Schizophr. Bull.* 26, 167–177.
- Mohamed, S., Paulsen, J.S., O'Leary, D., Arndt, S., Andreasen, N., 1999. Generalized cognitive deficits in schizophrenia: a study of first-episode patients. *Arch. Gen. Psychiatry* 56, 749–754.
- Nieuwenstein, M.R., Aleman, A., de Haan, D.H., 2001. Relationship between symptom dimensions and neurocognitive functioning in schizophrenia: a meta-analysis of WCST and CPT studies. *J. Psychiatry Res.* 35, 119–125.
- Nuechterlein, K.H., 1983. Signal detection in vigilance tasks and behavioral attributes among offspring of schizophrenic mothers and among hyperactive children. *J. Abnorm. Psychol.* 92, 4–28.
- Nuechterlein, K.H., Dawson, M.E., Gitlin, M., Ventura, J., Goldstein, M.J., Snyder, K.S., Yee, C.M., Mintz, J., 1992. Developmental processes in schizophrenic disorders: longitudinal studies of vulnerability and stress. *Schizophr. Bull.* 18, 387–425.
- Pantelis, C., Barnes, T.R., Nelson, H.E., Tanner, S., Weatherley, L., Owen, A.M., Robbins, T.W., 1997. Frontal-striatal cognitive deficits in patients with chronic schizophrenia. *Brain* 120, 1823–1843.
- Paulhus, D.L., Robins, R.W., Trzesniewski, K.H., Tracy, J.L., 2004. Two replicable suppressor situations in personality research. *Multivar. Behav. Res.* 39, 303–328.
- Peña, J., Ojeda, N., Segarra, R., Eguiluz, J.I., García, J., Gutiérrez, M., 2011. Executive functioning correctly classified diagnoses in patients with first-episode psychosis: evidence from a 2-year longitudinal study. *Schizophr. Res.* 126, 77–80.
- Penadés, R., Catalán, R., Puig, O., Masana, G., Pujol, N., Navarro, V., Guarch, J., Gastó, C., 2010. Executive function needs to be targeted to improve social functioning with Cognitive Remediation Therapy (CRT) in schizophrenia. *Psychiatry Res.* 177, 41–45.
- Peralta, V., Cuesta, M.J., 1994. Validation of Positive and Negative Symptom Scale (PANSS) in a sample of Spanish schizophrenic patients. *Actas Luso Esp. Neurol. Psiquiatr. Cienc. Afines* 22, 171–177.
- Reed, R.A., Harrow, M., Herbener, E.S., Martin, E.M., 2002. Executive function in schizophrenia: is it linked to psychosis and poor life functioning? *J. Nerv. Ment. Dis.* 190, 725–732.
- Reichenberg, A., 2010. The assessment of neuropsychological functioning in schizophrenia. *Dialogues Clin. Neurosci.* 12, 383–392.
- Rhinewine, J.P., Lencz, T., Thaden, E.P., Cervellione, K.L., Burdick, K.E., Henderson, I., Bhaskar, S., Keelisen, L., Kane, J., Kohn, N., Fisch, G.S., Bilder, R.M., Kumra, S., 2005. Neurocognitive profile in adolescents with early-onset schizophrenia: clinical correlates. *Biol. Psychiatry* 58, 705–712.
- Robbins, T.W., Arnsten, A.F., 2009. The neuropharmacology of fronto-executive function: monoaminergic modulation. *Annu. Rev. Neurosci.* 32, 267–287.
- Rocca, P., Montemagni, C., Castagna, F., Giugiario, M., Scalese, M., Bogetto, F., 2009. Relative contribution of antipsychotics, negative symptoms and executive functions to social functioning in stable schizophrenia. *Prog. Neuropsychopharmacol. Biol. Psychiatry* 33, 373–379.
- Saykin, A.J., Shtasel, D.L., Gur, R.E., Kester, D.B., Mozley, L.H., Stafniak, P., Gur, R.C., 1994. Neuropsychological deficits in neuroleptic naive patients with first-episode schizophrenia. *Arch. Gen. Psychiatry* 51, 124–131.
- Tirupati, S.N., Padmavati, R., Thara, R., McCreadie, R.G., 2006. Psychopathology in never treated schizophrenia. *Compr. Psychiatry* 47, 1–6.
- Torrey, E.F., 2002. Studies of individuals with schizophrenia never treated with antipsychotic medication: a review. *Schizophr. Res.* 58, 101–115.
- Van den Oord, E.J., Rujescu, D., Robles, J.R., Giegling, I., Birrell, C., Bukszar, J., Murrelle, L., Möller, H.J., Middleton, L., Muglia, P., 2006. Factor structure and external validity of the PANSS revisited. *Schizophr. Res.* 82, 213–223.
- Van der Gaag, M., Hoffman, T., Remijsen, M., Jihman, R., de Haan, L., van Meijel, B., van Harten, P.N., Valmaggia, L., de Hert, M., Cuijpers, A., Wiersma, D., 2006. The five factor model of the Positive and Negative Syndrome Scale II: a ten-fold cross-validation of a revised model. *Schizophr. Res.* 85, 280–287.
- Velligan, D.I., Mahurin, R.K., Diamond, P.L., Hazelton, B.C., Eckert, S.L., Miller, A.L., 1997. The functional significance of symptomatology and cognitive function in schizophrenia. *Schizophr. Res.* 25, 21–31.
- Wallwork, R.S., Fortgang, R., Hashimoto, R., Weinberger, D.R., Dickinson, D., 2012. Searching for a consensus five-factor model of the Positive and Negative Syndrome Scale for schizophrenia. *Schizophr. Res.* 137, 246–250.
- Weickert, T., Goldberg, T., Gold, J., Bigelow, L.B., Egan, M.F., Weinberger, D.R., 2000. Cognitive impairment in patients with schizophrenia displaying preserved and compromised intellect. *Arch. Gen. Psychiatry* 57, 907–913.
- White, L., Harvey, P.D., Opler, L., Lindenmayer, J.P., 1997. Empirical assessment of the factorial structure of clinical symptoms in schizophrenia. A multisite, multimodel evaluation of the factorial structure of the Positive and Negative Syndrome Scale. The PANSS Study Group. *Psychopathology* 30, 263–274.
- Wolthaus, J.E., Dingemans, P.M., Schene, A.H., Linszen, D.H., Knegtering, H., Holthausen, E.A., Cahn, W., Hijman, R., 2000. Component structure of the Positive and Negative Syndrome Scale (PANSS) in patients with recent-onset schizophrenia and spectrum disorders. *Psychopharmacology (Berlin, Ger.)* 150, 399–403.