The "Obsessive Paradox"

The Complex Relationship Between Cognitive and Obsessive Dimensions in Schizophrenia

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Abstract: The objective of the study was to investigate the relationship between cognitive functions and obsessive-compulsive dimension in schizophrenia and a possible moderating effect of schizophrenia symptom dimensions on this association. Sixty-one schizophrenia patients were administered the Positive and Negative Syndrome Scale, the Yale-Brown Obsessive-Compulsive Scale (YBOCS), and the Matrics Consensus Cognitive Battery. A U-shaped curve described a gradual transition from an inverse association to a positive relationship between YBOCS and processing speed scores, along a severity gradient of obsessive dimension. This effect ("the obsessive paradox") was not moderated by other symptom dimensions. The present study suggests that severe obsessive-compulsive symptoms may participate to counterbalance processing speed impairment independently from other symptom dimensions. These results highlight the complexity of the relationship between cognitive and obsessive dimensions in schizophrenia.

Key Words: Obsessive-compulsive symptoms, processing speed, negative symptoms, disorganization, dimension

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Schizophrenia is highly heterogeneous in clinical presentation and course (Lee et al., 2009). A dimensional approach, rather than a categorical one, may better grasp this heterogeneity due to multiple interactions of relatively distinct psychopathological dimensions (Insel, 2010; Tandon et al., 2009). After the "classical" tripartite model (positive, negative, disorganization dimensions; Liddle, 1987), schizophrenia is currently described as a more complex architecture including positive, negative, disorganization, cognitive, mood and motor symptom dimensions (Tandon et al., 2009). Therefore, the different clinical features and outcome in schizophrenia may partly reflect a constellation of multiple interactions among different symptom dimensions. In the last decade, obsessive-compulsive (OC) dimension has received increasing attention because of the high rates of OC symptoms (OCS) in schizophrenia (up to 30% of schizophrenia patients; De Haan et al., 2013; Swets et al., 2014) and its association with a greater disability and poorer prognosis (Schirmbeck et al., 2013; Tonna et al., 2015). Interestingly, our previous studies have suggested that OC dimension interacts with other symptom dimensions (namely, disorganization) in impacting social functioning with a "dual" effect ("Janus Bifrons" effect) along a severity continuum (from protective to adverse; Tonna et al., 2016a, 2016b).

Because cognitive deficits in schizophrenia are highly stable over time and associated with functional impairment (Grover et al., 2017; Ventura et al., 2009), the relationship between comorbid OCSs and cognitive function has been extensively investigated.

The "double jeopardy" hypothesis proposes that in patients with schizophrenia OCS may induce additional cognitive deficits in those domains typically impaired in "pure" OC disorder (OCD; Bottas et al., 2005; Lysaker et al., 2000; Tibbo and Warneke, 1999), such as processing speed, visuo-spatial memory, and executive functions (Chamberlain et al., 2005). However, whereas some studies found a specific pattern of cognitive impairment in OCS-comorbid patients (Michalopoulou et al., 2014; Patel et al., 2010; Schirmbeck et al., 2013), others failed to find significant differences with respect to non-OCS patients (Kazhungil et al., 2017). Some studies even reported a better performance in specific cognitive domains in the "schizo-obsessive" group (Kontis et al., 2016). The apparent inconsistency of results may be partly explained by the differences in the definition of diagnostic criteria for OCS, the heterogeneity of the neuropsychological tests used, or by a scarcely exhaustive neurocognitive assessment (Michalopoulu et al., 2014). Moreover, previous studies do not take into account the complexity of relationship between OC dimension and other schizophrenia symptom dimensions; particularly the possibility that the association between OCS and specific cognitive domains may be mediated and/or moderated by other symptom dimensions. With this respect, it is noteworthy that negative symptoms appear to mediate the relationship between neurocognition and outcome (Ventura et al., 2009) and that disorganization moderates the association between neurocognition and metacognitive processes (Minor et al., 2015). Moreover, strong associations have been found among symptoms of psychosis, OCS, and metacognitive beliefs in a nonclinical sample (Hagen et al., 2017).

Therefore, the aim of the present study was to investigate the association between OCS and cognitive impairment in schizophrenia through the lens of a pure dimensional model and using an exhaustive and specific neuropsychological battery for schizophrenia cognitive impairment. The second objective was to evaluate if the relationship between OCS and cognitive functions might be mediated and/or moderated by other schizophrenia symptom dimensions.

MATERIAL AND METHODS

Participants

All participants were recruited from the Psychiatric Unit of the University Hospital of Parma from January 2014 to December 2015. Patients were included in the study if 1) they were aged older than 17 years; 2) they received a diagnosis of schizophrenia, according to *DSM-IV* criteria (American Psychiatric Association, 2000); 3) a written informed consent to study participation was obtained; and 4) the resolution of the acute phase of illness was reached, defined as the achievement of a clinical stabilization phase with initial symptom response and reduced psychotic symptoms severity (American Psychiatric Association, 1997). The latter was described as a reduction in psychoticism dimension (hallucinations and delusions) to a low to mild symptom intensity level (Andreasen et al., 2005). Patients were excluded if they were affected by 1) a current mental disorder related to a general medical condition

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or to a drug or alcohol abuse or dependence; and 2) a cognitive disorder (Mini-Mental State Examination score lower than 25), which could impair the compliance with testing procedures.

Instruments and Procedures

The Structured Clinical Interview for *DSM-IV* (SCID-I; Mazzi et al., 2000) confirmed the diagnosis of schizophrenia. The three-factor model of the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987) was adopted to assess the severity of psychotic symptoms. In addition to PANSS positive, negative, and general psychopathology scores, we sought to evaluate the disorganization dimension since its clinical relevance. The PANSS disorganization score was computed by summing the items of conceptual disorganization (P2), difficulty in abstraction (N5), stereotyped thinking (N7), mannerism (G5), disorientation (G10), poor attention (G11), lack of judgment and insight (G12), and disturbance of volition (G13; van der Gaag et al., 2006). The severity of OCS was measured with the Yale-Brown Obsessive-Compulsive Scale (YBOCS; Goodman et al., 1989). The Matrics Consensus Cognitive Battery (Nuechterlein et al., 2008) was adopted for the cognitive assessment of all participants. This battery, specifically designed to measure neurocognitive functioning in schizophrenia, assesses seven neurocognitive domains: processing speed, attention, working memory, verbal learning, visual learning, reasoning and problem solving, and social cognition. In this study, we calculated a neurocognitive composite score that included all MATRICS subtests with the exception of the Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) that measures social cognition. The neurocognition composite was created excluding the MSCEIT and providing equal weight to the remaining six domains (Minor et al., 2015).

A trained psychiatrist interviewed patients after the resolution of the acute phase of illness to guarantee an adequate cooperation to the assessment.

Treatment

All patients were treated with antipsychotics. Patients who had moderate to severe OCSs also received a serotoninergic medication.

Statistical Analysis

First, Spearman's correlations (two tailed) were used to investigate the relationship among neurocognition (MATRICS total scores), sociodemographic features, OC dimension (YBOCS total score), and schizophrenia symptom dimensions (PANSS total, positive, negative, disorganization scores).

A curve fit analysis was then conducted to investigate the relationship between cognitive functioning (dependent variable: MATRICS domains score) and OCSs (independent variable: YBOCS total score). In particular, the analysis was used to evaluate whether the relationship between OC dimension and cognitive functioning differed at varying levels of OCS severity. Next, a multivariate curvilinear regression analysis (enter method) was performed to evaluate whether OCS predicted cognitive functioning regardless of other clinical and demographic features. In each model, YBOCS score and PANSS positive, disorganization, general psychopathology, and negative symptoms scores were entered as independent variables, whereas MATRICS domains score was the dependent variable. The historical and sociodemographic features, previously found to be related to MATRICS domains score in bivariate correlations, were controlled for in the regression analyses.

Subsequently, in case of association between YBOCS total score and the other covariates in the prediction of the outcomes (*i.e.*, cognitive functioning as dependent variable), we aimed at performing a series of mediation and moderation analyses using PROCESS for SPSS (model 1–4; Hayes, 2013) covarying as appropriate. All statistical analyses were performed with SPSS for Windows (version 23.0; SPSS Inc, Chicago, IL).

RESULTS

Participants

Sixty-one patients, 42 male (68.9%) and 19 female (31.1%), were enrolled into the study. The historical, sociodemographic, and clinical features are reported in Table 1.

Treatment

Fifty-five patients (90.2%) were treated with oral antipsychotics, and the remaining six patients (9.8%) received a long-acting antipsychotic. Twenty-one (34.4%) received a first-generation antipsychotic and 32 (52.5%) a second-generation antipsychotic. Eight patients (13.1%) were treated with clozapine. The mean chlorpromazine equivalent dose was 432 ± 121 mg/d.

OCS and Cognitive Functions

The YBOCS and MATRICS scores are reported in Table 1, and their correlations with schizophrenic symptoms are depicted in Table 2.

No association was found between MATRICS total score and PANSS positive symptoms score or YBOCS total score; a correlation

TABLE 1. Sociodemographic and Clinical Features in Patients With Schizophrenia

	Patients (n = 61)	
	n	**%**
Sex		
Male	42	68.9
Marital status		
Never married	49	80.3
Married	7	11.5
Divorced/widowed	5	8.2
Working status		
Never occupied	41	67.2
Occupied/student	20	32.8
Living status		
Living alone	6	9.8
Living with someone	55	91.2
	Mean ± SD	
Age, yrs	38.41 ± 12.53	
Age at onset, yrs	23.89 ± 5.96	
Illness duration, yrs	41.13 ± 11.87	
Hospital admission, *n*	2.98 ± 2.46	
PANSS		
Positive score	14.87 ± 5.92	
Negative score	22.48 ± 7.03	
General psychopathology score	38.98 ± 10.28	
Disorganization score	19.75 ± 5.74	
Total score	75.98 ± 17.26	
MATRICS		
Processing speed	26.52 ± 13.44	
Attention/vigilance	36.16 ± 11.63	
Working memory	36.16 ± 11.83	
Verbal learning	37.00 ± 7.12	
Visual learning	39.52 ± 14.61	
Problem solving	35.67 ± 8.75	
Total score	211.05 ± 49.67	
YBOCS score	10.08 ± 11.65	

TABLE 2. Spearman's Correlations Between Cognitive Function, Obsessive Dimension, and Schizophrenic Symptoms in the Study Sample ($n = 61$)

Variables	1	1a	1b	1c	1d	2	3	3a	3b	3c	3d	3e	3f
1 PANSS total scores	-												
1a. Positive scale	0.631**	-											
1b. Negative scale	0.684**	0.228	-										
1c. Disorganization	0.673**	0.433**	0.622**	-									
1d. General psychopathology	0.866**	0.408**	0.384**	0.520**	-								
2 YBOCS score	0.073	−0.114	0.016	−0.108	0.132	-							
3 MATRICS total score	−0.167	0.079	−0.338**	−0.375**	−0.097	−0.192	-						
3a. Processing speed	−0.175	0.065	−0.324*	−0.363**	−0.103	−0.282*	0.899**	-					
3b. Attention/vigilance	−0.160	−0.066	−0.143	−0.156	−0.115	−0.114	0.483**	0.346**	-				
3c. Working memory	−0.136	0.093	−0.241	−0.324*	−0.117	−0.114	0.797**	0.719**	0.237	-			
3d. Verbal learning	−0.073	0.080	−0.370**	−0.143	0.057	−0.066	0.739**	0.636**	0.262*	0.587**	-		
3e. Visual learning	−0.074	0.023	−0.220	−0.297*	−0.002	−0.082	0.740**	0.598**	0.165	0.472**	0.525**	-	
3f. Problem solving	0.077	0.245	−0.051	0.042	0.046	−0.186	0.681**	0.588**	0.159	0.501**	0.396**	0.461**	-

**$p \leq 0.01$; *$p \leq 0.05$.

was found between MATRICS total score and PANSS negative and disorganization symptoms scores. Furthermore, a significant correlation was found between Processing Speed (PS) and YBOCS total score as well as between PS and both PANSS negative and disorganization symptoms score.

Curve Fit Analysis and Curvilinear Regression

The quadratic model was significant over the linear one ($B = 0.042$; $p = 0.011$; 95% confidence interval [CI], 0.010–0.074; change $R^2 = 0.106$; $p = 0.011$; Table 3). Therefore, a U-shaped curve described a gradual transition from an inverse association between YBOCS and PS scores to a positive relationship, along a severity gradient of OC dimension. Particularly, PS impairment worsened at increasing severity of YBOCS till to the inflexion point corresponding to YBOCS value of 18.5 (b1/2 × b2), then PS deficits improved for higher YBOCS scores (Fig. 1). The multivariate curvilinear regression analysis (enter method) confirmed the aforementioned pattern, after controlling for the effect of schizophrenia symptom dimensions and other potentially confounding variables (Table 4).

To evaluate the specificity of the above findings, cubic and exponential models were also tested, but none was found to explain a significantly higher amount of the variance in PS scores than the quadratic mode.

Moderation Analyses

Since no correlations were found between YBOCS total score and PANSS positive, negative, or disorganization scores, we did not further investigate any mediation mechanism due to schizophrenia symptoms in the relationship between OCS severity and PS deficits. Finally, we evaluated whether symptom dimensions of schizophrenia interacted with OCS in influencing PS score, following Hayes's (2013) procedure for assessing conditional effects of the moderator (PROCESS model 1). No significant interaction was detected between OCS and, respectively, negative, or disorganization symptoms in predicting PS deficits (PANSS negative symptoms X YBOCS^2 scores: $B = 0.001$; $p = 0.609$; 95% CI, −0.003 to 0.005; PANSS disorganization symptoms X YBOCS^2 scores: $B = 0.004$; $p = 0.272$; 95% CI, −0.003 to 0.011).

TABLE 3. Curve Estimation Analysis Comparing Linear and Quadratic Models for the YBOCS/PS Relationship in the Overall Sample

	Model Fit			Parameter Estimates		
	R^2	F	p	Constant	b1	b2
Linear model	0.059	3.679	0.060	29.343	−0.280	
Quadratic model	0.152	5.204	0.008	32.127	−1.480	0.040

DISCUSSION

The present study was aimed to evaluate the relationship between OC dimension and cognitive impairment under the specific interaction with schizophrenia symptom dimensions.

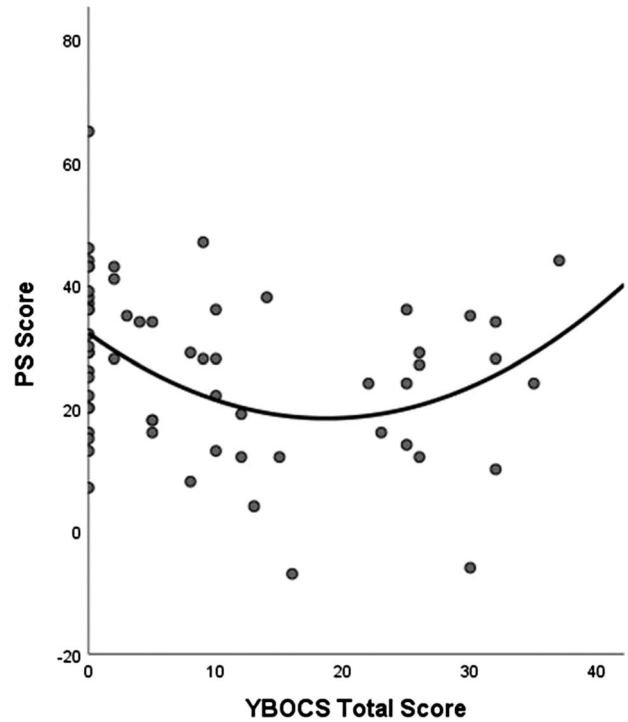

FIGURE 1. Curve fit estimation of the relationship between YBOCS and PS score in the overall sample.

TABLE 4. Curvilinear Regression Showing the Association between Obsessive-Compulsive Symptoms (YBOCS Score) and Processing Speed Symptoms and Demographic Covariates (Dependent Variable) Controlling for the Schizophrenia

	B	*SE*	*p*	95% CI
Education years	0.355	0.564	0.533	[−0.78, 1.49]
PANSS positive scale	0.345	0.298	0.252	[−0.25, 0.94]
PANSS negative scale	−0.296	0.276	0.289	[−0.85, 0.26]
PANSS disorganization	−0.712	0.365	0.057	[−1.45, 0.02]
$YBOCS^2$ score	0.037	0.16	0.020	[0.01, 0.068]

Although other studies investigated the association between cognitive functioning and OCS severity in schizophrenia (Meijer et al., 2013; Sahoo et al., 2018), the strength of the present study is the strictly dimensional model adopted. In fact, a dimensional model based on a gradient of OCS severity (rather than a categorical one) may better capture the complexity and heterogeneity in clinical presentation and outcome of schizophrenia spectrum (Insel, 2010; Tandon et al., 2009) as well as the different impact of OCS on other dimensions along a gradient of OC severity (Tonna et al., 2016a). Particularly, we sought to test if the relationship between cognitive performances and OCS might vary along a severity continuum of OC dimension.

Our results demonstrate a relationship between OC dimension and PS. The present finding was quite expected since PS has been found to be impaired in "pure" OCD patients compared with healthy controls (Chamberlain et al., 2005). Consistently, previous studies observed that schizophrenia patients with OCS had lower levels of PS score compared with schizophrenia patients without OCS, either in cross-sectional (Michalopoulu et al., 2014) or in longitudinal evaluations (Schirmbeck et al., 2013).

Interestingly, in the present study, PS score was differently associated with the severity of OCS. In fact, we observed a gradual transition from an inverse association (for mild and moderate OCS) to a direct relationship (for severe OCS) between YBOCS and PS scores; namely, PS score worsened up to the YBOCS value of 18.5, then it improved at higher YBOCS scores. This finding is in contrast with previous studies (Michalopoulu et al., 2014), which found PS impairment independent of the severity of OCS. The different model adopted in the studies (dimensional *vs*. categorical) may explain the conflicting results. In fact, a categorical approach might not be appropriate to capture such dual relationship of PS impairment along a severity continuum of OC dimension. The finding of a direct association between severe OCS and PS scores (the "obsessive paradox") is in line with previous studies, which suggested a positive effect of comorbid OCS on specific cognitive functions (especially executive functions and working memory) either in patients with schizophrenia (Borkowska et al., 2003; Kontis et al., 2016; Lee et al., 2009) or in individuals with at-risk mental states for psychosis (Soyata et al., 2018; Zink et al., 2014).

PS impairment is supposed to be a core feature in schizophrenia (Dickinson et al., 2007; Knowles et al., 2010; Ojeda et al., 2012), and it is also present either in individuals at high risk of schizophrenia (Chan et al., 2018; Niendam et al., 2007; Soyata et al., 2018) or in unaffected relatives of schizophrenia patients (Wang et al., 2007). PS appears to underlie higher cognitive processes, such as working memory and executive functions (Ojeda et al., 2012). Therefore, the present results would suggest that OC dimension exerts a role upon a key point of the hierarchical structure of neurocognition in schizophrenia.

Neuroimaging investigations have linked PD impairment with abnormal prefrontal cortex activity (Woodward et al., 2013) and disrupted brain connectivity (Karbasforoushan et al., 2015).

Consistently, our results also found a correlation between PS impairment and both negative and disorganization symptoms, which have been associated respectively with underactivity of prefrontal cortex (Dibben et al., 2009; Ventura et al., 2009) and disrupted connectivity between temporal and frontal lobes (Chan et al., 2018). On the contrary, positive symptoms did not exert any effect.

In the present study, the direct association of severe OCS on PS was confirmed also after controlling for other schizophrenia symptom dimensions; furthermore, this relationship does not occur through an interaction with negative or disorganization symptoms. Different symptomatic features of OCD (*e.g.*, intrusive thoughts, mental rituals) imply a specific impairment in cognitive inhibition processes (representing control over internal cognitions; Chamberlain et al., 2005). Although PS is impaired in "pure" OCD patients, we speculate that, in schizophrenia, severe OCS, leading to a failure to inhibit or shift attention from ongoing thoughts, may contribute to maintain PS, partly compensating cognitive impairment due to negative or disorganization symptoms.

Although the "dual effect" of OC dimension on functioning (with a transition from an improving to an adverse impact along a severity gradient) was replicated in the study, the effect of OC dimension on specific cognitive domains (PS) showed an opposite trend (with a transition from an inverse to a direct association). These data confirm that there are many different paths to social dysfunction, and that higher cognition may not necessarily led to higher social abilities (Lysaker et al., 2004). Moreover, the present data would confirm that the interplay among cognitive, psychopathologic, and psychosocial variables may be better captured by multiple, nonunidirectional pathways (Galderisi et al., 2018), which tend to vanish within a strict categorical model.

In keeping with the historical concept of "pseudoneurotic schizophrenia," (Hoch and Polatin, 1949), which emphasized the complex interplay between "neurotic" symptoms (including obsessive phenomena) and a primary psychotic illness (O'Connor et al., 2009), we suggest that indeed obsessive dimension may have a clinical relevance in schizophrenia spectrum. Particularly, in the present study, severe OCSs are associated with better cognitive performances (PS), independently from other symptom dimensions, whereas low OCS can mitigate functional impairment balancing the effect of underlying low disorganization symptoms. Altogether, these results highlight the clinical relevance of those forms of schizophrenia that have been neglected by a prototypical approach to diagnosis (Parnas, 2005).

It is still debated whether cognitive impairment associated to comorbid OCS in schizophrenia precedes the onset of OCS (Poyurovsky et al., 2012) or, alternatively, it represents their consequence (Moritz et al., 2012; Schirmbeck et al., 2016). Our finding of a dependency of PS on OCS severity would support the view that additional cognitive deficits related to OCS comorbidity may have a "state" component. However, the cross-sectional design of the study does not exclude that an OC cognitive impairment is already present before the development of OCS.

In the present study, we failed to find any correlation between OCS and higher cognitive processes (*i.e.*, memory or executive functions). We cannot exclude a counterbalancing effect of other basic cognitive processes on PS deficits such as to preserve higher cognitive functions (Holthausen et al., 2003).

The main limitation of our study concerns its cross-sectional design. In fact, the complex relationship between OC and cognitive dimensions, as well as the possible interactions with other symptom dimensions might vary over time. Moreover, these results should be viewed with the caveat of the small sample size. Larger longitudinal studies are needed to confirm our data. Another important limitation concerns the assessment of cognitive domains through the MATRICS consensus cognitive battery. In fact, the MATRICS is a comprehensive neurocognitive test-battery for schizophrenia, and it is not specifically focused on OCD related domains. Particularly, potential additional deficits (*e.g.*, cognitive and behavioral inhibitory control) due to comorbid OCS (Chamberlain et al., 2005) have not been investigated. Finally, the dosage of pharmacological medication was

not included as a possible confounder in the association between YBOCS and PS.

In summary, the present study highlights the complexity of the relationship between cognitive functions, OC, and schizophrenia symptom dimensions in schizophrenia. Particularly, our results suggest that in schizophrenia, severe OCS may participate to counterbalance PS impairment independently from other symptom dimensions.

DISCLOSURE

There are no conflicts of interest to declare.

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