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Executive control in chronic schizophrenia: A perspective from manual stimulus-response compatibility task performance

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Abstract

Background—Antisaccade deficits are a well-documented pathophysiological characteristic in schizophrenia. However, it is yet unclear whether these findings reflect a specific oculomotor deficit, general psychomotor impairment or disturbance in executive control mechanisms.

Methods—Performance in a manual stimulus-response compatibility (SRC) task and a neuropsychological test-battery covering different cognitive and motor domains were obtained in 28 patients with chronic schizophrenia. It was compared with a normative cohort of healthy subjects and validated by comparison with a sub-sample of that cohort consisting of 28 age, gender and education matched controls.

Results—Patients showed significantly worse performance than controls in tests requiring maintenance or manipulating of multiple components but were unimpaired in simple motor, memory or executive tasks. In the SRC task patients had a significantly worse performance in the congruent condition and also a significantly higher increase in error rate from the congruent to the incongruent condition. There were, however, neither a group difference nor a group-by-condition interaction with respect to reaction times.

Interpretation—Our results provide evidence against an isolated oculomotor deficit but also against an undifferentiated psychomotor dysfunction in chronic schizophrenia. Rather, in synopsis with previous reports on antisaccade performance, it becomes evident that the degree of impairment follows closely the amount of executive control required in a task, which in turn may relate to dysfunctional top-down bias of the prefrontal cortex arising from unstable task instructions.

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Keywords

Antisaccades; neuropsychology; integration; manual; inhibition; executive control

1. Introduction

Acute schizophrenic episodes are predominantly characterized by productive-psychotic symptoms. These, however, appear to have little influence on long-term quality of life, social and functional outcome (Eack and Newhill, 2007; Green, 1996; Palmer *et al.* 2009; Velligan and Bow-Thomas, 1999), while negative symptoms, cognitive and psychomotor impairments severely affect several outcome domains (Green, 1996; Morrens *et al.* 2007; Palmer *et al.* 2009). These data indicate the importance of considering neuropsychological deficits in treatment concepts. In this respect, executive dysfunction has been discussed as a core symptom of schizophrenia. Executive functions are a group of higher-order cognitive abilities which allow to plan and carry out goal-directed behavior enabling adaptive behavior, independent living and productivity. Consequently, patient's functional outcome seems to correlate with executive deficits (Green *et al.* 2000; Green, 1996; Velligan *et al.* 2000) and cognitive rehabilitation may enhance social and vocational outcome (Velligan and Bow-Thomas, 1999; Woodward *et al.* 2005; McEvoy, 2008).

A well-studied task for the assessment of executive dysfunction in schizophrenia is the antisaccade paradigm (Broerse *et al.* 2001). It entails the suppression of the reflexive prosaccade, shift of spatial attention, and initiation the correct antisaccade (Munoz and Everling, 2004). Antisaccades have been shown to be consistently impaired in schizophrenia (Broerse *et al.* 2001; Fukushima *et al.* 1988) as well as their unaffected relatives (Calkins *et al.* 2004) including non-schizophrenic co-twins (Ettinger *et al.* 2006) and have thus been proposed as an endophenotype of schizophrenia (Hutton and Ettinger, 2006; Karoumi *et al.* 2001; Turetsky *et al.* 2007). While this has raised the notion of abnormal fronto-striatal circuitry resulting in impaired anti-saccade execution, however, it remains unclear, whether these deficits relate to (a more specific) deficit in oculomotor control (Hutton and Ettinger, 2006; Munoz and Everling, 2004) or to (a more general) aberration in the executive control of goal-directed actions (Pierrot-Deseilligny *et al.* 2002).

The aim of the current study was to characterize the cognitive and psychomotor deficits in chronic schizophrenia. To address whether the known antisaccade deficits generalize to other effectors, patients and healthy controls performed a manual stimulus-response compatibility task. We expected results similar to those of saccade paradigms, which would indicate an overarching impairment of executive action control and stimulus-response mapping. In order to find associations between results of the SRC-paradigm and different neuropsychological domains, we additionally included a neuropsychological test battery covering motor, memory and executive functions at different stages of task complexity. In combination data from the SCR-paradigm, motor-, memory- and executive function tests should allow to address the hypothesis of an overarching executive control deficit in schizophrenia that extends well beyond the anti-saccade paradigm.

2. Material and Methods

28 patients (7 females; 20 inpatients, 4 day-treatment, 4 outpatients) with paranoid-hallucinatory schizophrenia (F20.0 in the ICD-10) were recruited. Diagnosis was established by review of the clinical records and two independent interviews with experienced clinical psychiatrists (K.H., S.H., M.B.-L., S.B.E., M.D.). As summarized in table 1, disease duration and symptomatology (as measured by the PANSS) were not particularly high in our sample,

which should allow to more specifically test for schizophrenic pathology rather than the marked general decline in cognitive functioning seen later in the course of the disease (Green *et al.* 2000; Palmer *et al.* 2009; Velligan and Bow-Thomas, 1999). The majority of patients (25) was treated by atypical anti-psychotics, 8 patients received (additionally) typical antipsychotics. Only 4 patients received other psychotropic medications (1× valproat, 2× SSRI, 1× venlafaxine), none had taken benzodiazepines for at least a week preceding the testing. Patients were free of psychiatric or neurological comorbidity, organic mental illness or developmental impairments and at least six months abstinent from illegal drugs. Significant extrapyramidal symptoms constituted an exclusion criteria and were not assured to be absent in the 28 patients included in this study by detailed clinical examination. Psychopathology was assessed by the Positive and Negative Syndrome Scale (PANSS).

As a control cohort, we recruited 68 healthy subjects (16 females) by local announcements. Exclusion criteria were family history of psychosis (to 2nd degree), a history of significant neurological or psychiatric illness (including substance or alcohol addiction) of the subjects or 1st degree relatives, any illegal drug use or intake of psychotropic medication in the last six months. All subjects age, (parental) education and intelligence estimates fell within the range of values seen in patients. All patients and controls gave informed written consent to the study protocol approved by the ethic committee of the RWTH Aachen University Hospital.

2.1 Neuropsychological test battery

Finger Tapping—Subjects tapped as rapidly as possible for 10s using the right and left index finger. Median number of taps from 3 trials per hand (separated by short breaks to prevent muscular fatigue) was used as the test score.

Pointing task—Subjects performed rapid horizontal pointing movements between two spots 30 cm apart using the right or left index finger (cf. CAPSIT Parkinson's disease test battery; (Defer *et al.* 1999)). Median number of 3 trials per hand represented motor coordination.

Digit Span subtest of the Wechsler Adult Intelligence Scale (Wechsler, 1981)—

The digit span forward (DS-F, repeating verbally presented sequences of numbers), is a measure of immediate verbal memory and attention, the digit span backward (DS-B, repeating the sequences backward), measures the ability to manipulate information in working memory.

Trail Making Test—In subtest A, participants were asked to connect numbered circles, subtest B required switching from numbers to letters. Here longer times indicate poorer performance. The TMT-A score mainly reflects visuoperceptual abilities, whereas the TMT-B score reflects working memory and task-switching (Sanchez-Cubillo *et al.* 2009).

Intelligence estimate—Crystalline (and hence presumably premorbid) intelligence was estimated by a multiple-choice vocabulary test (MWT-B; (Lehrl, 1989)), requiring to mark the actual word among four pseudo-words with increasing difficulty without time limitation.

2.2 Manual Stimulus-Response-Compatibility (SRC) Task

Participants were to respond as fast and as correctly as possible to briefly presented (200 ms) lateralized visual stimuli (red dot) by pressing a button using the right or left index finger (Cieslik *et al.* 2010): In the congruent condition, subjects were instructed to respond with the ipsilateral hand, i.e., responding with the left index finger to a left stimulus. In the incongruent condition they had to respond with the contralateral hand, i.e., pressing with

their left index finger to a right-sided stimulus. Task blocks were periodically alternated with short rest periods and started with a 500 ms instruction, informing the subject which of the two experimental conditions had to be performed in the upcoming block. Regardless of the condition, 21–24 events per block (randomized 50% left/right stimuli, number of events randomized to avoid anticipation-effects) were presented. The interstimulus interval was uniformly jittered (1300 – 1700 ms). Each condition (congruent, incongruent) was presented in 30 blocks. To make the testing more comfortable and prevent decreasing attention, the 30 blocks were split into five sessions (each containing 3 congruent / incongruent blocks). Between the sessions subjects had the possibility to rest up to five minutes. Order of blocks was pseudo-randomized and counterbalanced across sessions and subjects.

From the recorded data, the following measures were extracted: error rate (ER), reaction time (RT) for correct and erroneous responses congruent and incongruent responses as well as the incongruency effect, i.e., the difference in ERs or RTs between congruent and incongruent condition. RTs less than 150 ms or greater than 1600 ms were regarded as anticipation errors / missing responses and discarded from the analysis.

2.3 Data analysis

All measurements were analyzed offline using MATLAB (Mathworks, Natick, MA). First, variance in the data that could be explained by the confounding factors age, education, parental education and intelligence were removed by using a multiple regression model across both groups. This approach adjusted the obtained neuropsychological and experimental data for any variance systematically explained by (known) confounds. Subsequently, differences between the groups were analyzed by Wilcoxon–Mann–Whitney rank-sum tests. Correlations between measures of cognitive and motor performance as well as clinical characteristics were analyzed using Spearman's rank correlation coefficient. Correlations were deemed significant if they passed a threshold of $p < 0.05$ (Bonferroni-corrected for multiple comparisons).

Using a larger control cohort after data adjustment has a major advantage over the more conventional pair-wise matching strategy that it reduces the potential impact of the control group. Even if patients and controls are well matched, inter-individual variability in each group may influence the results of the ensuing comparison. By using a larger control cohort population variance will be approximated and effects due to outliers minimized. In order to evaluate this procedure against the more conventional matching approach, we also performed an additional analysis using only the data of a sub-group from this cohort, consisting of 28 healthy controls that were matched to the patients for age, gender, own and parental education as well as crystalline intelligence as measured by the MWT-B (cf. Table 1).

Results

3.1 Manual Stimulus-Response-Compatibility Task

The primary aim of this study was to assess whether schizophrenic patients show performance deficits in the manual SCR-task. From the well-documented abnormalities in an oculomotor SCR-task, i.e., the anti-saccade paradigm, we would hypothesize that patients would show an increased incongruence-effect on both error rates and reaction times also in the employed (manual) paradigm.

Error rate (ER)—In the SRC paradigm (Table 3), the mean ER of the patients was significantly increased in both conditions. Importantly, the difference in ERs between the congruent and the incongruent condition (incongruence-effect [ICE] on the ER) was also

significantly higher in patients, indicating worse switch-performance. These findings were completely replicated in the pair-wise matched sample.

Reaction times (RT)—RTs of patients were not significantly different from healthy subjects in either condition. Likewise, the ICE on RTs were not significantly different between groups. As higher ERs in patients could be a result of a higher impulsiveness, i.e., reflexive answers, we additionally analyzed the RTs of erroneous trials. Here, we assessed the difference between the RTs for correct and incorrect trials for either condition. Again, there was no significant difference between groups. Findings were replicated in the smaller control sample.

3.1 Neuropsychological test-battery—The secondary aim was to test whether find impairments in other functional domains (motor, memory, executive functions) were present in the same population of (moderately affected) schizophrenic patients. If there were a general deficit in executive control, we would hypothesize that patients show aberrant performance in particular in the more difficult tests in each domain.

In the basic motor tests, patients did not differ significantly from the control population in tapping speed but they were significantly slower in the more demanding pointing task (Table 2). Patients and controls performed similar on the TMT-A, but patients were significantly slower on the more complex subtest B. However, there was only a trend towards a group $\times$ difficulty interaction. While patients' immediate memory recall (DS-F) was not unimpaired, they were significantly worse than healthy controls when manipulation of memory content was required in the digit span backwards task. The results of this comparison between the patients and the larger control population were all replicated in the comparison with the smaller matched sample of controls with the exception of a significant difference emerging for the TMT - A performance in the latter comparison.

3.2 Associations between variables

In an additional, exploratory, analysis we furthermore assessed correlations between the different measures obtained from the SRC-task, the neuropsychological test battery as well as the socio-demographic and clinical data (Table 4). These correlations indicated an association between different measures of response time and psychomotor speed. In particular, RTs for correct responses in the congruent condition were correlated with the time needed for TMT-A and the pointing task. Time needed for the TMT-A, TMT-B and pointing tasks were also positively correlated with each other. RTs for erroneous responses in the incongruent condition were negatively correlated with finger tapping speed, i.e., patients who tapped faster were also faster in (erroneous) incongruent responses. In contrast, higher RTs in the congruent condition were negatively associated with higher chlorpromazine-equivalent dose.

ER in the congruent condition was positively correlated with duration of illness, while the incongruency effect on the ER (increase in errors) was positively correlated with the chlorpromazine-equivalent dose. TMT-B time (worse performance) was negatively correlated with the MWT-B intelligence estimates but positively correlated with higher general psychopathology as assessed by the PANSS and the number of hospital admissions. Time for the pointing task was correlated with the number of hospital admissions.

Finally, we observed several associations between test scores from the SCR-task or the neuropsychological battery and the individual item scores of the PANSS scale. All these correlations showed poorer performance to be associated with stronger psychopathology.

4. Discussion

The present study was intended to assess the hypothesis of an overarching executive control deficit in schizophrenia that spans multiple functional domains, including deficits in a manual version of the anti-saccade task (manual stimulus-response compatibility task). Patients with (early) chronic schizophrenia and a relatively low symptomatology nevertheless showed significantly worse performance in tasks that required maintaining or manipulating multiple components (DS-B, TMT-B, pointing) as compared to simpler tasks like the DS-F, TMT-A and finger tapping. In the SRC task there was a significant group main effect on task performance and a significant 'group $\times$ condition' interaction with the patients showing a greater increase in ER in the incongruent condition. There was, however, no group differences in any RT measure. In general these observations are well in line with the rather good clinical condition, confirming that the assessed patients do not (yet) show a general decline in overall cognitive and motor performance. Rather they seem to feature specific deficits related to the amount of required executive control. These deficits are well in line with the original hypothesis and may represent a core pathology in this disorder.

4.1 Neuropsychological impairments

The neuropsychological test battery indicated a consistent pattern of impairments in chronic schizophrenia with decreased performance seen in the more complex task of each. In the motor tests, this distinction was seen between the finger tapping and pointing task which poses higher demands on coordination and visuospatial monitoring. Similarly, immediate verbal recall (DS-F) was normal, while the ability to manipulate information in the working memory (DS-B) was reduced. Finally, performance was impaired in the TMT-B but not the TMT-A, indicating deficits in task switching and executive control. Correlations between the various task-completion times agree with the notion of psychomotor slowing in schizophrenia (Morrens *et al.* 2007). Such slowing, however, may be influenced by executive dysfunctions such as reduced processing speed or difficulties in attentional focusing. As performance in simple tests was unimpaired, our data support the notion that executive control deficits may contribute to psychomotor slowing. It should be noted, however, that this may particularly be the case in patients, which shows only mild overall impairment as psychomotor slowing in more long-standing and severe illness may become an independent pathological feature or side effect of medication. This again highlights the benefit of assessing patients with a relatively high overall level of functioning, as deficits in these may point more specifically to pathophysiological features of schizophrenia rather than a 'general' decline.

Executive control reflects the integration of sensory-motor and cognitive aspects by the prefrontal cortex (Koechlin and Summerfield, 2007). The anterior DLPFC maintains episodic information such as task instructions and preceding stimuli, the posterior DLPFC contextual information of the current stimulus and the dPMC the stimulus itself. In this model, each region integrates information from preceding (anterior) regions if necessary. While the dorsal premotor cortex (dPMC) thus leads to behavioral outcomes (actions), overarching representations in the anterior DLPFC should become more important with task complexity. Within the discussed model of executive control, the observed impairments in more complex tasks is thus in line with previous evidence for prefrontal dysfunction in schizophrenia (Friston, 1992; Weinberger *et al.* 1994; Carlsson, 2006) that may result in altered top-down modulation of sensory-motor regions (Yoon *et al.* 2008).

4.2 Manual stimulus-response compatibility and antisaccades

Healthy subjects show an speed-accuracy trade-off in manual SRC tasks as evidenced by anti-correlated performance and RTs (Cieslik *et al.* 2010). There was, however, no evidence

for a similar (systematic) trade-off between speed and accuracy in patients. These findings in our manual SRC task must evidently be considered against the backdrop of the already well documented antisaccade deficits in schizophrenia (Broerse *et al.* 2001; Fukushima *et al.* 1988; Turetsky *et al.* 2007; Reuter *et al.* 2005; Crawford *et al.* 2002). Our SRC paradigm may be regarded as a manual version of this task, as both require a bottom-up facilitated congruent response in one condition (prosaccade or ipsilateral button press) and a voluntary top-down modulated response in the other (antisaccade or contralateral button press). In prosaccade tasks, latency and accuracy seem largely unimpaired in patients (Broerse *et al.* 2001), while we found elevated ERs (though not RTs) in the congruent condition. These differences may relate to the fact that visual-guided saccades are highly stimulus-driven, needing little executive control, while the prepotency in the congruent condition of the SRC-task is lower. That is, while eye movements towards a visual stimulus are almost completely reflexively, the congruent manual SRC condition in the current experiment requires some executive control (stimulus-response mapping) in spite of the fact that visual stimuli do create a prepotency to shift attention and initiate a movement towards them (Rosen *et al.* 1999; Cisek and Kalaska, 2005; Cieslik *et al.* 2010). In the incongruent condition, the bottom-up facilitated response does not match the biasing information by the anterior DLPFC posing increased demands on executive control. Consequently, ERs are increased in both groups, though specifically stronger in patients. This matches the well-replicated finding of increased antisaccade errors in schizophrenia. However, compared to ERs of 25–71% in antisaccade tasks, the ER of 9% in our manual task appears rather low. This may again be explained by the fact that the prepotency that must be overcome to perform an antisaccade is stronger compared to a contralateral button press. In particular it seems, that the impairment closely follows the executive control requirements, from prosaccades (lowest) to ipsilateral manual responses, contralateral manual responses and antisaccades (highest). A similar though less distinct pattern may also be observed in the RTs, which are normal in prosaccades (Broerse *et al.* 2001), slightly but not significantly elevated in the manual SRC and higher for antisaccades (Fukushima *et al.* 1988; Turetsky *et al.* 2007).

In summary, when comparing the current results to the literature on anti-saccade movements, several important aspects seem to emerge. i) Anti-saccade aberrations in schizophrenia seem to be a specific instantiation of an overarching deficit rather than pointing to a more specific dysfunction of the oculomotor system. Manual SRC tasks may hence provide a more tractable assessment of anti-movement performance than the experimentally often challenging recording of eye movements. ii) While several similarities between saccadic and manual anti-movements may be noted in schizophrenia (most noteworthy, the increased incongruence-effect), there are several, potentially crucial, distinctions between the observed patterns of effects. In particular, relative to controls, the error rate for congruent movements is only increased in the manual task, reaction times for incongruent movements is only increased in the saccade task. iii) It must be noted, that in spite of the conceptual similarities of both types of anti-movement paradigm, they differ substantially from each other with respect to the required level of stimulus-response mapping. Whereas saccades entail little mapping as stimulus and response pertain to the same functional domain and body part, mapping from visual stimulation to manual responses is considerably more complex. iv) Acknowledging the conceptual similarities (anti-movements) and differences (stimulus-response mapping) between saccadic and manual SRC, the observed patterns of impairments may be interpreted as an expression of an overarching executive control deficit, which also became evident in the neuropsychological assessment.

4.3 Mechanisms for executive control deficits

Given the consistency of anti-movement deficits in schizophrenia it is worth reconciling the different mechanisms proposed for this observation: Theories of deficient inhibitory control explain erroneous antisaccades by an insufficient inhibition of the prepotent response (e.g. Nyffeler, 2007). A similar mechanism may have contributed to the increased incongruence-effect in patients in the current manual SRC-task. However, it is noteworthy, that ERs were also elevated in the congruent conditions, which may not be explained by deficient inhibition as in these conditions the prepotent response is required (but still needs stimulus-response mapping). Moreover, patients' RTs for erroneous responses in the incongruent condition were not decreased as would be expected in the case of deficient inhibition. We would thus conclude that deficient inhibitory control is at least not the dominant mechanism for the observed deficits. The response competition theory (Reuter *et al.* 2005) states, that prepotent and top-down initiated response compete for execution. Under this assumption, an erroneous prosaccade (executed instead of the actually required antisaccade) may result from two instances. Either, the prepotent response is activated too strong or the voluntary response is not activated strong enough. Insufficient activation of a voluntary response may well reflect aberrant top-down mechanisms (goal-activation) as part of an executive control deficit (Nieuwenhuis *et al.* 2004). While providing a good model for the effects observed in (anti-) saccade paradigms, the response competition theory, however, does not completely account for the observations from the current, manual SRC task. In particular, deficient response competition in patients would not be able to explain the significantly increased number of errors in the congruent (ipsilateral) responses. In this condition, bottom-up and top-down information is congruent and hence there should be no competition between them. As noted above, however, an insufficient goal-activation in schizophrenia may be considered part of a more general executive control deficit, including the inability to sufficiently maintain task information. Such inability to hold task instructions stably online makes the adequate response selection difficult and may give rise to fundamentally stochastic action selection (Redgrave *et al.* 1999). In other words, instable task-representations as an executive control deficit may account for errors of commission made in the congruent condition of the current task (by stochastic errors in response selection even when bottom-up and top-down information is congruent) as well as for the anti-movement deficits seen in oculomotor and manual tasks (by an insufficient activation of the voluntary response in a response competition).

4.4 Conclusions and open questions

Our results argue against a specific oculomotor deficit in schizophrenia and towards an overarching deficit in the integration of current stimuli with a-priori task (goal) representations. As neuropsychological tests indicated impairments with increasing task-complexity, the observation that (compared to the ocular version) the manual SRC task yields higher ERs in the congruent and lower ones in the incongruent condition indicates an executive control deficit. Here the degree of impairment relates to the required amount of executive control with (in-) congruent button presses holding an intermediate position between pro- and antisaccades. Finally, these findings indicate impaired goal-activation by top-down (executive) control in a competition model.

The current data, however, raises several important questions. In particular, it will be essential to assess manual- and oculomotor-SCR performance in the same patients to directly assess the implied relation between them. Likewise, a comparison of manual- and oculomotor-SCR performance with independent measures of inhibitory control, such as performance in a stop-signal or go/no-go task.

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Socio-demographic data of the patients, the cohort of 68 controls, the sub-group of 28 controls from this cohort that were precisely matched to the patients, as well as clinical data of the patient sample. For each cell, median (across the diagnostic group) and interquartil-range (IQR) are provided.

Table 1

	Patients		68 subjects control population		28 matched controls	
	Results		Results	p-value	Results	p-value
Age	36.2 (IQR: 18.0)		31.0 (IQR: 14.5)	0.3249	32.0 (IQR: 13.5)	0.6109
Education	12.1 (IQR: 3.0)		13.0 (IQR: 7.0)	0.0265*	12.5 (IQR: 2.5)	0.5229
P-Education	11.6 (IQR: 2.9)		10.5 (IQR: 4.5)	0.3998	11.3 (IQR: 4.3)	0.5647
MWT-B	23.9 (IQR: 5.0)		27.0 (IQR: 6.0)	0.0184	25.0 (IQR: 5.0)	0.5327
PANSS +	11 (IQR: 9.75)					
PANSS -	14 (IQR: 8.50)					
PANSS general	29 (IQR 14.5)					
DOI (years)	7 (IQR: 7.50)					
Admissions	3 (IQR: 3.75)					
CPE (mg)	749 (IQR: 730.5)					

Significance was assessed using a Wilcoxon-Mann-Whitney two-sample rank-sum test

* p<0.05;

** p<0.005.

P-Education: Parental years of education; PANSS+: Positive syndrom subscore; PANSS-: Negative syndrome Subscore; PANSS general: General psychopathology subscore; DOI: Duration of illness; Admissions: Number of hospital admissions; CPE: Chlorpromazine-equivalent dose.

Table 2

Results obtained from the neuropsychological test-battery. For each cell, median (across the diagnostic group) and interquartil-range (IQR) are provided.

	Patients	Healthy Controls	<i>p-value</i>
Tap	52.4 (IQR: 7.3)	52.9 (IQR: 6.8)	0.9012
Pointing	8.4 (IQR: 3.5)	7.3 (IQR: 2.3)	0.0305*
DS-F	7.9 (IQR: 2.8)	7.5 (IQR: 2.7)	0.3884
DS-B	5.7 (IQR: 1.6)	7.1 (IQR: 3.1)	0.0102*
TMT-A	26.2 (IQR: 7.3)	22.6 (IQR: 9.3)	0.1292
TMT-B	48.0 (IQR: 21.9)	44.0 (IQR: 21.4)	0.0413*
TMT B-A	22.5 (IQR: 20.6)	17.9 (IQR: 15.0)	0.0838

Significance was assessed using a Wilcoxon–Mann–Whitney two-sample rank-sum test

*
p<0.05

Tap: Finger tapping test; DS-F: Digit span forwards; DS-B: Digit span backwards; TMT-A/B: Trail marking test version A/B; TMT B-A: Difference in time taken for the two versions of the trail making test

Table 3

Results obtained from the SRC-task. For each cell, median (across the diagnostic group) and interquartil-range (IQR) are provided.

	Patients	Healthy Controls	<i>p-value</i>
ER-C	5.6 (IQR: 12.0)	3 (IQR: 5.5)	0.0107*
ER-ICE	3.4 (IQR: 7.6)	1.8 (IQR: 2.9)	0.0152*
RT-C	339.8 (IQR: 78.9)	328.4 (IQR: 55.2)	0.1629
RT-ICE	49.1 (IQR: 37.4)	45.9 (IQR: 22.9)	0.4247
RT-Errors-C	57.4 (IQR: 114.8)	62.0 (IQR: 69.7)	0.4630
RT-Errors-IC	-36.8 (IQR: 53.2)	-33.5 (IQR: 46.6)	0.6857

Significance was assessed using a Wilcoxon–Mann–Whitney two-sample rank-sum test

*
p<0.05;

**
p<0.005.

ER-C: Error rate in the congruent condition; ER-ICE: Incongruence-effect on the error rates; RT-C RT for correct responses in the congruent condition; RT-ICE: Incongruence-effect on the RT for correct responses; RT-Errors-C: RT for erroneous responses in the congruent condition; RT-Errors-ICE: Incongruence-effect on the RT for erroneous responses.

Table 4

Spearman's rank correlations of the neuropsychological, SRC-task test results and the clinical characteristics of the patients

			r-value	p-value
RT-C	-	TMT-A	0.44	0.021 *
RT-C	-	Pointing	0.49	0.008 *
RT-Errors-ICE	-	Tapping	-0.39	0.042 *
TMT-B	-	TMT-A	0.64	<0.001 **
TMT-A	-	Pointing	0.51	0.006 *
TMT-B	-	Ponting	0.52	0.005 *
TMT-B	-	MWT-B	-0.41	0.029 *
TMT-B	-	Genreal psychopath.	0.42	0.03 *
TMT-B	-	Admissions	0.50	0.015 *
Pointing	-	Admissions	0.43	0.041 *
Correct-C	-	Duration of illness	0.56	0.006 *
Correct-ICE	-	Chlorpromazin-e.	0.50	0.013 *
RT-C	-	Chlorpromazin-e.	-0.48	0.017 *
Sessions completed	-	Positive Symptoms	-0.046	0.015 *

* p<0.05;

** p<0.005.