Schizophrenia Research: Cognition 10 (2017) 1–6

Contents lists available at ScienceDirect

Schizophrenia Research: Cognition

journal homepage: www.elsevier.com/locate/scog

Speed and capacity of working memory and executive function in schizophrenia compared to unipolar depression

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ARTICLE INFO

Keywords:
Schizophrenia
Depression
Working memory
Processing speed
Executive functioning

ABSTRACT

Schizophrenia is associated with deficits in working memory (WM) and executive functioning (EF) that are present from prodrome to chronic stages of the disease and are related to social and occupational functioning. Recent empirical findings suggest that schizophrenia patients might suffer from a specific speed deficit regarding WM operations that also affects EF. To test this hypothesis, executive functioning (EF) and working memory (WM) performance of 20 schizophrenia (SC) patients, 20 patients suffering from Major Depressive Disorder (MDD) and 40 healthy control (HC) subjects were compared. While schizophrenia patients performed worse in the measure of EF, no difference between the SC and the MDD patients was found regarding WM capacity. However, the SC group was shown to have an impaired speed in encoding, retrieval and manipulation of WM contents compared to the HC group whereas the MDD group showed no such deficit. Furthermore, while in the MDD group only WM capacity was linked to EF performance, in the SC group EF was determined by both WM capacity and WM speed. Hence, increasing the speed of WM operations might be a fruitful target for future therapeutic interventions, and assessing not only the capacity but also the speed of WM might be helpful in identifying candidates for endophenotypic cognitive markers of SC.

1. Introduction

Beyond the symptoms listed in diagnostic manuals, schizophrenia patients often also suffer from a broad range of persistent cognitive deficits (Schaefer et al., 2013) affecting duration and further course of illness (Wölwer et al., 2008; Trapp et al., 2013) as well as social and occupational functioning (Green et al., 2004). In this context, executive functioning (EF), commonly defined as the ability to utilize higher-level cognitive processes controlling and coordinating more elementary cognitive processes (Banich, 2009; Alvarez and Emory, 2006), is particularly relevant for the functional outcome (Greenwood et al., 2005).

Although, at least at first glance, schizophrenia patients appear to suffer from a general and uniform cognitive impairment, working memory (WM) deficits (Silver et al., 2003; Green and Glausier, 2016; Barch and Ceaser, 2012; Park and Gooding, 2014) have repeatedly been regarded as core deficit that might be 'rate limiting' for other cognitive functions. WM can be considered as a system of limited capacity, capable of temporarily maintaining and manipulating information while working on a problem (Baddeley, 1992). Current models of working memory functions, such as Baddeley's model (Baddeley, 1986), propose several subcomponents: Separate storage buffers for visuospatial and verbal information (the so called 'visuo-spatial sketch pad' and the 'phonological loop') are controlled by a 'central executive' (CE) that is responsible for manipulation, retrieval and storage of information in the two buffers mentioned above. Recently, a more complex 'episodic buffer' for the integration of multimodal and more complex cognitive elements serving as an interface between WM and long-term memory has been added to the model (Baddeley, 2000).

Moreover, two recent meta-analyses (Dickinson et al., 2007; Knowles et al., 2010) provided evidence that the impairment of schizophrenia patients in speed tests with a high WM load, such as category fluency tests or the Digit Symbol Coding Task, is significantly larger than in other cognitive measures. Thus, in schizophrenia, not only WM capacity but also the speed of WM operations might be additionally impaired.

Therefore, the aim of this study was to examine potential deficits in schizophrenia with respect to speed and capacity of working memory and their relevance for EF. To investigate, whether these deficits are specific for schizophrenia, a group of MDD patients was included as a clinical control group, as it has been shown, that depressive patients

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http://dx.doi.org/10.1016/j.scog.2017.07.002
Received 2 May 2017; Received in revised form 10 July 2017; Accepted 11 July 2017

exhibit a similar, albeit less pronounced cognitive deficit profile, including impairments in EF (Bora et al., 2013; Lee et al., 2012).

We hypothesized that WM processing speed might be particularly impaired and linked to EF performance in schizophrenia but not in MDD patients, whereas WM capacity deficits might be present and relevant for EF performance in both patient groups.

2. Methods

2.1. Participants

40 inpatients of Department of Psychiatry, Psychosomatic Medicine and Psychotherapy at the Social Foundation Bamberg, Germany, as well as a sample of 40 control subjects without history of any psychiatric or neurological disorders, recruited among medical and nonmedical staff or their relatives, were included. All inpatients fulfilled the International Classification of Diseases-10 (ICD-10) as well as the Diagnostic and Statistical Manual of Mental Disorders-IV (DSM-IV) criteria for schizophrenia (n = 20) or MDD (n = 20) and were diagnosed based on the Structured Clinical Interview for the DSM-IV (SCID). The patients were recruited within the last week before discharge and were thus under stable medication and respondent to antidepressive or antipsychotic treatment. Exclusion criteria were medical diagnoses associated with neurocognitive impairment and uncorrectable deficits in vision or hearing that would preclude their ability to perform the cognitive tasks. After a complete description of the study, written informed consent was obtained from all subjects. The study adhered to the principles of Good Clinical Practice of the International Conference on Harmonization and the Declaration of Helsinki and was approved by the ethics board of the University of Bamberg.

2.2. Measures

2.2.1. Symptoms

Symptom levels were assessed in all participants using German versions of the 2nd edition of the Beck Depression inventory (BDI, Hautzinger et al., 2009) as self-report questionnaires as well as the Hamilton Depression Rating Scale (HAMD, Hamilton, 1960) and the Positive and Negative Syndrome Scale (PANSS, Kay et al., 1987) as observer ratings.

2.2.2. Neurocognitive tests

Working memory and executive functioning were assessed for the schizophrenia and the MDD group using the digit span forward and backward subtest of the German version of the Wechsler Memory Scale (WMS-R, Wechsler, 1987) as a routine measure of verbal WM and the Wisconsin Card Sorting Test (WCST, Young and Freyslinger, 1995) as a measure of EF. The primary WCST score used was the total number of errors. Additionally, the numbers of perseveration errors were recorded. As it was not our primary aim to determine the degree of neurocognitive impairments of both patient groups compared to unimpaired persons but rather to find differences in their neurocognitive profile, we did not administer these tests to the control group.

2.2.3. Assessment of working memory processing speed

As standard neuropsychological tests of working memory are either not capable of assessing working memory speed, or are too stressful for patients suffering from schizophrenia, all participants were additionally asked to complete a computer task developed by the first author, which was designed in a gamified manner. This was done in order to avoid too much pressure to achieve, because WM processing speed might be particularly sensitive to non-cognitive influence factors like low motivation, unfavourable negative cognitions or the participants' fear of not being able to successfully master the tasks.

To complete the task, a “flower shop” had to be run “as profitably as possible” (see also screenshots and detailed descriptions in Fig. 1). In three subtasks, verbal and spatial information had to be encoded (step 1), recalled (step 2) and finally sequenced in a different order than during presentation in step 1 (step 3).

Participants were permitted to take as much time as they wanted to encode, recall and reorder the items. A total of three runs of step 1 to step 3 had to be managed by the participants following a comprehensive training of about 5 min preceding the task to ensure that the task was fully understood by all participants, and in order to compensate for possible differences in their computer skills.

WM encoding, WM retrieval and WM manipulation speed indices were computed on the basis of the average time used per item and were then corrected by the number of errors during step 1 to step 3.

In order to determine the computer task's concurrent validity, “WM buffer” and “WM manipulation” performance scores were computed based on the percentage of correct answers in steps 1 to 3.

2.3. Statistical analyses

Univariate analyses of variance with Scheffé a posteriori comparisons were performed to compare the subsamples (controls, MDD and schizophrenia patients) with respect to age, years of education and duration of illness. Chi-square tests were used to test for differences in male to female ratio and relationship status.

t-Tests for independent samples as well as Cohen's d effect sizes were computed to compare schizophrenia and MDD patients' performance in all neurocognitive measures.

To evaluate the computer task's concurrent validity, its performance scores were correlated with the neurocognitive test scores using Pearson correlation coefficients.

To compare the three subsamples with respect to their WM speed, univariate analyses of variance with Scheffé and Tukey HSD a posteriori comparisons were performed. Partial η^2 estimators of effect size for the interaction effects were converted into Cohen's d values according to the algorithm described in Cohen (1988).

In order to figure out to what extent EF performance is influenced by working memory capacity and speed, the three WM processing speed indices of the computer task as well as the digit span scores were correlated with the WCST scores using Pearson correlation coefficients. In order to determine whether WM capacity, WM speed or both are independently relevant for EF performance in each group, two linear stepwise regression analyses were performed separately for the MDD and the schizophrenia group. The two WCST scores were used as dependent variables and the digit span scores all well as the speed measures from the computer task as predictors.

Finally, in order to evaluate whether WM processing speed was influenced by the patients' residual depressive and psychotic symptoms, Pearson correlation coefficients of the BDI, HAMD and PANSS scores with the three WM processing speed indices were computed separately for both patient groups.

3. Results

3.1. Sample characteristics

Clinical and demographic characteristics as well as neurocognitive measures of all participants are described in Tables 1 and 2 respectively. The groups do not differ in gender, relationship status, age, years of education, or duration of illness. As expected, higher PANSS and PDS-P scores were obtained for the schizophrenia patients than for the depressive patients, who did not differ from the control sample (Scheffé and Tukey HSD a posteriori comparisons $p < .0005$ each). Control subjects achieved lower BDI and HAMD scores compared to the two patient samples (Scheffé and Tukey HSD a posteriori comparisons $p < .0005$, each); higher BDI (Scheffé a posteriori comparison $p = .002$, Tukey HSD a posteriori comparison $p < .0005$) but no significantly higher HAMD scores were found in the MDD patients

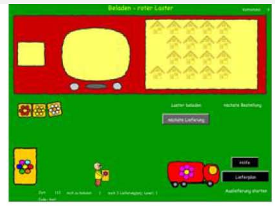
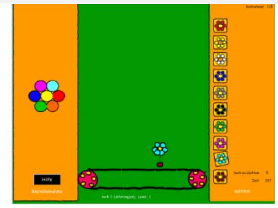
	step		
	1	**2**	**3**
screenshot			
task	memorize flower shop orders ("color of flower" and "position of customer in city map")	recall all orders and load the flower truck	grow new flowers (consecutively from top to bottom by the color indexed on the right side of the screen and not in the order of presentation) replacing those that had been delivered
targeted neurocognitive domain	encoding into temporal WM buffers	retrieval from temporal WM buffers	manipulation of WM buffer contents by CE
extracted WM speed measure	***encoding speed:*** average time used to memorize each item, multiplied by (-1)	***retrieval speed:*** average time needed to recall each item, corrected by number of errors (unstandardized residuals from regression of the average recall time per item on the number of errors as predictor), multiplied by (-1)	***manipulation speed***: average time needed to recall each item, corrected by number of errors (unstandardized residuals from regression of the average recall time per item on the number of errors as predictor), multiplied by (-1)
extracted WM performance measure	--	***buffer score:*** percentage of correct answers	***manipulation score:*** percentage of correct answers

Fig. 1. Screenshots, tasks, targeted neurocognitive domains and extracted WM speed measures of the computer task. WM: working memory.

compared to the schizophrenia patients (Scheffé a posteriori comparison p = .188, Tukey HSD a posteriori comparison, p. 161).

3.2. Neurocognitive tests

Table 2 displays descriptive statistics for the neurocognitive measures as well as *t*-test results for differences between patient groups. Patients of the schizophrenia sample committed significantly more WCST total errors but only a tendency towards a higher number of perseveration errors ($p < .10$). In all measures of working memory, no statistically significant differences were found between schizophrenia and MDD patients.

3.3. Computer task – concurrent validity

While significant correlations of the 'WM buffer' performance score with all digit span scores could be found, there were no significant correlations with the WCST errors at an alpha-level of .05 level (see

Table 1
Demographic and clinical characteristics.

Characteristic	Control group (n = 40)		Schizophrenia (n = 20)		MDD (n = 20)		χ^2 (2)	p
	N	%	N	%	N	%		
Gender							3.308	.191
	Male	21	52.5	11	55.0	6	30.0	
	Female	19	47.5	9	45.0	14	70.0	
In relationship	21	52.5	8	40.0	7	35.0	1.919	.383
	Mean	SD	Mean	SD	Mean	SD	$F_{(2,79)}$	p
Age	34.98	12.52	40.45	10.03	34.55	11.38	1.747	.181
Years of education	13.45	1.99	13.30	2.23	12.75	1.68	.847	.433
Duration of illness (years)			8.20	7.94	6.50	7.72	.686	.497
HAMD	.57	.90	7.84	5.09	9.68	3.42	70.869	< .005
BDI	2.90	3.13	13.47	4.89	22.33	13.34	47.106	< .005
PANSSP	7.05	.22	10.00	2.16	7.05	.23	53.973	< .005
PANSSN	7.00	.00	9.84	2.57	7.11	.32	35.369	< .005
PDS-P	1.90	2.27	11.44	6.18	4.56	3.29	39.946	< .005

Table 2
Performance of MDD and schizophrenia patients in the computer task and the neurocognitive tests. WMS: Wechsler Memory Scale, WCST: Wisconsin Card Sorting Test, WM: working memory, CE: central executive, MDD: major depressive disorder, CNT: healthy control subjects.

Measure	Schizophrenia (n = 20)		MDD (n = 20)		CNT (n = 40)		t	p	d
	Mean	SD	Mean	SD	Mean	SD			
Working memory									
WMS digit span forward	7.30	2.15	7.20	1.58			.168	.868	−.05
WMS digit span backward	5.80	2.21	6.60	2.19			1.150	.257	.36
WMS digit span total	13.10	3.91	13.80	2.91			.643	.524	.20
Executive function									
WCST total errors	36.56	44.15	8.20	5.75			2.850	.007	.90
WCST perseveration errors	9.06	15.14	3.15	3.00			1.710	.096	.54
WM speed indices							$F_{(2,77)}$	p	d
WM encoding speed	16.72	5.20	11.72	3.78	5.34	.85	6.019	.004	.79
WM retrieval speed	− 5.62	8.55	1.27	7.28	2.18	7.72	6.976	.002	.85
WM manipulation speed	− 2.75	7.16	1.32	2.72	.71	3.61	4.893	.010	.71

Table 3
Correlations between neurocognitive tasks and computer task performance.

Neurocognitive measure	Computer task	
	WM buffer score	WM manipulation score
Working memory		
WMS digit span forward	.37*	.33*
WMS digit span backward	.32*	.33*
WMS digit span total	.41**	.33*
Executive function (multivariate)		
WCST total errors	.31+	.45**
WCST perseveration errors	.18	.35**

** p < .01.
* p < .05.
+ p < .10.

Table 3). The ‘manipulation score’ co-varied significantly with the WCST scores and more weakly with two of the three digit span scores.

3.4. Computer task – WM speed measures

Significant between-group main effects were obtained for all processing speed measures. A posteriori comparisons yielded significantly lower encoding, retrieval and manipulation speed scores for schizophrenia patients compared to the MDD and control group (p-values for Scheffé a posteriori comparisons between .002 and .027, p-values for Tukey HSD a posteriori comparisons between .001 and .020), while MDD patients and controls did not differ significantly from each other in the three WM processing speed scores (p-values between .759 and .914). Speed indices were largely unaffected by the patients' symptom scores as no correlations were found (r between .02 and .32, p between .942 and .180) except for a positive correlation between BDI and encoding speed in the MDD group (r = .41, p = .074).

3.5. Prediction of EF performance

As can be seen in Table 4, WM capacity and WM processing speed scores are uncorrelated in both patient groups. However, in both groups, the digit span total scores and, to a lesser extent, the digit span forward scores are linked to the WCST scores.

While in the MDD group the WM processing speed measures were uncorrelated with all WCST scores, in the schizophrenia group significant correlations were found between manipulation speed and WCST total errors.

In the stepwise regression analyses for the MDD group, only the digit span total score remained as predictors of the total number of WCST errors (beta = −.494, p = .027, R^2 = .244). In the schizophrenia subsample however, WCST total errors were best predicted by a combination of the digit span total and the WM manipulation speed score (WCST total errors: R^2 = .535, beta = −.529 and .534, p = .009 and .008). WCST perseveration errors could not be predicted in any of the two patient groups.

4. Discussion

The main aim of the present study was to highlight impairments in working memory and their relevance for EF in schizophrenia compared to MDD patients.

Table 4
Correlations between digit span, WCST capacity and WM processing speed measures extracted from the computer task. CE: central executive, SCH: schizophrenia patients, MDD: patients suffering from Major Depressive Disorder, pers.: perseveration, forw.: forward, backw.: backward.

	Digit span						WCST errors			
	Total		Forw.		Backw.		Total		Pers.	
	MDD	SCH	MDD	SCH	MDD	SCH	MDD	SCH	MDD	SCH
Digit span										
Total							−.49*	−.50*	−.27	−.35
Forward							−.41+	−.50*	−.15	−.46+
Backward							−.37	−.37	−.26	−.14
Computer task										
Encoding speed	−.06	−.08	−.05	−.18	−.05	.03	.12	−.33	.31	.11
Retrieval speed	.15	−.08	.13	−.07	.11	−.09	−.05	−.32	.12	.07
Manipulation speed	.03	−.06	−.09	−.02	.10	−.07	.30	−.51*	.28	.05

* p < .05.
+ p < .10.

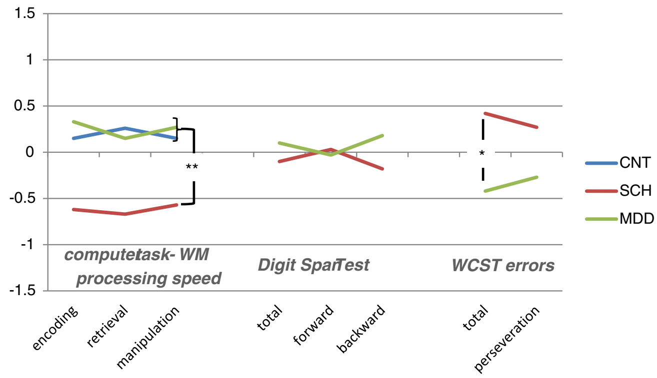


Fig. 2. z-Values of computer task speed indices, Digit Span Test and Wisconsin Card Sorting Test (WCST) scores. CNT: controls, SCH: schizophrenia patients, MDD: patients suffering from Major Depressive Disorder, WM: working memory. **: group differences: MDD and CNT > SCH in WM processing speed measures, $p < .01$; *: SCH > MDD in WCST total and WCST failure to maintain set errors, $p < .05$.

We found that schizophrenia patients performed worse than MDD patients regarding EF performance. While significant differences resulted for the WCST total score, the differences regarding the perseveration errors reached only a trend level. However, considering the moderate to large effect size for this measure, this finding might be nonsignificant due to the small sample size. There was no specific deficit in working memory capacity, but again, the effect size for one variable (digit span backwards) could be considered as moderate and might have reached significance in a larger sample size. The WM speed indices, however, point to an impaired speed of WM operations in the schizophrenia, but not the MDD patients (see Fig. 2 for a summary illustration). However, general processing speed deficits might underlie the WM processing speed deficits found in our schizophrenia group. On the other hand, recent evidence suggests that schizophrenia patients might be preferentially impaired in speed tests that put a high load on the CE module of WM by requiring participants to “rapidly and smoothly coordinate a complex assembly of elementary operations”, such as digit symbol coding or verbal fluency tasks (Dickinson et al., 2007; Knowles et al., 2010). Specifically, the corresponding effect sizes for those kinds of tests are much larger than for “pure” processing speed measures, such as part A of the Trail-Making Test, or for motor speed tests, such as finger tapping tasks. These findings indicate that WM processing speed specifically instead of processing speed in general might be particularly impaired in schizophrenia patients.

Also, in both patient groups WM capacity scores were correlated with EF performance, but only in the schizophrenia group was WM processing speed linked to EF performance independently. Notably, in neither of the two groups, WM processing speed indices and WM capacity measures were correlated and WM speed was shown to be unaffected by residual positive and negative symptoms in our sample.

Although we tried to limit the number of statistical tests as far as possible, we cannot rule out the possibility of false positive results due to multiple statistical testing.

Furthermore, as two different patient groups suffering from distinct mental disorders and therefore receiving different medical treatments were included, it is possible that differences in medication could account for at least some of the differences found in neurocognitive performance. However, effects of antipsychotic or antidepressive medication on performance in neurocognitive tasks have been proven low or nonexistent in former studies (Purdon et al., 2000; Elliot, 2000; Fossati et al., 1999) and it is thus unlikely that the differences found in the present study were influenced by medication effects to a larger degree.

In sum, our findings clearly indicate that WM processing speed might be independently and specifically impaired in schizophrenia patients. This could explain larger cognitive deficits characteristic of schizophrenia compared with other psychiatric illnesses and might in part be responsible for schizophrenia patients’ impaired community integration.

Therefore, increasing the speed of more complex mental operations could be an interesting target in future pharmacological or cognitive remediation approaches. Our own work group has demonstrated huge improvements in WCST performance using gamified speeded WM tasks with gradually increasing speed for remediation in schizophrenia patients (Trapp et al., 2013).

In case our results were confirmed in further studies including larger sample sizes and administering a broader array of verbal and spatial working memory tests (especially measures regarding maintenance and manipulation of WM contents, such as N-back tasks (e.g. Barch et al., 2002) or the Self-Ordered Pointing Test (Petrides and Milner, 1982)), the development of standardized WM tests providing measures for the speed of elementary WM operations would be a fruitful future topic.

Conflict of interests

None.

Funding sources

Study sponsors played no role in study design; data collection, analysis, or interpretation; manuscript preparation of decision to submit the paper for publication.

Acknowledgements

The authors wish to thank the patients who participated in this study, Karin Divers for proof reading and language editing of the manuscript and Dr. Klaus Drescher and Dr. Florian Bayerl for their help with the recruitment of participants.

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