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