THE OVERLAP OF COGNITIVE IMPAIRMENT IN DEPRESSION AND SCHIZOPHRENIA: A COMPARATIVE STUDY

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SUMMARY

Background: Schizophrenia (SCH) is primarily a cognitive dysfunction. Its specific cognitive impairment profile was identified and suggestions have been made to include it in present diagnostic instruments as a special differential diagnostic criterion. However, studies indicate a substantial overlap of cognitive deficits between SCH patients and those with depression (DEP). In order to elucidate the structure of cognitive functioning in both entities, principal cognitive domains of SCH and DEP patients were assessed in the acute phase of disease.

Subjects and methods: 44 SCH and 30 DEP patients, matched according to age, gender, education, IQ score, and duration of hospitalization were included. Neurocognitive assessments were performed in the first week of hospitalization using Digit Span test (working memory, attention), Trail Making Test (psychomotor speed, sustained attention, shifting), Rey's Complex Figure Test and Verbal Learning Test (perceptual organization, visual and verbal learning and memory). Results were evaluated according to demographically matched test norms. For statistics Student's t tests were used.

Results: In both study groups deficits in maintenance and shifting of attention during psychomotor tasks were found, while automatic processes (working memory, sustained attention) were preserved. In both groups memory and learning processes were impaired, in DEP however, deficits in attention shifting during cognitive tasks and delayed recall of visual material were more intense.

Conclusions: In the acute phase of schizophrenia and depression similar cognitive impairment profiles can be found. Further studies are needed to assess longitudinal dynamics and possible later development of specific patterns of cognitive functioning in these patients.

Key words: depression – schizophrenia - cognitive impairment - neurocognitive assessment – attention – memory - automatic processes - comparative study

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INTRODUCTION

In psychiatric disorders cognitive impairment represents an important issue regarding their differential diagnostics, success of treatment, rehabilitation and patient's social reintegration (Harvey 2008, Keefe 2008). Differentiation of cognitive impairment profiles and identification of possible specific deficits in individual cognitive domains among patients with different psychiatric diagnostic entities is therefore of significant importance.

Traditionally, schizophrenia (SCH) has been regarded primarily as a cognitive disorder (Harvey 2008). Cognitive deficits in SCH patients are considered to be of severe and persistent nature, largely independent of antipsychotic treatment (Keefe 2008). To different extent they are present in all phases of the disease prodromal, acute and remission phase (Green et al. 2004). In the majority of these patients cognitive deficits cover attention, working memory, executive functions and secondary or episodic memory. It is assumed that verbal memory is most profoundly impaired (Bowie & Harvey 2005, Keefe 2008). Basic dimensions of cognitive deficits in SCH patients were elucidated by the MATRICS programme, represented by the following separate cognitive factors: processing speed, attention/vigilance, working memory, visual learning and memory, verbal learning and memory, reasoning, problem solving and verbal comprehension (Green et al. 2004, Nuechterlein et al. 2004, Buchanan et al. 2005). On the basis of these findings, suggestions have been made that in SCH patients cognitive impairment should probably be included in the present diagnostic instruments as a special differential diagnostic criterion (Keefe & Fenton 2007, Harvey 2008). However, not enough evidence is present to support this. First, some studies have stressed the importance of heterogeneity in SCH spectrum disorders, which could lead to different cognitive impairment profiles among individual SCH diagnostic subtypes (Friedman et al. 2001, Turetsky et al. 2002). However, studies investigating this issue have not yielded consistent results (Palmer et al. 1997, Zalewski et al. 1998, Wilk et al. 2005). Second, there are relatively few comparative studies regarding cognitive impairment in SCH patients versus other diagnostic entities (Keefe 2008). Further research is needed in this field.

Cognitive impairment was confirmed in patients with depression (DEP) as well, but it is believed to resolve through clinical improvement (Chamberlain & Sahakian 2005), possibly as a consequence of antidepressant therapy (Fava 2003, Gualtieri et al. 2006). In contrast to impairment in SCH patients, it is regarded to be of milder and transient nature, largely interrelated to the intensity of affective disturbance itself (Chepenik et al. 2007, Ciesla & Roberts 2007). Cognitive deficits that are thought to be specific for DEP patients comprise psychomotor slowing, and memory or language functions (Gualtieri et al. 2006). Anyway, some reports indicate certain changes in working memory as well (Chamberlain & Sahakian 2004, Morrens et al. 2006, Morrens et al. 2007).

However, some studies do not support these findings. They have clearly shown that severe cognitive deficits often accompany affective disorders. These deficits frequently persist even into the period following symptomatic recovery (Austin et al. 2001, Chamberlain & Sahakian 2004, Gualtieri et al. 2006, Vanderhasselt & De Raedt 2009). Moreover, in DEP patients some authors reported the most severe cognitive deficits in exactly the same cognitive domains as were found for SCH spectrum disorders, namely in the areas of attention, memory and executive functions (Green et al. 2000, Chamberlain & Sahakian 2004, Chamberlain & Sahakian 2005). Along with above noted findings, in the case of both - SCH and DEP, a relative preservation of automatic cognitive processes was found, while cognitive domains which require psychophysical effort, were markedly impaired. For example, in DEP a deficit of verbal recall was found simultaneously with intact recognition, which is probably a consequence of fatigue, a common clinical characteristic of these patients (Austin et al. 2001). Similarly, in SCH patients an impairment of volitional deployment of mnemonic strategies was found with automatically deployed preserved (Bowie & Harvey 2005). retrieval Furthermore, due to specific cognitive deficits, a change in global cognitive functioning is noted in both, DEP and SCH patients (Lencz et al. 2005, Gualtieri et al. 2006).

Even though one may expect similar cognitive impairment profiles in SCH and DEP, their accurate delimitation and overlap between specific cognitive domains still remain relatively unclear (Maier 2006). With the exception of a few comparative studies addressing negative symptoms and cognitive functioning in DEP and SCH patients (Häfner et al. 2005, Winograd-Gurvich et al. 2006, Häfner 2010), and meta-analytical results on the overlap of cognitive disorders (Buchanan et al. 2005, Keefe & Fenton 2007), no extensive research in this respect is currently available. Our study aimed to assess and compare principal cognitive domains in SCH and DEP patients. According to previous studies, an overlap of deficits in domains of working memory, attention, perceptual organization and memory was expected to be found between the two clinical groups.

SUBJECTS AND METHODS

Subjects

A total of 46 patients with SCH and 35 with DEP, hospitalized at the University Psychiatric Clinic Ljubljana, in the period between March and December 2007, were invited to participate in the study. The study included male and female subjects, aged between 20 and 40 years who had the following admission diagnoses according to ICD-10 (World Health Organization 1993): schizophrenia (F20) and depression (F32, F33). The exclusion criteria were as follows: over 3 previous hospitalizations, depressive disorders with psychotic symptoms, bipolar disorder, depressive reaction as adjustment disorder or reaction to stress, neurasthenia, schizotypal, schizoaffective and delusional disorders, mental disorders of organic origin, mental retardation based on IQ test, psychoactive substance abuse, neurological diseases or brain injuries, severe visual, hearing or motor impairment of hand or fingers, deprivation of legal capacity and inability to provide independent informed consent for participation in the study.

The study was approved by the Medical Ethics Committee of the Republic of Slovenia. All participants signed an informed consent after appropriate oral information.

Methods

All assessments were performed by an experienced psychologist in the first week after admission to the hospital in a quiet ambulatory environment. The following psychometric tools were used:

- Rey Complex Figure Test (Meyers & Meyers 1995) to evaluate perceptual organization and visual memory. The test task was to copy a complex Rey-Osterrieth figure to a blank piece of paper (copy trial) as well as to memorize and draw the same figure 30 min later (delayed recall trial). There were no time limits at either task. The measures of performance were a copy score (which assesses the accuracy of the original copy and is a measure of visual-constructional ability) and a delayed recall score (which assesses the number of items of original figure correctly recalled and is a measure of visual information retained over time).
- Digit Span forwards and backwards tasks (Wechsler 1944) to evaluate working memory capacities. Subjects were asked to repeat strings of digits of increasing length (from 3 to 9) read aloud by the examiner in the same (forward) and in reverse (backward) order. The measure of performance was a maximal number of correctly recalled digits.
- Trail Making Test A (Reitan 1958) to assess sustained attention. The test required the subject to connect, by making pencil lines, 13 encircled numbers randomly arranged on a page in ascending

order. The measure of performance was time needed to complete the task.

- Trail Making Test B (Reitan 1958) to assess attention shifting. The test was administered immediately after the Trail Making Test A and required the subject to connect, by making pencil lines, 13 encircled numbers and letters from A to L in alternating order. Numbers had to be connected in ascending and letters in alphabetical order. Again the measure of performance was time needed to complete the task.
- Rey Auditory Verbal Learning Test (Schmidt 1996) to evaluate verbal memory. The AB test form was used. It consists of 15 nouns on the list A that are read aloud (with a 1 sec interval between words) for five consecutive trials, each trial followed by a free recall test (A1 to A5). The order of presentation of words remained fixed across trials. Instructions were repeated before each trial to minimize forgetting. On completion of Trial A5, an interference list of 15 words (list B) was presented, followed by a free recall test of that list. Immediately after this, delayed recall of the first list was tested (Trial A6) without further presentation of those words. After a 30 min delay period, the examinees were again required to recall words from list A (Trial A7). Finally, a written matrix array of 50 words (containing all items from the list A and B and 20 words that are phonemically or semantically similar to those in Lists A and B) was presented to identify words from List A (recognition). In this article immediate recall (A1), 5th repetition recall (A5), recall for interference stimuli (B), recall after interference stimuli (A7) and delayed recognition (total A) is shown.

Demographically appropriate test norms for the study participants were taken from the above-mentioned manuals and from Strauss et al. (2006). The data were analyzed using the SPSS for Windows 13.0 statistical package (Copyright(c) SPSS Inc., 1989-2004). Kolmogorov-Smirnov test statistics were calculated in order to detect whether data distribution significantly differs from normal. No such differences were found for p<0.05. Differences in continuous variables between patient groups were calculated using two-sided t-tests independent samples, while in normative for comparisons one-sided t-tests were used. For categorical variables Pearson's chi-square tests were applied. The differences were deemed statistically significant at p values lower than 0.05.

RESULTS

Sociodemographic and diagnostic characteristics of the sample

The study was completed by 30 DEP and 44 SCH patients. Dropout backgrounds were as follows: poor treatment compliance in 1 SCH and 1 DEP patient, premature termination of hospitalization in 1 SCH and 3

DEP patients, and suicide in 1 DEP patient. SCH group included 40 subjects with paranoid schizophrenia (F20.0) and 4 with unspecified schizophrenia (F20.9). DEP group included 6 patients with a severe depressive episode without psychotic symptoms (F32.2) and 24 patients with recurring depressive disorder (2 with mild (F33.0), 8 with moderate (F33.1), and 14 with severe current episode without psychotic symptoms (F33.2)).

Participants were demographically matched in terms of age (on average 39.0 years (SD 8.37) in DEP, and 35.8 years (SD 8.47) in SCH group) (t=-1.58; p=0.119), gender (14 (47%) males in DEP and 28 (64%) males in SCH group) (χ^2 = 2.09; p=0.148) and years of education (on average 11.9 years (SD 3.63) in DEP, and 12.5 years (SD 2.62) in SCH group) (t=0.68; p=0.502). No significant difference was present between study groups regarding the duration of current hospitalization (on average 9.0 weeks (SD 6.19) in DEP, and 8.5 weeks (SD 3.77) in SCH group) (t=-0.40; p=0.695), as well as regarding total IQ score of WAIS (Wechseler Adult Intelligence Scale) (on average 106.1 (SD 14.82) in DEP, and 108.5 (SD 12.72) in SCH group) (t=0.52; p=0.600).

Normative comparisons

Both study groups scored significantly lower according to demographically appropriate test norms in all tests, except for the Digit Span, as shown in Table 1. In the case of Digit Span no significant difference in regard to test norms was found in SCH group either in Forward or Backward subtest form. However, in DEP group, while no difference was observed in this comparison regarding Forward subtest, the score of Digit Span Backward Test was significantly lower compared to test norm.

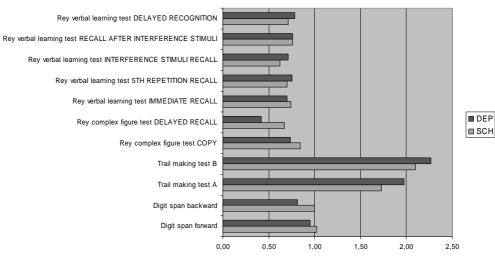
In Figure 1 average results in neurocognitive tests in DEP and SCH patients in comparison to demographically appropriate norms are presented. Deviations from the norms were the highest with the Trail Making Test A and B, since DEP and SCH patients exhibited markedly prolonged task execution times compared to the normative group. This is reflected in a highly elevated ratio of the study group vs. normative result (above 1.5 in the Trail Making Test A and above 2.0 in the Trail Making Test B). In Rey's Complex Figure Test and Rey's Verbal Learning Test deficient results of DEP and SCH patients are presented as low ratios, since their test scores were lower than test norms.

Inter-group comparisons

The comparative neurocognitive profile for DEP and SCH groups is shown in Table 2. Significant inter-group differences were found only in the case of Digit Span Backward task (t = -2.17; p = 0.037) and Rey's Complex Figure Test - delayed recall (t = -2.76; p = 0.009). In Digit Span Backward task DEP group achieved a significantly lower result (the average range of numbers was 3.5 (SD 1.11)) than SCH group (the average range of

numbers was 4.3 (SD 0.92). In Rey's Complex Figure Test, DEP group also had a lower result for delayed recall (score 7.2 (SD 3.93)) compared to SCH group

(score 11.5 (SD 5.42)). No other significant inter-group differences were found in the remaining neurocognitive tests.



The results are shown as the ratio between the average test score of the study group and a demographically matched test norm. Higher and lower ratios deviating from 1.0 indicate deficient results. DEP – patients with depression (n = 30); SCH – patients with schizophrenia (n = 44).

Figure 1. Neurocognitive test results in DEP and SCH patients

	DEP		SCH	
	t	р	t	р
Digit Span - Forward	-0.88	0.393	0.52	0.068
Digit Span - Backward	-2.74	0.016	0.001	0.999
Trail Making Test A	35.13	< 0.001	38.56	< 0.001
Trail Making Test B	91.63	< 0.001	111.06	< 0.001
Rey Complex Figure Test - Copy	-4.75	< 0.001	-4.95	< 0.001
Rey Complex Figure Test - Delayed recall	-10.46	< 0.001	-5.55	< 0.001
Rey Verbal Learning Test - Immediate recall	-4.84	< 0.001	-5.28	< 0.001
Rey Verbal Learning Test - 5 th repetition recall	-4.84	< 0.001	-4.98	< 0.001
Rey Verbal Learning Test - Interference stimuli recall	-4.78	< 0.001	-8.75	< 0.001
Rey Verbal Learning Test - Recall after interference stimuli	-3.73	0.002	-3.90	0.001
Rey Verbal Learning Test - Delayed recognition	-2.93	0.011	-3.45	0.002

DEP – patients with depression (n = 30); SCH – patients with schizophrenia (n = 44)

	DEP : SCH		
	t	р	
Digit Span - Forward	-1.26	0.229	
Digit Span - Backward	-2.17	0.037	
Trail Making Test A	1.27	0.212	
Trail Making Test B	0.35	0.726	
Rey Complex Figure Test - Copy	-1.44	0.158	
Rey Complex Figure Test - Delayed recall	-2.76	0.009	
Rey Verbal Learning Test - Immediate recall	-0.60	0.554	
Rey Verbal Learning Test - 5 th repetition recall	0.61	0.546	
Rey Verbal Learning Test - Interference stimuli recall	1.21	0.236	
Rey Verbal Learning Test - Recall after interference stimuli	-0.03	0.974	
Rey Verbal Learning Test - Delayed recognition	0.30	0.769	

DEP – patients with depression (n=30); SCH – patients with schizophrenia (n=44)

DISCUSSION

In accordance with the hypotheses of many authors (Green et al. 2000, Austin et al. 2001, Bowie & Harvey 2005, Chamberlain & Sahakian 2005), similar cognitive impairment profile was observed among DEP and SCH patients in our study. These results are therefore not in line with the findings that indicate certain cognitive deficits to be pathognomonic of DEP (general slow-down) and SCH (deficits in executive processes) (Friedman et al. 2001, Turetsky et al. 2002, Gualtieri et al. 2006).

In contrast to expectations based on the results of previous studies (Green et al. 2004, Nuechterlein et al. 2004, Buchanan et al. 2005), which found significantly impaired automatic processes in both patient groups, our DEP and SCH patients showed intact working memory capacities (demonstrated in Digit Span Forward scores). This indicates that automatic processes are preserved in these patients, but in regard of other results of the study, probably have little influence on memory and executive cognitive domains. On the other hand, compared to test norms, a general cognitive decline was observed in both patient groups. Both exhibited strongly impaired sustained and shifted attention in psychomotor tasks, poor perceptual organization, memory functions and learning processes, as well as impairment of their functioning in distracting conditions. Even though memory function of recognition has generally been assumed to remain intact (Bowie & Harvey 2005) in these patients, in our study it was found to be impaired.

Psychomotor slowing was not proved to be specific of DEP, since in both study groups prolonged task solving times were found when linking numbers in the Trail Making Test A. These results confirm previous findings of those authors who believe that due to a lack of energy in the case of DEP and avolition in the case of SCH, psychomotor retardation is one of the basic common symptoms of these two disorders (Crowe 1998, Chamberlain & Sahakian 2004, Morrens et al. 2006, Morrens et al. 2007). In our study it was reflected in solving mental effort tasks. No problems were seen in the case of automatic cognitive tasks, such as those included in the Digit Span Forward Test, in which neither DEP nor SCH group deviated from the normative group when asked to memorize numbers. However, caution is needed with such interpretations. First, in our study a total psychomotor slowing was assessed, which according to Morrens et al. (2006, 2007) may be misleading. They warn that psychomotor speed is influenced by both, sensorymotor and cognitive processes that may be unrelated. Therefore in future studies separate tests for these two components should be used. In addition, the score on Trail Making Test is influenced by a broad interval of other cognitive functions, which are supposed to be impaired in SCH and DEP patients, for example attention or visuospatial scanning. Also, it is possible that the neurocognitive test results of our patients were subjected to motivational

factors (Barch 2005), which however were not controlled for in our study.

The only important differences between our study groups were found to be the cognitive task of attention shifting and delayed recall of visual material, during which DEP patients had significantly worse results than did patients with SCH. Again, a possible explanation for this finding could be in uncontrolled motivational factors. Furthermore, the heterogeneity of diagnostic subcategories could have had a significant influence on our results, as the majority of patients from SCH group were diagnosed as paranoid, while DEP group was heterogeneous with respect to disease severity. According to Palmer et al. (1997), it should be pinpointed, that paranoid SCH subgroup could be constituted of cognitively better functioning patients. This is not very likely in the case of our SCH patients, since they scored below the normative results in tests of most basic cognitive dimensions. Similar results were obtained in other studies (Zalewski et al. 1998, Wilk et al. 2005, Gualtieri et al. 2006).

However, the findings of our study would be more reliable when overcoming some of its limitations. In addition to larger sample size, controlling for drug therapy and motivational factors, more precise neurocognitive tests should be included, together with another control group. Learning potential, verbal skills and social cognition could as well be monitored in both diagnostic groups.

CONCLUSIONS

In the acute phase of schizophrenia and depression similar cognitive impairment profiles can be found, indicating caution is needed when cognitive deficits are viewed upon as a possible differential diagnostic criterion. Further studies are necessary to assess longitudinal dynamics, intensity fluctuations and possible development of specific patterns of cognitive functioning in these patients.

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