

Chapter 5

Psychopathology and cognition in schizophrenia spectrum disorders: the role of depressive symptoms

Published:

Holthausen, E.A.E., Wiersma, D., Knegtering, R.H., van den Bosch, R.J., 1999.
Schizophr. Res. 39, 65-71.

Abstract

The cognitive correlates of five symptom dimensions based on PANSS ratings were examined in a group of 50 recent onset psychotic patients, using both objective and subjective cognitive measures. We were particularly interested in the depression dimension, since it has not been studied extensively thus far. The depression dimension showed a fairly high number of correlations with both objective and subjective cognitive measures, such as problems with simple and divided attention, psychomotor slowing and subjectively experienced distractibility, overload and diminished attentional control. The other dimensions, including the negative symptoms, had less cognitive correlates. It is possible that previous studies based on a three-dimensional model confounded correlates of negative symptoms with correlates of depressive symptoms. The results of this study suggest the need for more research into the mechanisms underlying the relationship between depressive symptoms and cognitive functioning in schizophrenia, and that patients with depressive symptoms are less efficient in information processing, but can compensate by investing more mental effort. Because subjective cognitive measures were related to mental effort in previous research they can be a useful tool in future research.

1. Introduction

Although schizophrenia is associated with a diversity of cognitive impairments, such as deficits in attention, memory, motor functioning and executive functioning (Gold and Harvey, 1993; Gourovitch and Goldberg, 1996; Rossel and David, 1997), it is not possible to specify a typical cognitive profile. This is partly due to the heterogeneity of the disease. Attempts to group patients into different subtypes of schizophrenia have not led to a solution. However, during the last decade a more promising dimensional approach has emerged, which categorizes symptoms instead of patients (Andreasen and Carpenter, 1993). Studies have consistently identified a positive, a negative and a disorganization dimension (Andreasen et al., 1994). Some, using a wider range of symptom ratings, also found excitement and depression-anxiety dimensions (Bell et al., 1992, 1994; Kay and Sevy, 1990; Lindenmayer et al., 1994, 1995). It has been suggested that the dimensions represent different pathological processes (Liddle et al., 1987; 1992). If this is true, it is likely that the symptom dimensions have specific cognitive correlates.

A number of studies have addressed the cognitive correlates of these dimensions of schizophrenia (Addington et al., 1991; Berman et al., 1997; Brown and White, 1992; Liddle, 1987; Liddle and Morris, 1991; Norman et al., 1997; Van der Does et al., 1996). Most included only positive, negative and disorganization symptom dimensions. The negative dimension has been shown to correlate with poor generation or execution of cognitive strategies, slow responses on simple attention tasks, poor abstract reasoning and impaired set shifting. The positive dimension appears to correlate mainly with poor verbal memory, and the disorganization dimension has been shown to correlate with attentional dysfunction and inhibition problems. Only two studies examined cognitive correlates of depressive symptoms, focusing on attention and verbal memory respectively. Van der Does et al. (1996) found a significant correlation with poor selective attention and Brebion et al. (1997) found that depressive symptoms correlated significantly with poor semantic encoding and reduced verbal recall and recognition.

It is well established that a proportion of the patients, ranging from 11% to 55% (Palmer et al., 1997), do not show cognitive deficits on neuropsychological or objective cognitive measures, although they often complain about their

cognitive functioning. It is possible that these individuals perform below the level they could have achieved if not ill. Another explanation might be that they are able to compensate for their cognitive deficits on neuropsychological tasks by investing more mental effort. These tasks usually measure basic cognitive functions over a short period, in a structured way, whereas in daily life patients probably reach their limits because the pressure on their information processing capacity is much larger. Ratings of subjective cognitive experiences could be helpful in obtaining an indirect measure of mental effort, because a recent study has shown that self-report ratings of increased mental effort are associated with subjective experiences of mental overload and distractibility (Van den Bosch & Rombouts, 1998).

Subjective cognitive deficits are failures or difficulties experienced by a person in the perception and processing of internal and external information, which are usually measured with self-report questionnaires. A small number of studies have examined subjective cognitive functioning in schizophrenia. These studies report a high prevalence of subjective cognitive deficits (Liddle et al., 1988; Peralta and Cuesta, 1998; Van den Bosch et al., 1993). There is a striking lack of correlation between objective and subjective measures. Williams et al. (1984) did not find a relation between self-report of cognitive difficulties and a choice reaction time task. Van den Bosch and Rombouts (1998) found no correlation between subjective cognitive dysfunctions and vigilance performance.

Our main objective in this study was to examine whether the five psychopathology dimensions have different cognitive correlates in recent onset psychotic patients. We were particularly interested in the depression dimension, because there is good evidence for its independent existence and it has not been studied extensively thus far. Although we do not know which specific cognitive functions are associated with this dimension, we hypothesized that it would have at least some cognitive correlates. Neuropsychological tasks addressed attentional, memory, executive and motor speed functions. To get an indirect measure of the amount of mental effort people invest to compensate for their cognitive deficits, we also included subjective ratings of cognitive functioning.

2. Method

2.1. Subjects

The study included fifty psychiatric patients who had recently experienced a first or second psychotic episode. Psychiatric diagnosis according to DSM-IV (American Psychiatric Association, 1994) was based on all information available, including a structured interview (Schedules for Clinical Assessment in Neuropsychiatry, SCAN; Wing et al, 1990). This study was part of a larger epidemiological study for which they gave informed consent. Exclusion criteria were severe mental retardation and a known systemic or neurological illness. Subject characteristics are given in table 1. There were no significant differences between the schizophrenic patients and patients with another psychotic disorder for sex (Chi-square = 0.02, ns), age ($F = 0.12$, ns), or educational level ($F = 1.62$, ns).

Table 1. Demographic characteristics of patients by diagnosis.

Diagnosis	n	age		sex m / f	educational level*	
		m	sd		m	sd
schizophrenia	32	24.8	6.3	22 / 10	3.8	1.3
schizophreniform disorder	10	23.7	6.3	7 / 3	2.4	0.7
delusional disorder	2	28.5	4.9	2 / -	4.0	1.4
brief psychotic disorder	2	18.	2.1	- / 2	3.5	0.7
psychotic disorder NOS	4	31.8	9.4	3 / 1	4.8	1.9
Total	50	25.0	6.6	34 / 16	3.6	1.4

* educational level goes from 1: primary school, up to 6: university degree

The average daily dosage of antipsychotic drugs was 6.1 mg haloperidol equivalents (range 1.0 - 20.0 mg). Seven patients were drug-free. Fifteen patients also used antiparkinsonian drugs.

2.2. Procedures and instruments

During the first week after admission patients were interviewed with the SCAN. Psychiatric diagnosis was made at a consensus meeting, seven weeks after admission. Only subjects with a diagnosis within the schizophrenia spectrum (schizophrenia, schizophreniform disorder, delusional disorder, brief psychotic

disorder, psychotic disorder NOS) were included. Patients were tested after a period of six weeks on stable medication. Within the same week their symptoms were rated on the Positive and Negative Syndrome Scale (PANSS; Kay et al., 1987). Dimensional scores were obtained by calculating sum scores of symptoms loading high on the five dimensions described in a large factor analytical study (Lindenmayer et al., 1995).

Objective cognitive functioning was measured using a neuropsychological battery measuring attention, memory, executive functioning and motor speed. Vigilance was measured with the sensitivity index d' of a double stimulus Continuous Performance Task (CPT; Van den Bosch et al, 1996). A computerized STROOP task measured reaction time in two simple (names, colors) and one complex selective attention task (interference). Forms A and B of a computerized version of the Trail Making Test were used to measure simple and divided attention respectively. The Digit Span subtest of the Wechsler Adult Intelligence Scale (WAIS; Stinissen et al., 1970) was used to measure immediate verbal memory, and the delayed recall score of the Dutch translation of the Rey Auditory Verbal Learning Task (RAVLT; Rey, 1964) was used to measure long-term verbal memory. Executive functioning was measured as the number of steps taken on a computerized Maze task and motor speed was measured by Fingertapping.

Subjective cognitive functioning was measured with the Test of Attentional Style (TAS; Van den Bosch et al., 1993). The TAS is a self-report questionnaire of 31 items containing five subscales. Responses are on a five point scale ranging from 1: "never" to 5: "always". The first two subscales refer to cognitive problems and are called (1) Distractibility and (2) Overload. The other three subscales measure perceived cognitive efficacy and are named (3) Processing capacity; (4) Attentional Control and (5) Conceptual Control. The last subscale was left out of analysis because it does not distinguish patients from normal controls (see Van den Bosch et al, 1993, for a more extensive description).

3. Results

Table 2 presents the data on the symptom dimensions and the cognitive measures. The symptom ratings, especially on the excitement and the disorganization dimensions, were fairly low. This is no surprise because patients were rated after a period of six weeks on stable medication.

	Mean	SD
Symptom dimensions		
positive (5 PANSS items)	9.9	5.0
negative (6 PANSS items)	12.4	5.0
disorganization (5 PANSS items)	7.7	2.7
depression (4 PANSS items)	9.3	3.3
excitement (3 PANSS items)	3.7	1.1
Neuropsychological tests		
CPT d'	3.6	0.9
STROOP names (s) ¹	53.6	9.1
STROOP colors (s)	50.4	9.3
STROOP interference (s)	68.0	15.3
Trail Making A (s) ¹	84.6	39.2
Trail Making B (s)	103.3	40.6
Mazes number of steps ²	280.5	108.0
Fingertapping (10 s)	50.9	12.5
Digit Span WAIS	12.8	3.6
Delayed recall RAVLT	9.4	2.6
Subjective Cognitive Functioning ³		
Distractibility	23.1	4.7
Overload	16.8	4.6
Processing Capacity	17.8	3.4
Attentional Control	15.2	2.3

Table 2. Symptom dimensions, neuropsychological tests and subjective cognitive functioning six weeks after admission.

The excitement dimension was left out of analysis because of the very low variability in scores. We do not give the norm-scores for the objective cognitive variables because the tasks were standardized on different groups. In general the STROOP, Trail Making and Maze tasks were performed poorly. Performance on the CPT, Fingertapping, Digit Span and verbal learning tasks were within

the normal range. All variables resembled the standard normal distribution, except the positive and the disorganization dimensions, which were skewed to the left. Therefore we used parametric as well as nonparametric correlation analysis. Because we predicted higher levels of symptomatology to be associated with poorer cognitive performance, one-tailed tests of significance were used (table 3).

The depression dimension in particular correlated significantly with a number of objective and subjective cognitive variables: slow performance on STROOP colors, Trailmaking A and B, Fingertapping and subjectively experienced distractibility, overload and diminished attentional control. The other symptom

¹ This computerised version takes longer than the paper and pencil test.

² Minimum number of steps, which means an excellent performance, is 205.

³ For mean scores and standard deviations of a normal control group see: Van den Bosch et al (1993).

dimensions showed less significant correlations with these variables. The positive dimension correlated with poor delayed verbal recall and slow Trailmaking B, as well as subjective overload experiences. The disorganization dimension correlated with subjective distractibility and overload experiences, but not with objective test measures. The negative dimension correlated with poor Fingertapping and the subjective experience of distractibility and diminished processing capacity.

Table 3. Correlations between symptom dimensions and cognitive variables.

cognitive variables	positive dimension †	disorganization dimension †	negative dimension ‡	depression dimension ‡
Objective				
CPT d'	0.10	-0.05	-0.04	0.06
STROOP names	0.01	0.03	0.08	0.23
STROOP colors	0.13	0.09	0.13	0.35**
STROOP interference	0.07	0.02	0.09	0.23
Trail Making A	0.15	0.04	0.12	0.26*
Trail Making B	0.32*	0.17	0.24	0.29*
Mazes number of steps	-0.08	0.05	0.12	0.15
Fingertapping	-0.19	-0.02	-0.25*	-0.28*
Digit Span WAIS	-0.01	-0.05	-0.18	-0.17
Delayed recall RAVLT	-0.33*	-0.05	0.07	0.19
Subjective				
Distractibility	0.20	0.24*	0.30*	0.49***
Overload	0.31*	0.25*	0.22	0.44**
Processing Capacity	0.05	0.03	-0.26*	-0.07
Attentional Control	-0.11	-0.09	-0.12	-0.33**

† Spearman rank-order correlation coefficients; ‡ Pearson product-moment correlation coefficients. One-tailed significance, * $p < .05$, ** $p < .01$, *** $p < .001$

The associations between objective and subjective cognitive measures were examined with one-tailed tests for significance on the Pearson product-moment correlations. Distractibility correlated significantly ($p < .05$) with the STROOP interference (0.27), Fingertapping (-0.25) and Digit Span (0.34). Processing capacity correlated significantly ($p < .05$) with Trail Making B (0.30), and Attentional control correlated significantly with Delayed verbal recall (0.35). The subjective experience of Overload had no objective cognitive correlates.

4. Discussion

In this study on recent onset psychotic patients we found significant correlations between several symptom dimensions and subjective as well as objective cognitive variables. Depressive symptoms were associated with a fairly high number of cognitive ratings such as problems with simple and divided attention, psychomotor slowing and subjective experiences of distractibility, overload and diminished attentional control. The other symptom dimensions showed fewer cognitive correlates, with some overlap with the depression dimension. Negative symptoms correlated with psychomotor slowing and the experience of distractibility, as did the depressive symptoms. However, there was a unique correlation with the experience of diminished processing capacity. Somewhat surprisingly, disorganization symptoms correlated only with subjective experiences of distractibility and overload but not with objective cognitive measures. Positive symptoms correlated with problems in divided attention and subjective experiences of overload, like depressive symptoms, but there was a unique correlation with poor verbal recall. The last finding is in accordance with other studies (Berman et al., 1997; Norman et al., 1997), whereas the findings concerning negative and disorganization symptoms are not. In most studies these dimensions correlate with executive and attentional tasks (Addington et al., 1991; Berman et al., 1997; Brown and White, 1992; Liddle, 1987; Liddle and Morris, 1991; Norman et al., 1997; Van der Does et al., 1996). Our negative findings regarding objective cognitive correlates of the disorganization dimension might be due to the fact that our patients had relatively few of these symptoms because they were on stable medication. There are several possible explanations for the lack of objective cognitive correlates of the negative symptoms in this study. First, in other studies this dimension usually correlates with less structured executive tasks like Verbal Fluency and Wisconsin Card Sorting, while we used an executive task (Mazes) which forces the subject to find the only possible solution. Second, the patient group also differed from other studies, most of which were based on more chronic patients. Studies of recent onset patients are not confounded by long-term medication or hospitalization, but these patients have a higher prevalence of depression (Addington et al., 1998; Koreen et al., 1993). This makes it more likely that cognitive correlates of depressive symptoms are identified. Moreover, studies

based on a three-dimensional model of symptomatology are likely to confound correlates of negative symptoms with correlates of depressive symptoms. Most studies have only looked at negative, positive and disorganization dimensions.

The evidence in favor of an independent dimension of depressive symptoms in schizophrenia is quite strong, as is shown by several factor analytical studies (Bell et al., 1992; 1994; Kay and Sevy, 1990; Lindenmayer et al., 1994; 1995), correlational studies (Kuck et al., 1991; Newcomer et al., 1989), and studies investigating the differences between schizophrenic patients with and without depression (Kohler et al., 1998; Lindenmayer et al., 1991). It is important to study these symptoms and their cognitive correlates in addition to the core symptoms of psychosis. If the causal mechanisms of the symptom dimensions and their cognitive correlates are the same regardless of the diagnostic category, then the causal mechanisms of some cognitive problems of psychotic patients with depressive symptoms could be the same as those in affective disorder patients. Depressive patients are less efficient in effortful information processing, and this would show in a slowness in reacting and responding (King and Caine, 1996). This agrees well with our findings on objective cognitive tasks.

The correlations of depressive symptoms with subjective cognitive complaints are also interesting. There is a relationship between depressive symptoms and subjective experiences of distractibility and mental overload. Previous research showed that in schizophrenic patients these subjective complaints were strongly related to ratings of the amount of mental effort people felt they had to spend on cognitive tasks (Van den Bosch & Rombouts, 1998). It could be speculated that depressive symptoms are accompanied by less efficient information processing, as a result of which patients have to invest more effort, which, in turn, results in subjective cognitive complaints in spite of normal results on neuropsychological tasks. This points to the importance of subjective measures for cognitive research. There were some correlations between subjective and objective cognitive tasks, but subjective mental overload had no objective cognitive correlates. This could mean that this scale addresses problems, which cannot easily be assessed by neuropsychological tasks.

The results of this study suggest that more research should be directed at the mechanisms behind the relationship between depressive symptoms and cognitive dysfunctioning in schizophrenia. In this study, the depression

dimension of the PANSS was used. In future research more sophisticated depression scales might be used. Subjective cognitive ratings and psycho-physiological measures of mental effort could be helpful in unraveling the relationship between depressive symptoms and cognition.

References

- Addington, J.D., Addington, D., Maticka-Tyndale, E., 1991. Cognitive functioning and positive and negative symptoms in schizophrenia. *Schizophr. Res.* 5, 123-124.
- Addington, D., Addington, J., Patten, S., 1998. Depression in people with first-episode schizophrenia. *Br.J.Psychiatry. Suppl.* 33, 90-92.
- American Psychiatric Association, 1994. *Diagnostic and Statistical Manual of Mental Disorders*, 4th ed. American Psychiatric Association, Washington DC.
- Andreasen, N.C., Carpenter, W.T.Jr., 1993. Diagnosis and classification of schizophrenia. *Schizophr.Bull.* 19, 199-214.
- Andreasen, N.C., Nopoulos, P., Schultz, S., Miller, D., Gupta, S., Swayze, V., Flaum, M., 1994. Positive and negative symptoms of schizophrenia: past, present, and future. *Acta Psychiat. Scand. Suppl.* 384, 51-59.
- Bell, M., Milstein, R., Beam Goulet, J., Lysaker, P., Cicchetti, D., 1992. The Positive and Negative Syndrome Scale and the Brief Psychiatric Rating Scale. Reliability, comparability, and predictive validity. *J. Nerv. Ment. Dis.* 180, 723-728.
- Bell, M.D., Lysaker, P.H., Beam Goulet, J.L., Milstein, R.M., Lindenmayer, J.P., 1994. Five-component model of schizophrenia: assessing the factorial invariance of the positive and negative syndrome scale. *Psychiat. Res.* 52, 295-303.
- Berman, I., Viegner, B., Merson, A., Allan, E., Pappas, D. Green, A.I., 1997. Differential relationships between positive and negative symptoms and neuropsychological deficits in schizophrenia. *Schizophr. Res.* 25, 1-10.
- Brebion, G., Smith, M.J., Amador, X., Malaspina, D., Gorman, J.M., 1997. Clinical correlates of memory in schizophrenia differential links between depression, positive and negative symptoms, and two types of memory impairment. *Am. J. Psychiatry* 154, 1538-1543.
- Brown, K.W., White, T., 1992. Syndromes of chronic schizophrenia and some clinical correlates. *Br. J. Psychiatry* 161, 317-322.
- Gold, J.M., Harvey, P.D., 1993. Cognitive deficits in schizophrenia. *Psychiat. Clin. North. Am.* 16,295-312.
- Gourovitch, M.L., Goldberg, T.E. 1996. Cognitive deficits in schizophrenia: attention, executive functions, memory and language processing. In C. Pantalis, H.E. Nelson, T.R. Barnes. (Eds.). *Schizophrenia: a neuropsychological perspective.* (pp 71-87). Wiley, Chichester, pp 71-87.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The Positive and Negative Syndrome Scale (PANSS) for schizophrenia. *Schizophr. Bull.* 13, 261-276.
- Kay, S.R., Sevy, S., 1990. Pyramidal model of schizophrenia. *Schizophr. Bull.* 16,537-545.
- King, D.A., Caine, E.D., 1996. Cognitive impairment and major depression: beyond the pseudodementia syndrome. In I. Grant, K.M. Adams (Eds.). *Neuropsychological assessment of neuropsychiatric disorders.* Oxford University Press, New York, pp 200-217.
- Kohler, C., Gur, R.C., Swanson, C.L., Petty, R., Gur, R.E., Mozley, L.H., 1998. Depression in schizophrenia: Association with neuropsychological deficits. *Biol. Psychiatry* 43, 173-180.

- Koreen, A.R., Siris, S.G., Chakos, M., Alvir, J., Mayerhoff, D., Lieberman, J., 1993. Depression in first-episode schizophrenia. *Am.J.Psychiatry* 150, 1643-1648.
- Kuck, J., Zisook, S., Moranville, J.T., Heaton, R.K., Braff, D.L., 1992. Negative symptomatology in schizophrenic outpatients. *J.Nerv.Ment.Dis.* 180, 510-515.
- Liddle, P.F., 1987. Schizophrenic syndromes, cognitive performance and neurological dysfunction. *Psychol. Med.* 17, 49-57.
- Liddle, P.F., Barnes, T.R., 1988. The subjective experience of deficits in schizophrenia. *Compr. Psychiatry* 29, 157-164.
- Liddle, P.F., Morris, D.L., 1991. Schizophrenic syndromes and frontal lobe performance. *Br. J. Psychiatry* 158, 340-345.
- Liddle, P.F., Friston, K.J., Frith, C.D., Hirsch, S.R., Jones, T., and Frackowiak, R.S., 1992. Patterns of cerebral blood flow in schizophrenia. *Br.J.Psychiatry* 160, 179-186.
- Lindenmayer, J.P., Grochowski, S., Kay, S.R., 1991. Schizophrenic patients with depression: psychopathological profiles and relationship with negative symptoms. *Compr.Psychiatry* 32, 528-533.
- Lindenmayer, J.P., Bernstein Hyman, R., Grochowski, S. A., 1994. A new five factor model of schizophrenia. *Psychiat. Quart.* 65, 299-322.
- Lindenmayer, J.P., Grochowski, S., Hyman, R.B., 1995. Five factor model of schizophrenia: replication across samples. *Schizophr. Res.* 14, 229-234.
- Newcomer, J.W., Faustman, W.O., Yeh, W., Csernansky, J.G., 1990. Distinguishing depression and negative symptoms in unmedicated patients with schizophrenia. *Psychiat. Res.* 31, 243-250.
- Norman, R.M., Malla, A.K., Morrison Stewart, S.L., Helmes, E., Williamson, P.C., Thomas, J., Cortese, L., 1997. Neuropsychological correlates of syndromes in schizophrenia. *Br. J. Psychiatry* 170, 134-139.
- Palmer, B.W., Heaton, R.K., Paulsen, J.S., Kuck, J., Braff, D., Harris, M.J., Zisook, S., Jeste, D.V., 1997. Is it possible to be schizophrenic yet neuropsychologically normal? *Neuropsychology* 11, 437-446.
- Peralta, V., Cuesta, M.J., 1998. Subjective experiences in psychotic disorders: diagnostic value and clinical correlates. *Compr. Psychiatry* 39, 11-15.
- Rey, A., 1964. *L'examen clinique en psychologie*. Presses Universitaires de France, Paris.
- Rossel, S.L., David, A.S., 1997. The neuropsychology of schizophrenia: recent trends. *Curr. Opin. Psychiatry* 10, 26-29.
- Stinissen, J. Willems, P.J., Coetsier, P., Hulsman, W.L.L., 1970. *Manual of the Dutch translation of the Wechsler Adult Intelligence Scale*. Swets, Amsterdam.
- Van den Bosch, R.J., Rombouts, R.P., Asma, M.J.O., 1993. Subjective cognitive dysfunction in schizophrenic and depressed patients. *Compr.Psychiatry* 34, 130-136.
- Van den Bosch, R.J., Rombouts, R.P., and van Asma, M.J.O., 1996. What determines continuous performance task performance? *Schizophr.Bull.* 22, 643-651.
- Van den Bosch, R.J., Rombouts, R.P., 1998. Causal mechanisms of subjective cognitive dysfunction in schizophrenic and depressed patients. *J.Nerv.Ment.Dis.* 186, 364-368.

Van der Does, A.J., Dingemans, P.M., Linszen, D.H., Nugter, M.A., and Scholte, W.F., 1996. Symptoms, cognitive and social functioning in recent-onset schizophrenia: a longitudinal study. *Schizophr.Res.* 19, 61-71.

Williams, R.M., Alagaratnam, W., Hemsley, D.R., 1984. Relationship between subjective self-report of cognitive dysfunction and objective information processing performance in a group of hospitalized schizophrenic patients. *Eur. Arch. Psychiat. Neurol. Sci.* 234, 48-53.

Wing, J.K., Babor, T.F., Brugha, T.S., Burke, J., Cooper, J.E., Giel, R., Jablensky, A., Regier, D.A., Sartorius, N., 1990. SCAN Schedules for Clinical Assessment in Neuropsychiatry. *Arch.Gen. Psychiatry* 47, 589-593.