Neurocognitive performance and negative symptoms: Are they equal in explaining disability in schizophrenia outpatients?

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Abstract

Objective: The aim of this study is to assess if cognitive variables and symptom dimensions can predict disability in a sample of outpatients with schizophrenia.

Method: A cross-sectional sample of 113 individuals with a diagnosis of schizophrenia (DSM-IV criteria) was selected from a computerized register of five Community Mental Health Centers. Patients were assessed by two trained psychologists, with a neuropsychological battery comprising measures for verbal memory, attention, operative memory and abstraction and flexibility functions. Symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS); a socio-demographic and clinical questionnaire, comprising the Disability Assessment Scale (DAS), was also completed. Test scores were standardized (t scores) to performance of healthy controls. To assess the relationship between clinical and sociodemographic factors and disability and cognitive functioning Pearson’s correlation coefficients were computed. In order to establish the predictive capacity of the cognitive, clinical and symptom variables on disability linear regression models were fitted.

Results: Mean age of patients was 41.6 years and 68% were male. Higher ratings in the negative dimension were associated with more cognitive deficits. Association with the positive dimension was present but less strong. All disability areas, except for disability in occupational functioning, were partially explained by the negative dimension. Disability in family functioning was also partially explained by attention and number of admissions since onset.

Conclusion: Negative symptoms are the major source of disability of our sample and are also associated to cognitive functioning. The present findings suggest that further investigation on the mediators between clinical and social outcomes may help to design specific treatments to reduce disability.

Keywords: Schizophrenia; Psychopathology; Positive and Negative Syndrome Scale (PANSS); Cognitive functioning; Disability
1. Introduction

Schizophrenia is frequently associated with disability in different areas of daily life and impaired social functioning (Murray and Lewis, 1987; Obiols, 2001). Disability is defined as disordered or deficient functioning in roles and domains compared to what it is regarded as normal in a particular society, by the family or social group or by the person affected (World Health Organization, 1988). It is considered one of the most relevant outcome measures of schizophrenia (Strauss and Carpenter, 1974; Strauss and Carpenter, 1972).

Social and role functioning requires the performance of abilities which include the performance of complex cognitive tasks (Ertugrul and Ulug, 2002). Thus impaired cognitive functioning should be related to impaired social functioning. For instance, verbal memory and attention deficits should affect the acquisition of social abilities (Addington and Addington, 1999) and impaired executive functions could also lead to an array of social and occupational difficulties (Liddle, 2000). Even though some studies have reported association between cognitive and social impairment (Dickerson et al., 1996; Ertugrul and Ulug, 2002), the positive effects of remediation programs on cognition do not directly translate to improved social functioning (Greenwood et al., 2005).

On the other hand, several studies have reported associations between symptom measures, specially negative symptoms, and domains of functioning (Norman et al., 2000; Greenwood et al., 2005), but it has not been established how negative symptoms directly influence social outcomes (Green, 1996) and they have been assumed to contribute mostly indirectly through their link with cognition or other mediators with social outcomes (Greenwood et al., 2005; Dickerson et al., 1999). In a previous study with a different sample of patients (Ochoa et al., 2005) the author found that symptom severity was also related to patient needs.

Until now, the association between negative symptoms and cognitive deficits and their relation with disability in social functioning has widely been reported (Penades et al., 2001; Grawe and Levander, 2001; Liddle, 2000; Hammer et al., 1995); but it is unclear how much of this functional impairment can be attributed to the presence of psychiatric symptoms or to impaired cognitive functioning (Dickinson and Coursey, 2002).

Efficient treatment should not only lead to symptom reduction but also decrease the disability of patients (Ertugrul and Ulug, 2002; Voruganti et al., 1997). The search for mediators between clinical variables (symptoms and cognition among others) and functional outcome is important since it will help to understand the relationships between clinical variables and disability and it will also help to reasonably define targets of interventions (Green et al., 2000).

The present study was designed to determine how cognitive variables and symptom dimensions can predict disability in our sample of outpatients with schizophrenia. Specifically, it was hypothesized that: (1) cognitive deficits would be most related to the negative component of the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987; Peralta, 1994) and (2) these deficits together with the negative symptoms would have an important role in explaining disability.

2. Method

2.1. Subjects

A cross-sectional sample of 113 individuals (94 completed the entire assessment) with a diagnosis of schizophrenia was selected from a computerized register of five Community Mental Health Centers (CMHC) belonging to Sant Joan de Déu-Mental Health Services. The catchment area of the centers was a well-defined area of the city of Barcelona and surroundings. Inclusion criteria were: (a) primary diagnosis of schizophrenia (DSM-IV-TR (American Psychiatric Association, 2000) criteria as well as confirmed diagnosis by a psychiatrist different from the treating one); (b) age between 18 and 65 years; (c) to live in the catchment areas of the participating CMHC; and (d) to at least have received one outpatient visit during the 6 months previous to the beginning of the study. Patients with a diagnosis of mental retardation, substance abuse or neurological disorder were excluded.

All selected individuals received a complete description of the study by their psychiatrist and provided his/her written informed consent to participate voluntarily in the study which was previously approved by Sant Joan de Déu-Mental Health Services Ethics Committee.

2.2. Procedure and measures

Patients were assessed by two trained psychologists, using a neuropsychological battery comprising measures for verbal memory, attention, operative memory and abstraction and flexibility tasks. Inter-rater reliability was assessed in a pilot study with kappa index above 0.80.
The neuropsychological battery included a number of tests which were classified based on theoretical cognitive function dimensions:

- Measures of abstraction and flexibility abilities which included the Wisconsin Card Sorting Test (WCST-64: CV) (Heaton, 2000) and the Stroop Test (Golden, 1994).
- Measures of attention (Hill et al., 2002) as the Continuous Performance Test (CPTII) (Conners, 2002), Trail Making Test part A (TMTA) (Reitan and Wolfson, 1993), digit span and digit symbol Wechsler Adult Intelligence Scale subscales (WAIS-III) (Wechsler, 1999).
- Measures of verbal memory as the Test de Aprendizaje Verbal España Complutense (TAVEC) (Benedet and Alejandre, 1998).
- Measures of operative memory as the Semantic and Phonemic Verbal fluency Tasks (Benton and Hamsher, 1976) and the Trail Making Test part B (TMTB) (Reitan and Wolfson, 1993).

Measures of executive functioning were grouped into the summary of cognitive abstraction and flexibility abilities and the summary of operative memory. The first summary was defined based on the studies that report the WCST to require cognitive abilities of abstraction/problem solving and ability to shift strategies and the Stroop test to require abilities of response inhibition (Bozikas et al., 2004; Friis et al., 2002). The summary of operative memory includes the Verbal Fluency Tasks, considered to be an operative memory measure (Kieler et al., 2002; Hill et al., 2002), and Part B of the TMT. Part B of the TMT has also been described as an operative memory measure (Bousoño et al., 2004; Asarnow, 1999) and it has been previously analyzed together with verbal fluency measures (Ehmann et al., 2004), even though it also requires the ability to shift strategies.

Symptoms were assessed with the Positive and Negative Syndrome Scale (PANSS) (Kay et al., 1987; Penalta, 1994). Disability was assessed with the Disability Assessment Schedule-short version (DAS-sv) (World Health Organization, 1992). This is a brief schedule designed to evaluate the disability caused by psychiatric disorders. It measures the severity and duration of the disability in four areas: personal care, family functioning, occupational functioning and social functioning. A socio-demographic and clinical questionnaire was also administered.

2.3. Data analysis

To provide a Standard metric for comparisons across cognitive subtests, tests were scored as specified in test manuals, with conversions to demographically corrected $t$ scores. Scores for each cognitive function assessed (abstraction and flexibility, verbal memory, operative memory and attention) were obtained by computing the mean of tests involved in each function (Hill et al., 2002).

As syndromes obtained by factor analysis of the PANSS are unstable over time, (Hill et al., 2002) we considered appropriate to use the factors resulting after a Principal Component Analysis (PCA) for the ratings obtained by the subjects of our sample. The PCA resulted in four principal components with eigenvalues over 1.5 that accounted for 56.22% of the variance. After oblimin rotation, these factors were identified as Negative, Excitement, Affective and Positive components in decreasing order of relative importance (Villalta-Gil et al., in press).

To assess the relationship between clinical factors, disability and cognitive functioning Pearson correlation coefficients were computed. Only those correlation coefficients with a $p$-value lower than 0.01 were reported as significant, in order to reduce Type I errors.

To establish the predictive capacity of the four cognitive summaries (attention, verbal memory, operative memory and abstraction and flexibility abilities) and clinical variables (negative, excitative, affective and positive dimensions and number of admissions) on the four areas of disability (personal care, occupational functioning, family functioning and social functioning), a linear regression models were fitted. Besides these variables, the model also included gender, age, education, years since onset and age at onset. Model reduction was conducted with a stepwise method.

3. Results

Table 1 shows the characteristics of the patients included in the study. 68% of the sample were male (77 men and 36 women), mean age of the sample was 41.64 (SD=12.75) years and 74.3% of the sample had a medium educational background (between 5 and 12 years of education). Most subjects were single (74.3%), while only the 16.8% were married. A total of 55.8% of the patients were living with their parents, followed by a 17.7% who lived with their own family. Subjects receiving some kind of pension accounted for 79.6% of the sample and only a 7.1% were working at the time of the assessment. Patients had been admitted to hospital a mean number of 3.38 (SD=4.06) times since onset, although a 17.1% of the sample had never been hospitalized. The clinical profile indicated that the illness onset was in the early twenties and years since onset were near twenty; so we are in front a chronic sample of
Patients in our study have severe difficulties when undertaking complex tasks and managing responsibilities, which is confirmed by the high percentage of them living with their parents and receiving some kind of pension. The chronic course of the disorder could be aggravating the disability (Usall et al., 2002).

Negative symptoms have been significantly associated with disability in family functioning and in social functioning. People with more severe negative symptoms show worse or scarce interactions with family members and with members of the community (friends, colleagues, neighbors ...). Considering that the assessment of negative symptoms comprises the assessment of social functioning, this relation could have been expected (Addington and Addington, 1999; Dickinson and Coursey, 2002). Disability in social functioning is also associated with positive symptoms, and this finding is consistent with previous studies (Dickinson and Coursey, 2002). Considering that positive symptoms are less present in our sample than negative symptoms, this finding indicates us that they are disruptive enough to relate significantly to poor social functioning.

Disability in personal care tends to be associated with negative symptoms. In a previous study about patient needs that assessed a different sample of patients with schizophrenia, families could not predict disability. Disability in occupational functioning was not explained by any variable. These multivariate findings were independent of gender, education, age, age at onset and years since onset.

### 4. Discussion

Results suggest two different relations between symptoms, cognition and disability. The first refer to direct associations between symptoms and disability and cognition and disability, while the second type of relations refer to the specific load of each of the symptom and cognitive variables in explaining disability.

#### 4.1. Symptoms and disability

Negative symptoms have resulted to be associated with disability (personal care, family and social functioning and total score), except for disability in occupational functioning which has not been related to any of the variables analyzed. Disability in occupational functioning of the patients in our sample is much more severe than in the rest of areas and shows little variation among them, which probably causes that no variable has been associated with it.

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### Table 1

<table>
<thead>
<tr>
<th>Description of clinical, cognitive and disability variables of the patients</th>
<th>Mean</th>
<th>SD</th>
<th>Min–Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>41.64</td>
<td>12.75</td>
<td>19.53–80.29</td>
</tr>
<tr>
<td>G.A.F.</td>
<td>43.48</td>
<td>10.41</td>
<td>20.00–70.00</td>
</tr>
<tr>
<td>Years since onset</td>
<td>18.91</td>
<td>11.16</td>
<td>0.77–54.08</td>
</tr>
<tr>
<td>Age at onset</td>
<td>22.91</td>
<td>6.85</td>
<td>7.75–43.03</td>
</tr>
<tr>
<td>Admissions since onset</td>
<td>3.38</td>
<td>4.06</td>
<td>0–25</td>
</tr>
<tr>
<td>Disability: Personal Care</td>
<td>0.62</td>
<td>0.80</td>
<td>0.00–3.00</td>
</tr>
<tr>
<td>Disability: Occupational Functioning</td>
<td>4.21</td>
<td>1.61</td>
<td>0.00–5.00</td>
</tr>
<tr>
<td>Disability: Family Functioning</td>
<td>1.33</td>
<td>1.15</td>
<td>0.00–5.00</td>
</tr>
<tr>
<td>Disability: Social Functioning</td>
<td>1.83</td>
<td>1.06</td>
<td>0.00–5.00</td>
</tr>
<tr>
<td>Disability: Total Score</td>
<td>7.95</td>
<td>3.31</td>
<td>0.00–16.00</td>
</tr>
<tr>
<td>Negative PANSS</td>
<td>19.97</td>
<td>6.26</td>
<td>9.37–32.89</td>
</tr>
<tr>
<td>Excitative PANSS</td>
<td>4.10</td>
<td>1.01</td>
<td>2.79–7.26</td>
</tr>
<tr>
<td>Affective PANSS</td>
<td>6.02</td>
<td>2.02</td>
<td>3.71–14.06</td>
</tr>
<tr>
<td>Positive PANSS</td>
<td>9.99</td>
<td>3.32</td>
<td>4.96–18.76</td>
</tr>
<tr>
<td>Verbal Memory</td>
<td>38.09</td>
<td>8.12</td>
<td>14.77–53.07</td>
</tr>
<tr>
<td>Operative Memory</td>
<td>30.99</td>
<td>8.70</td>
<td>6.45–53.00</td>
</tr>
<tr>
<td>Abstraction and Flexibility abilities</td>
<td>50.21</td>
<td>9.08</td>
<td>34.38–72.50</td>
</tr>
<tr>
<td>Attention</td>
<td>61.01</td>
<td>27.61</td>
<td>17.00–199.08</td>
</tr>
</tbody>
</table>

Patients in our study have severe difficulties when undertaking complex tasks and managing responsibilities, which is confirmed by the high percentage of them living with their parents and receiving some kind of pension. The chronic course of the disorder could be aggravating the disability (Usall et al., 2002).
Table 2
Pearson correlation coefficients between clinical, symptom, cognitive and disability variables

<table>
<thead>
<tr>
<th></th>
<th>Clinical variables</th>
<th>Symptoms</th>
<th>Cognitive functioning</th>
<th>Disability</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Age</td>
<td>Years since onset</td>
<td>Age at onset</td>
<td>Admissions since onset</td>
</tr>
<tr>
<td><strong>CLINICAL VARIABLES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td>0.842**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years since onset</td>
<td></td>
<td>0.478**</td>
<td>0.202*</td>
<td>0.303**</td>
</tr>
<tr>
<td>Age at onset</td>
<td></td>
<td>0.478**</td>
<td>0.202*</td>
<td>0.303**</td>
</tr>
<tr>
<td>Admissions since onset</td>
<td></td>
<td>0.202*</td>
<td>0.071</td>
<td>0.036</td>
</tr>
<tr>
<td><strong>SYMPTOMS</strong></td>
<td></td>
<td>0.121</td>
<td>0.166</td>
<td>0.061</td>
</tr>
<tr>
<td>PANSS Negative</td>
<td></td>
<td>0.071</td>
<td>0.039</td>
<td>0.209*</td>
</tr>
<tr>
<td>PANSS Excitative</td>
<td></td>
<td>0.073</td>
<td>0.112</td>
<td>0.072</td>
</tr>
<tr>
<td>PANSS Affective</td>
<td></td>
<td>0.074</td>
<td>0.185</td>
<td>0.190</td>
</tr>
<tr>
<td><strong>COGNITIVE FUNCTIONING</strong></td>
<td></td>
<td>0.184</td>
<td>0.242*</td>
<td>0.071</td>
</tr>
<tr>
<td>Attention</td>
<td></td>
<td>0.020</td>
<td>0.045</td>
<td>0.067</td>
</tr>
<tr>
<td>Verbal Memory</td>
<td></td>
<td>0.071</td>
<td>0.112</td>
<td>0.045</td>
</tr>
<tr>
<td>Operative Memory</td>
<td></td>
<td>0.074</td>
<td>0.185</td>
<td>0.190</td>
</tr>
<tr>
<td>Abstraction and Flexibility</td>
<td></td>
<td>0.208*</td>
<td>0.264**</td>
<td>0.109</td>
</tr>
<tr>
<td><strong>DISABILITY</strong></td>
<td></td>
<td>0.189</td>
<td>0.253*</td>
<td>0.083</td>
</tr>
<tr>
<td>Disability: Personal Care</td>
<td></td>
<td>0.010</td>
<td>0.060</td>
<td>0.157</td>
</tr>
<tr>
<td>Disability: Occupational Functioning</td>
<td></td>
<td>0.137</td>
<td>0.182</td>
<td>0.065</td>
</tr>
<tr>
<td>Disability: Family Functioning</td>
<td></td>
<td>0.086</td>
<td>0.108</td>
<td>0.020</td>
</tr>
<tr>
<td>Disability: Social Functioning</td>
<td></td>
<td>0.196</td>
<td>0.245*</td>
<td>0.092</td>
</tr>
</tbody>
</table>

*p<0.05; **p<0.01.
schizophrenia (Ochoa et al., 2005), the authors also found an association between negative symptoms and needs in personal care. This result indicates that people with more severe negative symptoms tend to show impaired abilities in taking care of their food, self-care and health among others. As mentioned above, a high percentage of the patients of our sample live with their parents, who take care of their needs. Severity of symptoms is directly associated with the amount of formal and informal help that a patient receives in order to meet his/her needs in basic care areas (Ochoa et al., 2005). The formal and informal help received by the patients influences and hampers the evaluation of patient appearance and answers during assessment sessions and specific assessment of formal and informal caregivers should be included in future analysis.

4.2. Cognition and disability

The only significant association between cognitive functioning and areas of disability referred to operative memory and disability in social functioning; but some weak associations were revealed among other cognitive functions and areas of disability.

Disability in social functioning was associated with deficits in operative memory function. Operative memory is defined as a flexible computational system implied in managing and store information for a short period of time in order to allow the subject to undertake a wide range of cognitive tasks as learning, reasoning or comprehension. This cognitive function has been considered a frontal function (Boussoño et al., 2004; Lezak, 1995) and it has been previously related to disabilities in social functioning (Greenwood et al., 2005; Dickinson and Coursey, 2002).

Verbal memory showed a tendency, not statistically significant at $p<0.01$ level, to be associated with several areas of disability. The analysis indicated that patients with worse performance in verbal memory tasks seemed to show more disability in social functioning and family functioning areas. Other studies have also found this function to be related to social outcome (Green et al., 2000; Green, 1996; Addington and Addington, 1999). Verbal memory includes short term and long term verbal memory tasks and, as people usually communicates verbally, deficits in these functions would impede the patients to undertake complex social tasks (Green, 1996). Together with attention deficits, memory problems will impair patients to solve social problems as well as the acquisition of psychosocial skills and community daily activities (Green et al., 2000), thus affecting family and social functioning.

Our results support findings of other studies that have not found association between abstraction and flexibility abilities (both executive functions) and any area of social disability (Dickerson et al., 1996).

4.3. Symptoms and cognition

Our results confirm our first hypothesis: worse cognitive functioning is related to more severe negative symptoms. Verbal memory and operative memory are significantly associated with negative symptoms, and tend to associate with positive symptoms. These results are concordant with previous studies (Bryson et al., 2001; Berman et al., 1997; Hammer et al., 1995).

Contrary to most previous studies (Berman et al., 1997; Honey et al., 2003; Norman et al., 1997; Roth et al., 2004; Bryson et al., 2001; Cameron et al., 2002; Nieuwenstein et al., 2001), we have not found negative symptoms to be associated with deficits in abstraction and flexibility abilities (mainly assessed with the WCST). Only the negative dimension showed a weak association with attention (Nieuwenstein et al., 2001).
4.4. Do symptoms and cognition equally explain disability?

Studies have reported evidence suggesting that neurocognitive abilities are predictive of functional outcome in schizophrenia (Fujii and Wylie, 2003; Dickerson et al., 1996; Niendam et al., 2006) but longitudinal studies suggest that only symptoms, especially negative symptoms, predict social outcome (Dickerson et al., 1999). Our second hypothesis was not confirmed by our results. When adding symptoms to multivariate models, the negative factor partially explains impairment of most of the disability areas and total score, but neurocognitive factors are no longer predictors of disability. Disability is, then, partially explained by clinical variables, especially negative symptoms and unstable course of illness.

Even though positive symptoms show a significant relation with disability, their effects disappear when we adjust for negative symptoms and other covariates. We conclude that negative symptoms are the major source of disability in our sample of patients diagnosed with chronic schizophrenia.

Taking into account that treatment should focus on the reduction of disability levels (Ertugrul and Ulug, 2002) and that pharmacological treatments are most effective for positive symptoms (Feldman et al., 2003; Miller, 2004; Rueter et al., 2004), psychosocial rehabilitation programs should mainly focus on the effects of negative symptoms, more than in the treatment of cognitive deficits.

When analyzing the results, we should acknowledge that our sample is representative of outpatients with schizophrenia, but not all the population of patients with the disorder. Patients assessed in the study had a mean number of years since onset higher than 15; it is then possible that results will differ from those obtained for first-episode samples or for subjects with fewer years since onset. Also, patients who suffered an acute psychotic episode were not assessed during it, but when clinical stability was achieved. This fact has a clear implication on the PANSS scores, and positive symptoms were less prominent than negative symptoms.

The limitations of our study could be overtaken by future projects with longitudinal design and patients with shorter duration of illness. These studies could confirm that negative symptoms are more important predictors than cognitive functioning in defining disability and whether these findings are predictive of future course. Future research should also include the assessment of social cognition as a mediator between cognitive functioning and symptoms and disability as it seems to predict social functioning even when basic cognitive abilities are controlled (Ihnen et al., 1998; Pinkham et al., 2003).

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