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Apathy, poor verbal memory and male gender predict lower psychosocial functioning one year after the first treatment of psychosis

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ABSTRACT

Background: Apathy is a negative symptom associated with poor psychosocial functioning in schizophrenia but has not been sufficiently studied as predictor of poor functioning in first episode psychosis (FEP).
Objective: The main aim of the current study was to evaluate if apathy predicts poor functioning after 1 year in FEP patients in the context of other clinical variables with influence on outcome.
Method: Sixty-four FEP patients completed an extensive clinical and neuro-psychological test battery at baseline and 1-year follow-up. Symptoms were assessed with the Positive and Negative Syndrome scale (PANSS), apathy with the shortened Apathy Evaluation Scale (AES-C-12) and psychosocial functioning with the functioning score from the split version of the Global Assessment of Functioning scale (GAF-F).
Results: High levels of apathy, poor verbal memory and being male were the baseline variables that best predicted poor functioning at 1-year follow-up, explaining 34% of the variance in GAF-F. When PANSS negative factor was included in the analysis, the significance of AES-C-12 diminished.
Conclusion: These findings points to a robust role for apathy among the negative symptoms in the development of persisting psychosocial dysfunction in FEP and supports the current effort in targeting motivation to improve functioning.

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1. Background

Schizophrenia spectrum disorders are among the world's five leading causes of disability. In order to develop better and more specific treatments researchers and clinicians focus on identifying factors associated with long-term disability that can be assessed already at the initial treatment contact (Kirkpatrick et al., 2006). Studies of patients coming into treatment for their first episode of psychosis show that severity of psychotic symptoms at first treatment contact as well as diagnosis has a relatively weak association with poor psychosocial functioning (from now called "functioning") and is a poor predictor of future disability, while negative symptoms (Pogue-Geile and Harrow, 1985; White et al., 2009), male gender (Cotton et al., 2009), poor premorbid adjustment (Gonzalez-Ortega et al., 2013; MacBeth and Gumley, 2008; White et al., 2009), long duration of untreated psychosis (DUP) (Marshall et al., 2005; White et al., 2009), and cognitive dysfunction (Carlsson et al., 2006; Gonzalez-Blanch et al., 2010; Malla et al., 2002b) have been identified as stronger predictors.

The negative symptom complex consists of several symptoms including apathy, anhedonia, restricted affect, asociality and alogia. Recent research has focused on the specific relationship of these different symptoms to poor functioning with the aim of developing new and more specific treatment targets (Kirkpatrick et al., 2006). In particular apathy is thought to play a central role in the development of poor functioning (Barch, 2008; Brown and Pluck, 2000; Foussias and Remington, 2010; Medalia and Brekke, 2010), with seven different studies confirming this hypothesis so far (Evensen et al., 2012; Faerden et al., 2009, 2010; Foussias et al., 2009, 2011; Kiang et al., 2001; Konstantakopoulos et al., 2011), but all except one is cross-sectional studies. In all these studies, comprising samples of first episode psychosis (FEP) and chronically ill patients, apathy was found to have the strongest

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association with poor functioning, also when entered into multivariate analyses together with other symptom measures and measures of cognitive function with putative influence on outcome (Evensen et al., 2012; Faerden et al., 2009; Foussias et al., 2009; Kiang et al., 2001; Konstantakopoulos et al., 2011). The one follow up study is of chronic patients, with varied duration of illness, small sample size and only 6 months follow up. But prediction of functioning already from the start of coming into treatment is warranted. It is therefore of interest to study how apathy is able to predict functioning in FEP patients and with longer time to follow up (Birchwood et al., 1998; Faerden et al., 2009).

Apathy is not clearly defined in the most commonly used symptom measures, such as the Positive and Negative Syndrome Scale (PANSS), Scale for Assessment of Negative Symptoms (SANS) or Brief Psychiatric Rating Scale (BPRS) (Welham et al., 1999). The Apathy Evaluation Scale (AES) on the other hand, is based on a clear definition of apathy (defined as reduced motivation leading to reduced goal directed behavior not attributed to diminished level of consciousness, cognitive impairment or emotional distress), and is currently the most used measure of apathy in neuropsychiatric disorders (Marin et al., 1991). We have previously found a high correlation between the PANSS negative subscale (PANNS-N) and the AES at start of first treatment (Faerden et al., 2008) but no one has previously explored how they act together in explaining the variance in, and prediction of poor functioning. The main aim of the current study was to investigate the association between apathy, other clinical characteristics, and poor functioning in FEP patients at first treatment contact (baseline) and to what extent these baseline variables predict poor functioning at 1 year follow-up. A secondary aim was to study the interaction between the AES and the PANSS negative symptom in the prediction of poor functioning.

2. Methods

2.1. Participants

The present study includes 64 FEP patients with complete clinical and neuropsychological assessments at baseline who also participated in the scheduled 1 year follow-up. All patients were part of the ongoing Thematically Organized Psychosis (TOP) Study in Oslo, Norway (Faerden et al., 2010), consecutively recruited from three out of six catchment areas in Oslo, between July 2004 and the end of June 2006. Inclusion criteria for patients in the TOP study were: age between 18 and 65 years, with a first episode of psychosis and a DSM-IV diagnosis of either schizophrenia, schizophreniform disorder, schizoaffective disorder (constituting schizophrenia spectrum disorders); psychosis NOS, delusional disorder, brief psychotic disorder (constituting other psychotic disorders), or affective disorder with mood incongruent psychotic symptoms and bipolar I disorder (constituting affective psychotic disorders). Patients were eligible for inclusion in the study up to 1 year following the start of the first treatment. In the current study only those with a fluent understanding of Norwegian (=those having started primary school in Norway) were included. Seventy one patients met this criterion at baseline, but seven of these 71 did not meet for the 1-year assessment, making the current cohort to 64 patients. There was no statistically significant difference between the original cohort and the present study group regarding premorbid functioning scores, baseline demographics, symptoms scores or alcohol or drug use. A slightly significant statistical lower mean AES-C-12 score was found in the current study group compared to the original cohort (26 vs. 28 $p=0.040$) as well as a higher number with the diagnosis of schizophrenia (30/64 vs. 57/103 $p=0.049$).

2.2. Assessment

2.2.1. Measures

2.2.1.1. Assessment of diagnosis, symptoms and functioning. Diagnostic assessment was carried out with the Structural Clinical Interview for DSM-IV (SCID-I) (American Psychiatric Association, 1994). Positive and negative symptoms were assessed by the Structural Clinical Interview of the PANSS (SCI-PANSS) (Kay and Fiszbein, 1987). We used the positive (PANSS-pos) and negative (PANSS-neg) factor suggested by Wallwork et al. to represent PANSS positive and negative symptoms in the statistical analysis. Apathy was assessed with the clinical version of the Apathy Evaluation Scale (AES-C) (Marin et al., 1991). The questions of the AES-C are concerned with the degree of self-experienced motivation and interests. The AES does not include measures of degree of functioning. The items are scored on a likert scale ranging from 0 to 4, with higher total score indicating higher levels of apathy. We have previously shown that a shortened 12-item AES-C scale (AES-C-12) is a better measure of apathy than the full 18-item version in a FEP population (Faerden et al., 2008) and the shortened version was used in the present study. Depression was assessed with the Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1992). Level of alcohol and drug use during the last 6 months was assessed with the Alcohol Use Disorder Identification Test (AUDIT) and Drug Use Identification Disorder Test (DUDIT).

Premorbid function was assessed with the Premorbid Assessment of Functioning scale (PAS) (Cannon-Spoor et al., 1982). The PAS assesses the degree to which a person has attained certain developmental goals preceding the onset of an outbreak of psychosis and is divided into four age periods: PAS childhood (up until 11 years); PAS early adolescent (age 12–15); PAS late adolescent (16–18) and PAS adulthood (≥ 19). Five major social- and academic domains across each age period are assessed and rated from 0 (normal adjustment) to 6 (severe impairment). The PAS scores are used differently from one study to the other. We choose

Table 1
Sociodemographics and clinical variables at baseline ($N=64$).

	N (%) Mean (S.D.)
Gender (male/female)	36 (56%)/28 (44%)
Age	27.9 (8.4)
Premorbid function	
PAS[a]-childhood	0.27 (0.19)
PAS-early teen	0.28 (0.18)
PAS-late teen	0.33 (0.17)
PAS-adolescent	0.34 (0.24)
Years education	13.2 (2.9)
DUP[b] median/range (weeks)	31.5 (1–1040)
GAF-S[c]	42.9 (14.1)
GAF-F-B[d]	46.0 (14.3)
AUDIT[e] alchohol use	2.0 (0.8)
DUDIT[f] Drake drug use	1.8 (1.1)
Diagnostic distribution[g]	
Schizophrenia spectrum	30 (47%)
Affective psychosis	14 (25%)
Psychosis NOS	20 (31%)
Symptoms	
PANSS total[h]	60.7 (15.5)
PANSS-P	14.4 (5.2)
PANSS-N	14.7 (5.9)
PANSS-G	31.5 (7.7)
AES-C-12[i]	26.1 (7.2)
CDSS[j]	6.0 (4.4)
Cognitive tests	
NART[k]	16.2 (7.4)
WASI FIQ 4[l]	106.0 (13.1)
Psychomotor speed Digit symbol	63.7 (14.4)
Attention Digit span forward	5.7 (1.0)
Verbal memory CVLT II	52.8 (11.0)
Visual memory ROCF LTM	19.4 (6.8)
Working memory Letter number span frwd	9.7 (2.5)
Executive function	
Verbal fluency	39.3 (11.7)
Category fluency	40.0 (8.7)
Set shifting	12.6 (2.7)
Inihibition	62.6 (20.6)

[a] PAS: Premorbid Assessment of functioning scale.
[b] DUP: Duration of Untreated Psychosis.
[c] GAF-S: Global Assessment of Functioning Scale split version Symptoms.
[d] GAF-F: Global Assessment of Functioning Scale split version Functioning.
[e] AUDIT: Alcohol use disorders identification test.
[f] DUDIT: Drug use disorders identification test.
[g] Diagnostic distribution: DSM IV diagnosis.
[h] PANSS: Positive and Negative Syndrome Scale.
[i] AES-C-12: Apathy Evaluation Scale shortened 12 item version.
[j] CDSS: Calcary Depression Scale for schizophrenia.
[k] NART: National Adult Reading tests.
[l] WASI FIQ: Wechsler Abbreviated Scale of Intelligence.

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