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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).

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Author's contributions

AFae: Study design, collecting data, analysis, drafting and revising the manuscript. EAB: Collecting data and revising the manuscript. RN: Collecting data and revising the manuscript. AF: Conception of the study and revising of the manuscript. SF: Conception of the study and revising of the manuscript. SM: Conception of the study and revising of the manuscript. JV: Conception of the study and revising the manuscript. OAA: Conception of the study and revising the manuscript. IA: Conception of the study and revising the manuscript. IM: Conception of the study, study design, data analysis and revising the manuscript. All authors contributed to and have approved of the final version of the manuscript.

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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.

Keywords

Psychosis; Functional outcome; Predictors; Apathy; Verbal memory; Male gender; Negative symptoms

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 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 to use a total score for each developmental stage, excluding PAS adulthood to avoid confounding with change in functioning close to coming into treatment. Psychosocial functioning was assessed with the functioning score of the split version of the Global Assessment of Functioning Scale, the GAF-F (Pedersen et al., 2007). GAF-F is scored between 100 and 0 with each 10 point defined in relation to degree of functioning in the areas of independent living, degree of social relations and ability to work. Both baseline GAF-F (GAF-F-B) and GAF-F at 1 year (GAF-F-1 yr) were used in the analysis. Sociodemographic data and clinical assessments of the 64 participants are provided (Table 1).

2.2.2. Neuropsychological assessments—A comprehensive neuropsychological test battery was administrated to all 64 participants (Table 1). The tests cover domains shown to be sensitive to the neurocognitive dysfunction of psychosis: (1) psychomotor speed (Digit Symbol from WAIS-III), (2) attention (Digit Span forwards from WAIS-III), (3) verbal learning (California Verbal Learning Test; CVLT-II), (4) visual learning (Rey-Oesterrieth Complex Figure Test), (5) working memory (Letter Number Span from WAIS-III) and (6) executive function [represented with four different tests: Semantic and Phonetic Fluency, Category Switching (from the Verbal Fluency test) and the third trial from the Color–Word

Interference test (the “Stroop” test)]. Premorbid IQ was assessed with a Norwegian Research version of the National Adult Reading Test (NART); and current IQ with the Wechsler Abbreviated Scale of Intelligence (WASI). All participants showed adequate effort on the neuropsychological tests as indicated by two errors or less on the forced recognition trial of the CVLT-II.

2.3. Procedures

All participants gave written informed consent to participate, and the study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate in 2004. The data file has received an Audit Certificate from the Center for Clinical research at Oslo University Hospital in 2007.

The three investigators (AF, EAB, and RN) from the current study completed the structured assessment training and reliability program of the TOP study (Faerden et al., 2008). For DSM-IV diagnostics, assessment was carried out by raters trained to reliability using the Structural Clinical Interview for Structural Clinical Interview for DSM-IV (SCID-I) (Ventura et al., 1998). Mean overall kappa for the standard diagnosis of training videos was 0.77, and mean overall kappa for a randomly drawn subset of actual study patients was 0.77 (95% CI 0.60–0.94). Inter-rater reliability (Intra Class Coefficient (ICC) 1.1) for PANSS positive subscale was 0.82 (95% CI 0.66–0.94), PANSS negative subscale 0.76 (95% CI 0.58–0.93), AES-C 0.98 (95% CI 0.92–0.99) and GAF-F 0.85 (95% CI 0.76–0.92).

2.4. Analyses

2.4.1. Data and statistical analyses—A preliminary analysis was performed to examine the distribution of each variable and examined for outliers. Logarithmic transformation (ln) was performed for the DUP (lnDUP) scores due to the detection of a skewed data distribution. All t-tests were two-tailed, with a preset significance level of $p<0.05$. Pearson product moment correlation coefficient (r) and hierarchical multivariate regression analysis was used to address the study questions.

Only baseline independent variables (BIV) were used and were divided into five groups in order of their presumed developmental appearance and entered into the final hierarchical regression analysis in this order: BIV-1: demographical (sex, age), BIV-2: premorbid functioning (PAS), BIV-3: pre-onset variables (DUP), BIV-4: neuropsychological tests results, and BIV-5: baseline symptoms and baseline drug use (AES-C-12, PANSS-pos, CDSS, AUDIT, DUDIT). In groups with more than one BIV with a significant correlation to GAF-F-B (Table 2) preliminary regression analyses was performed in order to reduce number of variables. Only those BIVs that contributed significantly to GAF-F-B were used in the final analysis (Table 3). The PANSS-neg was not included in these analyses in order to avoid collinarity with the AES-C-12. AES-C-12 was entered in a last step in order to study its contribution when all other variables were controlled for. Diagnosis was not part of the analysis, since it per definition is based on clinical variables and degree of poor functioning, and thus represent collinarity with the other variables.

In a follow-up analysis we studied the combined contribution from apathy and PANSS negative symptoms in explaining the variance in GAF-F-B and predicting GAF-F-1 yr. This was done in two steps; first a multivariate regression analysis was performed with only PANSS-neg and AES-C12 as independent variables (Table 5). Lastly the effect of AES-C-12 was studied when also PANSS-neg was controlled for in the above final hierarchical analysis (Table 4, Model B).

3. Results

3.1. Clinical variables correlated to GAF-F at baseline and one year

The pattern of correlations between baseline demographic, clinical characteristics and GAF-F-B and GAF-F-1 yr were much the same, but with a slight decline in the strength of associations from baseline to 1-year follow-up (Table 2). The AES-C-12 was the variable with the strongest correlation at time points, explaining 25% of the variation in GAF-F at baseline and 18% at 1 year. Other demographic and clinical characteristics with a significant association to the GAF-F at both time points were gender (male), lnDUP, PAS-childhood and -early-youth from BIV-3, psychomotor speed and verbal memory from BIV-4 and PANSS-pos, CDSS, DUDIT from BIV-5.

3.2. Variables explaining the variance in GAF-F-B and predicting GAF-F-1 yr

The preliminary regression analysis from the three BIV-groups with more than one BIV with a significant association to GAF-F is shown in Table 3. PAS-childhood, verbal memory, PANSS-pos and AES-C-12 were the variables retrieved for the final analysis.

The result of the final regression analysis with GAF-F-B as dependent (Table 4), display that even when controlling for all other significant BIVs the AES-C-12 contributed significantly to the variance in GAF-F-B, explaining 7%, and the total model explaining 45% of the variance. In the final step the statistically significant contributions came from gender (male), PANSS-pos and AES-C-12; with AES-C-12 having the highest β-value.

In the analysis for prediction of the variance in GAF-F-1 yr (Table 4) also AES-C-12 made a significant contribution when all other variables were controlled for, adding 6% to the total model. In the last step gender (male), verbal memory and AES-C-12 were the three BIVs with independent significant predictive power. Also here AES-C-12 had the highest β-value. Together this model was able to predict 34% of the variation in GAF-F-1 yr.

In both models the significance of PAS-childhood was lost when AES-C-12 was entered into the model.

3.3. The relationship between AES-C-12 and PANSS negative factor in explaining the variance in GAF-F-B and GAF-F-1 yr

AES-C-12 and PANSS-neg have a significant correlation with GAF-F-B and GAF-F-1 yr of nearly equal strength (Table 2). They have a bivariate correlation of r=0.56, p <=0.000. Analyzed together they were able to explain 28% of the variance in GAFF-B and predict 20% of variance in GAF-F-1 yr and when controlling for PANSS-neg, AES-C-12 still had a significant contribution to both GAF-F-B and GAF-F-1 yr (Table 5). In the last step of these

analyses the two contributed close to equal; AES-C-12 having a slightly higher β-value at both time points.

When PANSS-neg was introduced to the final hierarchical regression analysis (Table 4, Model B), the contribution from AES-C-12 was significant for GAF-F-B and reduced to nonsignificant in prediction of GAF-F-1 yr. No BIV gave independent contribution in the last step in this model.

4. Discussion

The main finding of this study is that apathy is the clinical characteristic contributing most robustly and stable over the first year to the variation and prediction of poor psychosocial functioning and that the significance is sound, also when other variables are controlled for.

This is the first study we are aware of that investigated the role of apathy in association with other clinical and neurocognitive variables in predicting poor functioning in FEP patients. The finding that apathy is a significant predictor of functioning is in line with the follow up study of 6 months of Foussias et al. in a sample of more chronic patients (Foussias et al., 2011) and is supported by findings from the cross sectional studies. Degree of explained variance from apathy vary from one study to the other; being as high as 72% in the study by Foussias et al. and Konstantakopouos et al. (Foussias et al., 2011; Konstantakopoulos et al., 2011) and at 3% in the study by Evensen et al. (2012) and 7% in this study. One reason for these wide-ranging results most possibly lies in the use of different outcome variables to assess functioning and number of other variables in the analysis. Added together this supports the current focus on apathy among the negative symptoms as an important contributor to poor functioning (Erhart et al., 2006; Kirkpatrick et al., 2006; Medalia and Brekke, 2010; Medalia and Saperstein, 2011) and thus a potential new treatment target in psychotic disorders.

Results from the last part of this study show that PANSS-neg and AES-C-12 have a strong bivariate correlation, correlate close to the same strength with GAF-F and when comparing their contribution the AES-C-12 have a slightly stronger standardized Beta-value compared to PANSS-neg. When the influence from PANSS-neg is controlled for the AES-C-12 is still able to explain an additional 8% of the variation in GAF-F at baseline and predict an additional 5% at the 1-year follow up. This shows that the AES-C-12 and PANSS-neg represent overlapping phenomena, but also something distinct, and underlines the importance of apathy among the negative symptoms as assessed with the PANSS. But exactly what in the PANSS represent apathy we do not know. Apathy is not clearly defined in the PANSS, but both the item N2 (Emotional withdrawal), N4 (Passive/apathetic withdrawal) of the PANSS negative subscale and the item G13 (Disturbance of volition) of the PANSS general subscale have definitions that to a certain degree overlap with Marin's definition of apathy used in development of the AES (Marin et al., 1991). A former study of the same patient group found the highest correlation between AES-C-12 and the items N2 and N4 (Faerden et al., 2008), which was also found by Evensen et al. (2012). The advantage of the AES is that it was developed from a definition of apathy as reduced goal directed behavior based on theoretical, neurobiological, and clinical knowledge (Marin et

al., 1991). Apathy may therefore serve as a more proximate target to the pathophysiology of the brain than the combined negative symptoms or any of the items (Faerden et al., 2008). The AES also has the advantage of being clinically useful, an easily measured concept and has been used in all the recent studies focusing on apathy in psychotic disorders (Evensen et al., 2012; Faerden et al., 2010; Foussias et al., 2009, 2011; Kiang et al., 2001; Konstantakopoulos et al., 2011). This study therefore shows the potential advantage of using specialized scales for the study of the different negative symptom domains. But the study also shows that the PANSS negative symptom consist of more than the symptom of apathy. Factor analysis of the PANSS suggests that negative symptoms consist of two domains; apathy-anhedonia and affective flatteningalogia (Foussias and Remington, 2010), but we do not know how they interact and act upon functioning. This is of importance to gain more knowledge of in order to better understand how the negative symptoms influence outcome.

Among the other variables also impaired verbal memory and male gender were able to predict poor psychosocial functioning at 1-year follow up. Numerous previous studies ‘have indicated that males are at greater risk of developing persistent high levels of poor functioning (Chang et al., 2011). We have previously shown that men have a higher risk of persistent high levels of apathy (Faerden et al., 2010), but the current analyses indicate that the negative impact of male gender is not explained by higher levels of apathy alone.

Verbal memory is one of the cognitive domains found to be most frequently and severely impaired in FEP patients (Gonzalez- Blanch et al., 2007). Impaired verbal memory has also been implicated as an important mediator of poor functioning (Green et al., 2000). Previous studies have reported on the predictive power of verbal memory for poor functioning in FEP. One study reported verbal memory to be a significant marker for poor functioning among different cognitive domains (Bodnar et al., 2008) while two other studies found no such specific role (Gonzalez-Blanch et al., 2010; Holthausen et al., 2007). Our study supports an independent role for verbal memory in the prediction of functional outcome.

Male gender, poor premorbid function, cognitive dysfunction and negative symptoms are the independent variables that repeatedly have been shown to predict poor functioning in studies of FEP patients; despite both differences in methodology and time to follow up (Flyckt et al., 2006; Lucas et al., 2008; Malla et al., 2002b; Melle et al., 2008; Moller et al., 2010; White et al., 2009). The effect of premorbid functioning as a predictor of outcome disappeared when we entered AES-C-12 in the analysis. We have previously reported a significant association between poor premorbid function and degree of apathy at baseline in this patient group (Faerden et al., 2009), and thus baseline apathy may be a mediator of poor premorbid functioning or they share common underpinnings.

The strength of the current study is that this was a naturalistic study that included participants from a large catchment area who were consecutively recruited which increases generalizability of the findings. The generalizability is supported by stability in the incidence rate in this study and the previous Treatment and Intervention study (TIPS) (REF) which varied between 11 and 14/ 100000. The response rate of 81% for 1-year follow up is also in line with TIPS (Melle et al., 2004) and other studies (Addington et al., 2007; Malla et

al., 2002a) as is the response rate for neuropsychological assessment (Rodriguez-Sanchez et al., 2008; Rund et al., 2007).

There are two main weaknesses in the present study. One is that the time between first treatment contact and first assessment could be up to a year and we do not have data to control for this. One reason for this was that assessments were not part of the routine clinical assessment and written consent could not be asked for before patients were clinically stable. But this could also give an advantage by eliminating some of the acute phase variation. Also numbers of participants are in the lower limit of what is recommended for multivariate regression analysis and hence results have to be interpreted with this in mind.

4.1. Significance of study

The present study adds to recent findings that apathy or reduced motivation is a core symptom within the negative syndrome, found especially useful in the prediction of poor functioning in FEP. This study also demonstrated that poor functioning at 1-year follow-up is multi-determined with several significant predictors. This underscores the need for developing specific interventions for different aspects of FEP, and supports the choice of apathy as an intervention target. But there is also a clear need for additional studies and longer follow-up periods to establish the role of apathy as a feature of FEP.

Since this is the first follow up study in a FEP population pointing to a significant role for apathy in the development of poor functioning the clinical implications at this stage cannot be fully established. Also, additional and more specific studies of the other negative symptom domains are needed to reach a more complete understanding of the negative symptom complex.

Since apathy or reduced motivation can arise from different sources treatment of apathy is in need of a multidisciplinary approach and effectfull treatment may differ from one disorder to another. We have found one study of old date within the field of schizophrenia targeting treatment of apathy (Schaefer and Martin, 1966) and one of new date (Grant et al., 2012). In other medical disciplines there are newly published studies with pharmaceutical (Berman et al., 2012; Ishizaki and Mimura, 2011), cognitive (Buettner et al., 2011) and psychosocial interventions (Brodaty and Burns, 2012). Some of these interventions may be applicable to psychosis since apathy across disciplines share common traits (Roth et al., 2007).

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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)

	***N* (%) Mean (S.D.)**
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.

Table 2

Correlation (*r*) between baseline independent variables (BIV) and GAF-F.

All baseline assessment	GAF-F-B	GAF-F-1 yr
BIV-1	*r*	*r*
Gender	**–0.28**	**–0.29***
Age	–0.08	–0.16
BIV-2: Premorbid functioning		
PAS[a] *Childhood*	**–0.34****	**–0.28***
PAS Early youth	**–0.26***	–0.19
PAS Late youth	–0.25	–0.22
BIV-3: lnDUP[b]	**–0.37****	**–0.35****
BIV-4: Cognitive function		
NART[c]	–0.15	–0.15
WASI FIQ[d]	–0.04	–0.03
Psychomotor speed digit symbol	**0.31***	**0.25***
Attention Digit span forward	0.03	0.14
Verbal memory CVLT II	**0.33****	**0.36****
Visual memory ROCF LTM	0.23	0.2
Working memory Letter number span frwd	0.14	0.16
Executive function		
Verbal fluency	**0.25**	0.16
Category fluency	0.09	0.01
Set shifting	0.05	0.08
Inhibition	–0.23	–0.12
BIV-5: Symptoms and drug use		
PANSS-pos[e]	**–0.41****	**–0.34****
PANSS-neg[f]	**–0.48****	**–0.41****
CDSS	**–0.27***	**–0.30***
AES-C-12[g]	**–0.50****	**–0.42****
AUDIT[h]	–0.02	–0.08
DUDIT[i]	**–0.25***	–0.21

*Corr is sign at the > 0.05.

**Corr is sign at the > 0.01.

[a]PAS: Premorbid Assessment of functioning Scale.

[b]lnDUP: Logaritmic transformation of Duration of Untreated Psychosis.

[c]NART: National Adult Reading Test.

[d] WAS FIQ: Wechsler Abbreviated Scale of Intelligence.

[e] PANSS-pos: positive factor after Wallwork et al.

[f] PANSS-neg: negative factor after Wallwork et al.

[g] AES-C-12: Apathy Evaluation Scale shortened 12 item version.

[h] AUDIT: Alcohol use disorders identification test.

[i] DUDIT: Drug use disorders identification test.

Table 3

Preliminary hierarchical regression analysis with GAF-F-B as dependent and BIV groups 2,4 and 5.

	R	***R*² adjusted**	***R*² change**	***F* change**	**Sig *F* change**
BIV-2					
Step 1: PAS[a]-childhood	0.34	0.1	0.12	8.07	**0.006**
Step 2: PAS-early youth	0.34	0.09	0	0.59	0.88
BIV-4					
Step 1: Verbal memory	0.33	0.1	0.11	7.61	**0.008**
Step 2: Psychomotor speed	0.37	0.11	0.03	1.83	0.182
BIV-5					
Step 1: AES-C-12 [b]	0.5	0.24	0.25	20.35	**<0.001**
Step 2: PANSS-pos [c]	0.6	0.34	0.11	10.6	**0.002**
Step 5: CDSS [d]	0.6	0.33	0	0.37	0.548
Step 6: DUDIT [e]	0.61	0.33	0.01	1.2	0.279

[a] PAS: Premorbid Assessment of functioning Scale.

[b] AES-C-12: Apathy Evaluation Scale shortened 12 item version.

[c] PANSS-pos: Positive factor after Wallwork et al.

[d] CDSS: Calgary Depression Scale for Schizophrenia.

[e] DUDIT: Drug use Disorder Identification Test.

Table 4

Hierarchial regression analysis with multiple baseline variables explaining variance of GAF-F-B and predicting GAF-F-1 yr.

Model A	**GAF-F-B dependent**						**GAF-F-1 yr dependent**					
	R^2 adjusted	**R^2 change**	***F* change**	***p***	**Last step**		**R^2 adjusted**	**R^2 change**	***F* change**	***p***	**Last step**	
					β	***p***					***β***	***p***
Step 1: BIV-1: Gender	0.06	0.08	5.08	**0.028**	0.21	**0.034**	0.07	0.08	5.48	**0.022**	0.21	**0.044**
Step 2: BIV-2: PAS[a]-childhood	0.16	0.11	7.88	**0.007**	−0.16	0.12	0.13	0.07	5.24	**0.026**	−0.12	0.266
Step 3: BIV-3: LnDUP [b]	0.24	0.09	7.47	**0.008**	−0.15	0.151	0.2	0.08	6.04	**0.017**	−0.15	0.17
Step 4: BIV-4: Verbal memory (CVLTII)	0.29	0.06	4.8	**0.033**	0.16	0.112	0.26	0.08	6.25	**0.015**	0.22	**0.047**
Step 5: BIV-5: PANSS-pos [c]	0.38	0.1	9.75	**0.01**	−0.27	**0.01**	0.29	0.04	3.68	0.08	−0.2	0.08
Step6: AES-C-12 [d]	0.44	0.07	7.2	**0.003**	−0.32	**0.04**	0.34	0.06	5.31	**0.019**	−0.26	**0.025**
Model B												
Step 5: PANSS-neg [e]	0.37	0.09	8.91	**0.004**			0.31	0.06	5.33	**0.025**		
PANSS-pos	0.42	0.05	5.41	**0.024**			0.33	0.02	2,36	**0.13**		
AES-C-12	0.45	0.04	4.14	**0.047**			0.34	0.02	2,31	**0.134**		
Total explained variance model A: $R = 0.70$; R^2 adj = 44; $F(6,56) = 9.11$; $p < 0.000$							Total explained variance: $R = 0.64$; R^2 adj = 0.34; $F(6,56) = 6.41$; $p < 0.000$					
Total explained variance model B: $R = 0.71$; R^2 adj = 45; $F(7,55) = 8.16$; $p < 0.000$							Total explained variance: $R = 0.65$; R^2 adj = 0.34; $F(7,55) = 5,38$; $p < 0.000$					

[a] PAS: Premorbid Assessment of functioning Scale.

[b] LnDUP: log transformed Duration of Untreated Psychosis.

[c] PANSS-pos: Positive factor after Wallwork et al.

[d] AES-C-12: Apathy Evaluation Scale abridged 12 item version.

[e] PANSS-neg: negative factor after Wallwork et al.

Table 5

Regression analysis explaining variance of GAF-F-B and predictionof GAF-F-1 yr with PANSS-neg and AES-C-12 as independent variables.

	GAF-F-B dependent						**GAF-F-1 yr dependent**					
	R^2 **adjusted**	R^2 **change**	**F change**	**Last step**			R^2 **adjusted**	R^2 **change**	***F* change**	**Last step**		
				p	***β***	***p***				***p***	***β***	***p***
Step1: PANSS-neg[a]	0.22	0.23	18.65	**0.000**	–0.29	**0.026**	0.16	0.17	13.5	**0.001**	–0.26	0.061
Step 2: AES-C-12[b]	0.28	0.08	6.62	**0.013**	–0.33	0.013	0.2	0.05	4.19	**0.045**	–0.3	**0.045**
Total explained variance: $R = 0.55$; R^2 adj = 0.28; $F(2,61) = 13.48$; $p < 0.000$							Total explained variance: $R = 0.48$; R^2 adj = 0.20; $F(2,61) = 8.93$; $p < 0.000$					

[a] PANSS-neg: negative factor after Wallwork et al.

[b] AES-C-12: Apathy Evaluation Scale abridged 12 item version.