The Relative Contribution of Cognition and Symptomatic Remission to Functional Outcome Following Treatment of a First Episode of Psychosis (FEP)

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ABSTRACT

Objective: Functional recovery remains the primary goal following treatment of a psychotic disorder, especially after a first episode. Evidence regarding relative contributions of predictors of functional outcome, including symptoms and cognition, remains equivocal. The objective of the study was to determine the relative contribution of cognition, in particular verbal memory, and symptomatic remission to social and occupational functioning while controlling for established predictors of functioning in a large sample of patients presenting with a first episode (FE) of a schizophrenia spectrum or affective psychosis. *Methods*: Patients (aged 14-35) who met DSM-IV criteria for a first episode of a schizophrenia spectrum or affective psychosis and had been admitted to the Prevention and Early Intervention Program for Psychoses, Montréal, between 2003-2009 for treatment and follow-up for two years. Established predictors (DUP, medication adherence, age of onset, substance use, premorbid adjustment), verbal memory and length of positive and negative symptom remission were regressed on functioning (using the Strauss Carpenter Scale) at one (n =208) and two (n=159) years. Regressions were conducted with established predictors in the first step, followed by verbal memory and consecutive months of combined positive and negative symptom remission in the third step. Regressions were then repeated with length of positive and negative symptom remission, respectively. *Results:* Length of combined positive and negative symptom remission explained the most variance in functioning at one $\{R^2_{adj}=.35, F(9,129)=9.33, p<.001\}$ and two $\{R^2_{adj}=.38\ F(9,97)=8.21, p<.001\}$ years, and verbal memory contributed only slightly to such outcome. While length of remission of negative symptoms was a stronger predictor of functioning than remission of positive symptoms at

1 year, length of positive symptom remission also made a large contribution at two years. *Conclusions:* These results highlight the importance of achieving and maintaining remission of both negative and positive symptoms for longer periods in FEP patients and the need for effective interventions to do so.

Key words: Remission, cognition, functional outcome, first episode psychosis

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Introduction:

Trajectories of academic, employment, and social functioning, often interrupted with the onset of psychosis[1, 2], are important for recovery[3]. Cognitive deficits, especially in verbal memory, are present in many patients during their first episode of a psychotic disorder (FEP), most often within the schizophrenia spectrum. Furthermore, following treatment many patients do not meet criteria for a full remission of positive and negative symptoms. While a predominant role of cognition, in particular verbal memory, and a relatively limited role of symptom levels in determining social and community functioning among patients with a psychotic disorder has been promoted[4,5], some have demonstrated a more significant role for symptoms[6, 7], especially following treatment of a first episode. The recent consensus definition of remission in schizophrenia[8] has promoted an interest in exploring the role of symptom remission in functional outcome. Studies investigating the relative contribution of symptoms and cognition on functioning among FEP patients have produced mixed results. Some found that negative symptoms and cognition are important[7, 9], one revealed the primacy of negative symptoms[10] and another demonstrated cognition to be more important[11]. Studies exclusively examining *either* the role of symptoms[12] *or* of cognition[13, 14] have simply confirmed their respective importance.

Our primary objective was to determine the relative contribution of verbal memory and symptomatic remission to social and occupational functioning in patients treated for a FEP, thus validating the practical utility of recent remission criteria[8]. As a

secondary objective, we examined separately the relative contribution of positive and negative symptom remission to functioning.

Methods

Treatment Setting and Subjects

Participants included patients admitted (2003-2009) to the Prevention and Early intervention Program for Psychoses (PEPP-Montréal) for treatment of a first episode of a schizophrenia spectrum or affective psychosis (FEP). This is the only specialized early intervention service serving an urban population of 400,000 in the catchment area of south-west Montreal. Admission criteria are: diagnosis of a non-affective or affective psychotic disorder according to the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-*IV)* criteria; age 14-30; not having received antipsychotic medication for more than 1 month; IQ above 70 and an absence of an organic brain condition. Patients with a secondary diagnosis of substance abuse are included. Treatment mainly includes antipsychotic medication; case-management; family interventions and, where indicated, cognitive behavioural therapy[15]. This study was approved by the Ethics Board of Douglas Mental Health University Institute and informed consent was obtained from all study participants.

Materials

Patients presenting with the first episode of a schizophrenia spectrum disorders (schizophrenia; schizophreniform disorder; delusional disorder; or schizoaffective disorder) and affective psychotic disorder (bipolar or major depressive disorder with psychotic symptoms) were included. Diagnosis was established with the Structured Clinical Interview for *DSM-IV* and confirmed through consensus by two senior psychiatrists (AM & RJ) at baseline and at 1-year follow-up (Table 1). In the rest of the

manuscript all patients will be referred to as FEP for brevity and in agreement with vast literature published in the last twenty years.

Symptoms and Remission: Symptoms were evaluated using the Scale for Assessment of Positive Symptoms (SAPS) and Scale for Assessment of Negative Symptoms (SANS) [16, 17]. Inter-rater reliability coefficients revealed substantial agreement on the SAPS (Kappa=.74) and SANS (Kappa=.71). Using recent consensus remission criteria[8], participants were considered in total remission if they scored ≤ 2 on all 4 SAPS global subscale items (hallucinations, delusions, bizarre behaviour, thought disorder) and SANS global subscale items (affective flattening, alogia, apathy-avolition, asociality-anhedonia). Positive symptom remission was established when remission criteria on SAPS global items were met while participants were considered in negative symptom remission when criteria for SANS global items were met.

Symptoms were assessed at baseline and at 8 subsequent times during the 2-year period of treatment and follow-up (months 1, 2, 3, 6, 9, 12, 18 and 24). When no assessments were conducted (e.g., at months 4, 5, 7-11, 13-17, 19-23), positive symptom remission was established through clinical notes. The last observation carried forward (LOCF) technique was applied to SAPS data when sufficiently detailed notes were unavailable (e.g., evaluations from month 3 were carried forward to month 6). For missing negative symptom remission data, we applied the LOCF technique because of doubts about the reliability of evaluating negative symptoms based on clinical notes.

We examined the maximum number of continuous months in remission. If a participant was in remission for five consecutive months, followed by a period of no remission for three months, their maximum number of months in remission was recorded

as five. Previous research has demonstrated a 3-month time criterion for remission had equal predictive validity as a 6-month criterion in FEP[12]. Furthermore, using continuous variables may result in greater statistical accuracy and more face validity than categorical measures[18]. Comparing remission status based on SAPS ratings with that obtained through the LOCF procedure, for participants for whom 12 complete months of data was available, showed that 82.87% of our LOCF estimates were correct.

Cognition: Given the previously reported strong association of verbal memory with functional outcome[4, 19] and early remission[20], we tested the role of verbal memory (based on the WMS-III Logical Memory Immediate Recall, Delayed Recall and Recognition) in predicting functional outcome. Based on the Measurement and Treatment Research to Improve Cognition in Schizophrenia (MATRICS) recommendations[21], we also examined the following additional cognitive domains: attention/vigilance (D2 test of attention); working memory (Digit Span subtests of the WAIS-III-R; Spatial Span subtests of the WMS-III); visual learning and memory (WMS 3 Visual Reproduction); reasoning and problem solving (WAIS 3 Block Design; Trail Making Test, Part B); and speed of processing (Trail Making Test, Part A; WAIS-III Digit Symbol Coding). Tests were administered to participants when they were considered clinically stable, usually within the first three months after initiation of treatment. Clinical stability was based on patient's ability to tolerate and participate in at least an hour long cognitive assessment and arrived at through consensus between clinicians and the senior author (A.M.). The same battery was administered to age and gender-matched healthy controls (N=73), recruited from the same catchment area[18]. To create domains, scores were z-transformed based on the mean and standard deviations from healthy controls and then averaged. Each

domain was averaged and z- transformed to produce a global cognitive domain reflecting overall cognitive performance.

Established Predictors of Functioning. Based on their previously established influence on outcomes in FEP, we included age of onset[22], pre-morbid adjustment [23], duration of untreated psychosis (DUP)[24], gender[25], medication adherence[26] and substance use[27] as potential confounds. Premorbid Adjustment Scale (PAS) scores were considered for childhood (up to age 11) and early adolescence (12-16 years) on educational and social domains. Ratings from late adolescence and early adulthood were omitted because of potential overlap with onset of prodromal and/or psychotic symptoms. DUP was defined as the period between the onset of psychotic symptoms until treatment with antipsychotic medication for 30 days[28] using the Circumstances of Onset and Relapse Schedule[29]. Medication adherence was assessed through a previously validated method[12] using multiple sources (patients, families, case managers, and clinical notes) and patients were rated as being adherent (75-100% of the time) or non-adherent (0-74%). Presence or absence of a co-morbid SCID diagnosis of substance abuse/dependence at baseline was considered in analyses.

Functional Outcome. Functional outcome was measured using the Strauss Carpenter Scale (SCS; Strauss & Carpenter[30, 31]) at months 12 and 24 during face-to-face interviews. The SCS is a widely used and validated composite index of functioning[32]. Only the social adjustment (e.g., number of times friends are seen per month) and occupational functioning (e.g., amount of time employed during the past year) subscales were used as the other two subscales (e.g., re-hospitalization, psychiatric symptoms)

overlap with the concept of being in remission. Participation in educational courses replaced the employment variable, where appropriate.

Data Analyses: To evaluate the primary objective, the established predictors of functioning (e.g., DUP, medication compliance, gender, age of onset, substance abuse, PAS) were entered in the first step followed by verbal memory in the second step. Step 3 contained the maximum number of consecutive months in total (combined positive and negative) symptom remission. To evaluate the secondary objective, we again entered the established predictors in step 1, verbal memory in step 2, the maximum number of consecutive months of positive symptom remission in step 3, and lastly negative symptom remission in the fourth step. To determine if overall cognitive performance was as important for functioning as verbal memory, we also repeated each regression by substituting verbal memory with the global cognitive domain. All analyses were regressed on SCS scores at one and two years.

Results

Preliminary Analysis: Of the original sample (n = 318), 66 dropped out prior to completing 1 year of treatment, 38 refused to complete symptom assessments and 6 were reassessed as not having a psychotic disorder, yielding a final sample of 208 for the 1-year analysis. Of these (n=208), 36 dropped out of treatment between years 1 and 2, and 15 did not complete assessments, leaving a sample of 159 for year 2. Drop-outs were not different on demographic, cognitive or clinical characteristics compared to those who were included in treatment (Table 1).

DUP (weeks) was positively skewed and was corrected with a logarithmic transformation. No multi-colinearity among known predictors was detected.

62 participants (30%) were in total remission at month 12 for a mean of 2.4 (*SD*=3.25) months, while 141 (67.8%) and 69 (33.32%) were in positive or negative symptom remission for a mean of 7 (*SD*=4.17) and 2.9 (*SD*=3.55) months, respectively. Likewise, 66 (41.5%) were in total remission by month 24 (mean 5.7 months, *SD*=6.57), with 110 (69.2%) and 77 (48.4%) in positive and negative symptom remission, for a mean of 13.9 (*SD*=7.91) and 6.79 (*SD*=7.31) months, respectively. Cognitive profiles of participants and healthy controls were significantly different (*P* <.001) (Figure 1) with patients performing poorly on most dimensions.

Correlations between Cognitive Domains, Symptom Remission and Functional Outcomes. Correlations between positive and negative symptom remission were observed over one {*r*(207)=.327, *P* < .001} and two {*r*(158)=.369, *P* < .001} years. Furthermore, an extremely modest correlation between global cognition and negative symptom remission was found at one year {*r*(207)=.149, *P*=.043} which did not persist at two years {*r*(144)=.005, *P*=.96}. SCS scores at 1 and 2 years and length of remission (e.g., total, positive and negative symptom remission) were strongly correlated. SCS scores were not correlated with any cognitive domain (Table 2).

Primary Objective:

The regression on functional outcome at *one* year (Table 3) showed an effect for pre-morbid adjustment but the overall model at step 1 was not significant {*F(*6,132) = 1.700, *P* =126, R^2_{adj} = .030)}. Adding verbal memory to the model in the second step was significant {*F*(7,131)=2.97, *P* =.006)} and explained 9% of the variance in functioning (R^2_{adj} = .091) with male gender and verbal memory as significant predictors. Adding consecutive months in total remission in the final model explained an additional

20% of variance and in total 30% of the variance in functioning {R^2_{adj} =.302, F(8,130) = 8.48, P <.001}. Only consecutive months in total remission significantly predicted functional outcome in this model.

The analysis of functional outcome at *2* years (Table 3) showed a significant effect for the first step and absence of a substance use diagnosis and better PAS being significant among established predictors {F(6,100)=2.46, P =.029}. This step explained 8% of variance in functioning (R^2_{adj} =.076). The second model with verbal memory was also significant {F(7,99)=2.48, P=.022}, explained only 2% unique variance in the model, and accounted for 9% of total variance in functioning (R^2_{adj}= .089). The third step with addition of 'months in total remission' was significant {F(8,98)=6.51, P <.001} and represented a 19% increase in variance. In this final model, number of months in total remission and better pre-morbid adjustment were significant predictors and explained a total of 29% of variance in functioning (R^2_{adj} =.294).

Secondary Objective:

In the one year analysis (Table 4), gender, verbal memory and months in *positive* symptom remission were significant at Step 3, {F(8,130)=4.01, P <.001} explaining 15% of variance in functioning (R^2_{adj} =.148). In Step 4, adding months in *negative* symptom remission added 20% unique variance to the model which and was significant {F(9,129) = 9.33, P <.001} explained a total of 35% amount of variance in functioning *(*R^2_{adj} =.35). In this final model, younger age of onset and consecutive months in negative symptom remission were significant.

With respect to the analysis of two year outcome (table 4), adding consecutive months in positive symptom remission in the third step was significant {F(8,98)=5.33, P

<.001} and associated with 24% of variance in functioning (R^2_{adj} =.24). Better pre-morbid adjustment and the absence of a substance use diagnosis were also significant at this step. The addition of months in negative symptom remission in the final step added an additional 13% variance. This final model explained 38% of variance in functioning {(R^2_{adj} = .380, $F(9,97)=8.21$, P <.001)} and consisted of PAS, length of positive and negative symptom remission.

Post-hoc Tests:

When the analyses were repeated with global cognition replacing verbal memory, a greater effect of global cognition was not found, suggesting that verbal memory may be a stronger predictor of functioning than overall cognitive performance. All analyses were also repeated without the known predictors of functioning in the first step, yielding similar results to the original analyses with respect to verbal memory as well as total, positive and negative symptom remission.

Discussion

Our objective was to determine the relative contribution of cognition, specifically verbal memory, and symptom remission (positive and negative) to functional outcome in the first two years of treatment of FEP, after controlling for other known predictors. Results showed that sustained remission of symptoms, especially of negative symptoms, made a larger contribution to functional outcome than verbal memory.

The relatively strong contribution of negative symptom remission for functional outcome was particularly evident at one year. At two years, length of total symptom remission explained the largest proportion of variance in outcome, which was largely contributed by length of positive symptom remission with a relatively lower unique

contribution of negative symptom remission than observed at one year. Correlations between negative and positive symptom remission were stronger over 2 years than 1 year. Those who continued not to meet remission criteria may have had both residual positive and negative symptoms. Some patients, who achieved remission of positive symptoms early on, may have relapsed, not achieved full remission and maintained persistent positive symptoms, especially in the second year.

Our finding of a modest contribution of verbal memory to functioning is somewhat consistent with previous studies showing that performance on verbal tasks is important for outcome[21]. It has been proposed[33] that cognition imparts the capacity to function while negative symptoms determine the motivation and likelihood to perform these tasks. The role of poor motivation and apathy in functional outcome has been reported previously in a relatively small sample of more chronically ill schizophrenia patients[34]. This differential nature of contribution of cognition and negative symptoms may explain our findings and may also correspond to the importance of pre-morbid functioning as was reflected in our models. Of importance is that the negative symptom dimension is relatively independent of cognition and any overlap between these two domains cannot explain our findings.

It could be argued that there may be some overlap between the item content of some of the domains of negative symptoms (apathy and asociality) and items on the SCS. However, we examined correlations separately for the two relatively independent domains of negative symptoms (affective flattening-alogia and apathy-avolition) [35] with the SCS scores and found both to be equally correlated (r =.496 and .504, respectively) with the outcome variable (SCS scores). The role of amotivation in functional outcome,

as assessed by an independent apathy scale, has previously been demonstrated in a sample of chronically ill patients [34]. Further, we have used a composite definition of remission, currently recommended through expert consensus[8], which incorporates all domains of negative symptoms and has received support for its utility through validation with functional outcome[12]. Further, our results also show that at two years length of positive symptom remission makes a large contribution to functional outcome suggesting the importance of achieving lengthy remissions of both positive and negative symptoms.

Consecutive months in remission were predictive of functional outcome, suggesting that a fixed criterion of six months may not be necessary for examining associations between remission and functional outcome. Our results highlight the importance of persistent symptoms for their impact on functional outcome. More intensive treatment including the more targeted use of antipsychotic medication (e.g. early use of Clozapine), reducing substance abuse[36], improving adherence to medication[37] and intensive psychosocial interventions (e.g. family intervention) may result in improved rates and longer sustenance of remission.

Findings concerning the role of co-morbid substance abuse and pre-morbid adjustment[12, 38] were consistent with previous studies, especially at 2 years. This may suggest that pre-morbid adjustment is more of a trait variable and has a lasting effect on functioning[19] while substance abuse is more difficult to treat[39] and remains a significant predictor of relapse even in patients who are totally adherent to medication[36]. On the other hand, a significant impact of DUP[40] and earlier age of onset[41] were not confirmed in our study. Younger age of onset was associated with better functioning at one year, consistent with a recent study[22] perhaps due to the extra support received by younger

patients from their families. The effect of DUP on outcome may generally be overshadowed by other variables that come into play after the patient enters treatment as suggested by another study[42]. The absence of the effect of DUP on functional outcome may also reflect a relatively short DUP for majority of patients in this program, achieved through many years of active early case identification interventions in the community.

Strengths and Limitations

Our study has several strengths. Using a relatively large sample of well characterized patients, with minimal previous treatment, consecutively admitted to a specialized service for FEP in a defined catchment area with no alternative services is likely to make these results generalizable to FEP patients. Our data were derived from repeated prospective evaluations of symptoms and functioning at multiple time points and included a large number of variables known to influence functional outcome. This design is likely to reduce random variation of responses and increase confidence in interpreting the data. Further, we applied both a symptom and time criteria of remission while others[43, 44] have examined symptom severity only. Consecutive months of remission as a continuous measure may better reflect the influence of remission than a-priori fixed criterion creating a dichotomous variable. Using an operationalized definition of remission is likely to be of real clinical relevance and applicable in clinical practice as a goal of treatment.

Our choice of functional outcome (employment/education and social relations) is generally considered important from societal as well as personal perspectives. However, recent studies on recovery in psychotic disorders have suggested that patients' own perspectives on a variety of domains of recovery (illness related, social-functional and

psychological) may also be of importance[3]. Our results have examined at least two of these dimensions: remission (illness-related) and social-functional. Another limitation worth noting is that we did not assess social cognition which may be more likely to impact capacity for social interaction and overall functioning than verbal memory alone or global cognition.

Our results suggest that consecutive months in remission can be used reliably to predict functioning in FEP. Further, our findings support the validity of the Remission in Schizophrenia Working Group criteria for remission in this population except for the six month criterion as also suggested by an earlier study on an independent sample of FEP patients[12]. Clinically, our results highlight the importance of achieving and sustaining complete remission of symptoms as a meaningful treatment target in FEP. The difficulties associated with achieving complete remission underline the importance of searching for effective treatment of persistent positive and, especially, negative symptoms.

Clinical points: Our study highlights several issues relevant for the practising clinician. Achieving and sustaining remission of both positive and negative symptoms of psychotic disorders is extremely important to achieve a good functional outcome (e.g. employment and social relations) for patients, especially during the early years following onset. This is likely to involve maintaining adherence to antipsychotic medication, engagement in other therapeutic interventions and addressing other triggers of relapse such as, substance abuse and interpersonal stress. Patients not able to achieve or sustain remission may need more intensive specialized approach very early in the course of treatment.

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Tables:

Table 1: Demographic and Clinical Characteristics: Comparisons of Study Participants vs. Non-participants [a]

	Year 1 (N = 208)				Year 2 (N = 159)			
	Participants		**Non Participants**		**Participants**		**Non Participants**	
	f/M	***%/SD***	***f/M***	***%/SD***	***f/M***	***%/SD***	***f/M***	***%/SD***
Medication Compliance								
0-74% compliance	29	14.30%	50	50.50%**	12	7.50%	47	43.5**
75-100% compliance	174	85.70%	49	49.50%	147	92.50%	61	56.5
Age at Entry	22.69	4.01	23.34	4.09	22.75	4.01	23.24	4.03
Age of Onset	22.01	3.77	22.38	3.85	21.95	4.03	22.24	3.99
Gender								
Male	144	69.20%	70	70%	108	67.90%	82	71.9
Female	64	30.80%	30	30%	51	32.10%	32	28.1
Substance Abuse & Dependence								
No	81	40,.10%	41	45.60%	68	42.80%	47	42.7
Yes	121	59.90%	49	54.40%	56	89%	60	54.5
Education								
Less than high school	79	38.50%	34	36.20%	59	37.60%	37	33.6
High school or more	126	61.50%	60	63.80%	98	62.40%	73	66.4
Marital Status								
Single	188	90.40%	87	88.80%	145	91.20%	98	86.7
In a relationship	20	9.60%	11	11.20%	14	8.80%	15	13.3
Socioeconomic Status								
Upper class	36	18%	15	15.80%	30	19.60%	16	14.3
Upper middle	44	22%	25	26.30%	32	20.90%	26	23.2
Middle	43	21.50%	22	23.20%	32	20.90%	28	25.00%
Lower middle	62	31%	28	29.50%	49	32%	34	30.4
Lower	15	7.5%	5	5.30%	10	6.50%	8	7.10%
Diagnosis								
SSD	156	75%	72	73.50%	121	76.10%	88	78.60%*
Affective	51	24.50%	23	23.50%	38	23.90%	20	17.90%
DUP (log)	1.25	.64	1.32	.66	1.23	.64	1.35	1.35
Baseline Strauss Carpenter	4.11	2.12	4.53	1.99	4.2	2.17	4.12	4.12
Premorbid Adjustment	.25	.14	.24	.13	.24	.14	.24	.24

f = frequency; *M* = mean; *SD* = standard deviation; * = $P < .05$; ** = $P < .01$; Numbers may not add up to 208 and 159 for all variables due to missing data or rounding. [a]

Table 2: Bonferonni Corrected Pearson Correlations between Remission, Cognitive Domains and Functioning at 1 and 2 Years [b]

	Functional Outcome at Year 1		Functional Outcome at Year 2	
Variable	*r*	*P*	*r*	*P*
Remission				
Months in Total symptom remission	0.553	< .001*	0.507	< .001*
Months in Negative symptom remission	0.610	< .001*	0.530	< .001*
Months in Positive symptom remission	0.283	< .001*	0.329	< .001*
Cognition				
Verbal Memory	0.191	0.014	0.191	0.041
Processing Speed	0.055	0.481	0.129	0.173
Working Memory	0.131	0.088	0.177	0.056
Attention	0.071	0.378	0.168	0.081
Problem Solving	0.101	0.191	0.070	0.453
Visual Memory	0.153	0.059	0.092	0.343
Global Cognition	0.165	0.032	0.177	0.056

* = $P < .005$; *r* = Pearson Correlation Coefficient [b]

Table 3: Symptom Remission, Cognition and Other Predictors of Functional Outcome: Regression Analysis [c]

	Year 1		Year 2	
Block	SE β	β	SE β	B
DUP	.271	-.073	.369	.008
Medication Compliance	.516	.066	.807	.018
Age of Onset	.045	-.110	.052	-.001
Gender	.384	.152†	.472	-.029
Substance Abuse	.366	-.054	.029	-.212*
Premorbid Adjustment	1.252	-.199*	1.566	-.308**
Block 1 R^2 change	.072		.128	
DUP	.266	-.033	.372	.034
Medication Compliance	.504	.101	.801	.021
Age of Onset	.044	-.089	.051	.000
Gender	.378	.200*	.490	-.075
Substance Abuse	.360	-.003	.029	-.196*
Premorbid Adjustment	1.231	-.153†	1.600	-.272**
Verbal Memory	.133	.277**	.183	.162
Block 2 R^2 change	.065		.021	
DUP	.235	.030	.328	.058
Medication Compliance	.451	.003	.712	.082
Age of Onset	.039	-.138†	.045	.006
Gender	.340	.089	.432	-.060
Substance Abuse	.316	-.021	.025	-.153†
Premorbid Adjustment	1.083	-.108	1.436	-.179*
Verbal Memory	.121	.138†	.162	.104
Months in total remission	.048	.498**	.028	.468**
Block 3 R^2 change	.206		.198	
Block 3 R^2 adj	.302		.294	

† = $P < .1$; *= $P < .05$; **= $P < .01$ [c]

Table 4: Separating the Influence of Positive and Negative Symptom Remission on Functional Outcomes: Regression Analysis [d]

	Year 1		Year 2	
Block	SE β	β	SE β	B
DUP	.271	-.073	.369	.008
Medication Compliance	.516	.066	.807	.018
Age of Onset	.045	-.110	.052	-.001
Gender	.384	.152†	.472	-.029
Substance Abuse	.366	-.054	.029	-.212*
Premorbid Adjustment	1.252	-.199*	1.566	-.308**
Block 1 R^2 change	.072		.128	
DUP	.266	-.033	372	.034
Medication Compliance	.504	.101	.801	.021
Age of Onset	.044	-.089	.051	.000
Gender	.378	.200*	.490	-.075
Substance Abuse	.360	-.003	.029	-.196*
Premorbid Adjustment	1.231	-.153†	1.600	-.272**
Verbal Memory	.133	.277**	.183	.162
Block 2 R^2 change	.065		.021	
DUP	.258	-.013	.339	.021
Medication Compliance	.498	.048	.730	.000
Age of Onset	.043	-.135	.047	-.038
Gender	.366	.185*	.446	-.089
Substance Abuse	.349	-.018	.026	-.183*
Premorbid Adjustment	1.191	-.149†	1.456	-.268**
Verbal Memory	.132	.215*	.169	.080
Months in positive Remission	.040	.263**	.025	.404**
Block 3 R^2 change	.061		.154	
DUP	.226	.033	.309	.055
Medication Compliance	.437	.002	.706	.134
Age of Onset	.038	-.161*	.043	-.021
Gender	.333	.049	.412	-.013
Substance Abuse	.305	-.041	.024	-.141†
Premorbid Adjustment	1.050	-.081	1.353	-.183*
Verbal Memory	.119	.089	.154	.065
Months in positive remission	.036	.124	.027	.189*
Months in negative remission	.046	.517**	.029	.453**
Block 4 R^2 change	.196		.129	
Block 4 R^2 adj	.352		.380	

,† = $P < .1$; *= $P < .05$; **= $P < .01$ [d]