Spring 5-2023

Transdiagnostic Predictors Of Everyday Functioning: Examining The Relationships Of Depression And Reinforcement Learning

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A thesis presented to
Washington University in St. Louis
in partial fulfillment of the
requirements for the degree
of Master of Arts

May 2023
St. Louis, Missouri

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Acknowledgments

I thank Drs. Deanna Barch, Denise Head, and Desiree White for serving on my thesis committee and guiding me through this process. I would also like to offer thanks to the individuals who generously gave their time to participate in this study.

This work was supported by National Institute of Mental Health ROI1s (grant numbers MH084840 to Deanna M. Barch, MH084826 to Cameron S. Carter, MH084821 to James M. Gold, MH084861 to Angus W. MacDonald and MH084828 to Steven M. Silverstein). Author Nada Assaad Dalloul had full access to all study data and takes responsibility for the integrity of the data and accuracy of the data analysis. Deanna M. Barch, James M. Gold, Cameron S. Carter, Angus W. MacDonald, III, J. Daniel Ragland, Steven M. Silverstein, and Steven J. Luck developed the study concept and design and aided in interpretation and provided critical revisions.

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Washington University in St. Louis

May 2023

ABSTRACT

Background and Hypothesis. Identifying the factors contributing to functional deficits in psychotic disorders is essential to developing effective interventions. To address gaps in the literature, the current study had several goals: examine whether there are differential relationships across domains of neurocognition and function, assess whether reinforcement learning is related to function, identify how and if predictors of function are transdiagnostic, determine whether depression and positive symptoms contribute to function, and to further explore whether the modality of assessing function impacts the observed relationships.

Study Design. We examined the neurocognitive and symptomatic predictors of individual functional domains across three measures of function using data from 274 participants with Schizophrenia/Schizoaffective Disorder (SZ; n=195) and Bipolar Disorder with psychosis (BD; n=79).

Results. Two neurocognitive components, one working and episodic memory and the other negative and positive reinforcement learning, predicted different functional domains. Predictors of function were largely transdiagnostic with two exceptions: reinforcement learning had a positive association with self-reported interpersonal relationships for SZ and a negative association for BD, and the negative association between positive symptoms and self-reported social acceptability was stronger for BD than for SZ. The predictors of self- and informant-reported function differed in significant ways. Most notably, depression robustly predicted self-reported but not informant-reported function, and anhedonia predicted all domains of informant-reported function.

Conclusions. These findings imply that depression plays a critical role in self-perceived functional impairments, traditional domains of neurocognition and symptoms may be effective transdiagnostic targets for interventions, and reinforcement learning may differentially relate to function across disorders.

Key Words: Schizophrenia, Bipolar Disorder, Psychosis, Neurocognition

1 Introduction

Psychotic disorders are among the most disabling illnesses worldwide.[1] This disability extends across multiple functional domains, including social, occupational, interpersonal, and community functioning. Identifying the factors that are associated with, and possibly contribute to, these functional deficits is essential to inform effective interventions. However, there are still several open issues in the literature. This study focuses on clarifying the transdiagnostic relationships of neurocognition and symptoms with domains of function in schizophrenia and bipolar disorder.

There is robust evidence demonstrating that neurocognitive impairments in domains such as processing speed, working memory, and attention are core features of schizophrenia.[2] Further, neurocognition has been shown to play a crucial role in functional outcomes for individuals with schizophrenia.[3] Yet there is a lack of coherence in the literature regarding the differential relationships of general versus domain-specific components of both neurocognition and function. Largely, the relationship between neurocognition and function broadly defined has been shown to cut across cognitive domains.[4] However, there are indications that certain domains of cognition are more related to function than others. For example, some work suggests that processing speed is more strongly related to function than other domains of cognition,[5] while other studies show stronger relationships between verbal memory or executive function and function.[6,7]

Generally, the literature is most robust in linking work function to neurocognition when considering specific domains of function.[8] Work function has been associated with attention, processing speed, working memory, verbal memory, and reasoning/problem-solving.[9–12] Yet, the findings regarding the relationships between cognitive domains and other domains of function

are mixed.[8] Several studies found that general neurocognition is significantly related to social function,[7,9,13] and one reported that attention, verbal learning, and verbal memory are associated with social outcomes.[9] This is partially supported by studies linking attention, in particular, to social function.[4,14–16] However, a meta-analysis found no significant relationship between attention and social function,[17] and other studies that reported no significant association between any neurocognitive domain and social function.[6,18]

In contrast to the literature on schizophrenia, less work has been done to investigate the factors that are associated with function in bipolar disorder. Like schizophrenia, studies have demonstrated neurocognitive deficits in bipolar disorder,[19–21] predominantly in episodic memory, attention/concentration, and executive functions.[2,22] Additionally, these deficits have been associated with functional outcomes in bipolar disorder[23–29] and persist outside the context of active symptoms.[22,28,30] Although the cognitive and functional impairments in bipolar disorder are generally less severe than in schizophrenia,[20,31] the literature suggests that the relationships between neurocognition and function are present across both disorders.[22,24,28] Still, it is less clear whether the strength and pattern of these relationships across domains of cognition and function are the same across disorders.[22,32] Identifying the transdiagnostic nature of these deficits and relationships could inform interventions that are beneficial for both schizophrenia and bipolar disorder.[32]

The majority of the research described above focuses on what is often referred to as "cold" cognition, which does not include the domain of reinforcement learning. There are multiple elements of reinforcement learning, including implicit (i.e., outside of conscious awareness) and explicit (i.e., including the use of explicit representations about potential reward associations), as well as both positive reinforcement (i.e., learning about actions that lead to

reward) and punishment (i.e., learning to avoid actions that lead to loss) components.[33] Given that the bulk of the literature has centered on standard neurocognitive domains, there is less evidence about the potential role of reinforcement learning in functional outcomes across psychotic disorders. However, several recent studies have linked reinforcement learning to effort allocation, anticipated pleasure and motivation, and everyday function in schizophrenia and schizoaffective disorder.[34–36] Furthermore, there are hints that these relationships are transdiagnostic across the spectrum of psychotic disorders, in that more severe motivation and pleasure deficits are related to worse explicit reinforcement learning performance across diagnoses of schizophrenia, schizoaffective disorder, and bipolar disorder with psychosis.[33] Thus, investigating the relationships between reinforcement learning and function in psychotic disorders could help inform future transdiagnostic interventions.

The role of negative symptoms in functioning in psychotic disorders has also been widely supported.[32,37] Several studies found that negative symptoms are the most robust predictor of everyday function in schizophrenia.[38–42] Only a small body of research has investigated depression as a separate contributing factor from negative symptoms. This work has suggested that depression is associated with function and quality of life across psychotic disorders, but the magnitude of this relationship is unclear.[5,43] In bipolar disorder, depressive symptoms have been found to be more strongly correlated with functional impairments than manic symptoms.[44,45] On the other hand, while some studies reported that depression is more associated with function than psychotic symptoms in schizophrenia,[46,47] other studies found the contrary.[48,49] Moreover, the impact of positive symptoms has mixed support.[32] Much literature suggests that positive symptoms are less associated with general function than negative symptoms in schizophrenia and are related to different domains of function.[5,50] Also, while psychotic symptoms are not as

prevalent in bipolar disorder, there is evidence that they contribute to disability.[51] Overall, more work is needed investigating the presence, strength, and patterns of transdiagnostic relationships between symptoms and functional domains.

There is also a need to investigate whether these predictors differ across different modalities of assessment. Individuals with schizophrenia often have deficits in self-evaluating their illness and function.[52,53] Due to this, informant reports of function and performance on functional competence tasks are often used as alternative measures. Generally, prior work suggests that patients overestimate their function compared to informant-reported function. Variability in symptoms may influence the degree to which patients are able to accurately report their own function. Ermel[52] found that depression is related to the underestimation of interpersonal function and the magnitude of discrepancy between self- and informant-reported function. In contrast, Harvey[53] demonstrated that participants with higher self-reported depression more accurately report their function while participants with very low self-reported depression tend to overestimate their function.

To address the gaps in the literature described above, the study focused on the following questions: 1) Are there differential relationships across domains of neurocognition and function? 2) Is reinforcement learning related to function? 3) Are the predictors of function transdiagnostic? 4) Are depression, independent of negative symptoms, and positive symptoms related to function? and 5) Does the modality of assessing function impact the observed relationships?

2 Methods

2.1 Participants

Participant data (see below for final sample sizes) were collected from two studies with identical recruitment and assessment procedures conducted by the Cognitive Neuroscience Task

Reliability And Clinical applications for Serious mental illness (CNTRaCS) Consortium, which is comprised of 5 sites: University of California, Davis; Maryland Psychiatric Research Center; Rutgers University; University of Minnesota; and Washington University. Group differences in data from the first study are reported in Barch,[33] Gold,[54] and Moran,[55] and group differences in data from the second study are reported in Pratt.[56] Participants provided written informed consent based on the specific recruiting and informed consent procedures approved by each site's local Institutional Review Board. Exclusion criteria: (1) history of significant head trauma or neurological disease or pervasive developmental disorder, (2) diagnosis of substance dependence or abuse in the last six months, (3) score below six on the Wechsler Test of Adult Reading WTAR 57, (4) failing a drug or alcohol screen. Additional inclusion criteria for controls included no personal or 1st degree relative with a history of schizophrenia, schizoaffective, or bipolar disorder and no current major depression or dysthymia or psychotropic medication.

2.2 Procedure

A masters-level clinician conducted or supervised assessments using the Structured Clinical Interview for DSM-IV-TR, the 24-item Brief Psychiatric Rating Scale (BPRS), and the Clinical Assessment Interview for Negative Symptoms (CAINS) (See Table 1). As previously reported,[33] certified raters who were trained during on-site standardized SCID supervision and teleconferences achieved agreement (ICC = .80) with the "gold" standard ratings for at least six interviews.

Participants and individuals with information about the participants' function (e.g., family members, therapists) were asked to complete the Specific Levels of Functioning Scale (SLOF).[57] The SLOF assesses four domains: Interpersonal Relationships (e.g., effectively communicating), Social Acceptability (e.g., inappropriate or abusive behavior), Activities of

Community Living (e.g., managing household responsibilities) and Work Skills (e.g., employable skills). Each domain is scored from 1 to 5, with higher scores indicating better function.

Participants also completed the UCSD Performance-Based Skills Assessment (UPSA),[58] a performance-based measure of functional capacity. Participants are asked to perform various tasks, including manipulating money, making routine and emergency calls, reading maps and schedules, and performing shopping tasks. The UPSA total score used in this analysis is on a 0 to 100-point scale, with higher scores indicating better function.

Participants completed two cognitive testing sessions within one month. The cognitive tasks (described in Table 1) were Working Memory Change Detection and Change Localization, Running Span, Explicit Probabilistic Incentive Learning Task (E-PILT), and a Reversal Learning Task. In addition, three subtests of the MATRICS Consensus Cognitive Battery were administered: BACS Symbol Coding, Hopkins Verbal Learning Test (HVLT), and Letter Number Sequencing (LNS).

2.3 Data Analysis

2.3.1 Data Cleaning and Final Participant Totals

We identified four outliers as part of a multivariate outlier analysis using Mahalanobis distance. These 4 participants (3 schizophrenia/schizoaffective, 1 bipolar with psychosis) and 128 participants (96 schizophrenia/schizoaffective, 32 bipolar with psychosis) were removed for missing data as we used a complete case analysis. The participants with and without excluded data differed on years of education (by ½ year) but did not differ on age, parental years of education, gender, or diagnosis (see Supplemental Table 1). We analyzed data from 274 participants, comprised of 195 individuals with a diagnosis of schizophrenia or schizoaffective

disorder (SZ; 113 M 82 F; M_{age} = 36.70, SD_{age} = 10.42), and 79 individuals with a diagnosis of bipolar disorder with psychosis (BD; 30 M 49 F; M_{age} = 37.16, SD_{age} = 10.92). Data from both studies were combined, and numerical variables were standardized to have a mean of 0 and a standard deviation of 1. For regression analyses, participants' diagnoses were coded either as -.5 (BD) or .5 (SZ). Of the 274 participants, 166 had informant-report SLOF data (42 BD; 124 SZ).

2.3.2 Principal Component Analysis

We conducted a principal component analysis with all 13 neurocognitive variables see Table 1), using an oblique rotation and a Catell's Scree Test to determine the optimal number of components.

2.3.3 Prediction

A both-direction stepwise linear regression was used to explore the predictors of UPSA total score and of the four SLOF self-report and informant-report scales. Each model included the following independent variables: age, sex, diagnosis, symptom variables, scores from the three neurocognitive PCA components, and interactions of each variable with diagnosis. Each final model was selected with Bayesian Information Criterion because this approach penalizes more complex models and is likely to select a "true" model with large datasets.

In follow-up analyses to test whether depression was more significantly associated with self- or informant-reported function, a series of three linear regressions were conducted on the domains of function that were significantly predicted by depression. These models included depression as the dependent variable and self- and informant-report SLOF scales as independent variables.

3 Results

3.1 Descriptives

The racial and ethnic composition of the groups is show in Supplemental Figure 1. SZ

participants had higher BPRS positive symptoms, CAINS Anhedonia (Motivation and Pleasure Sympotoms), and CAINS affective blunting scores than BD participants but did not differ on any other variables (See Supplemental Table 2).

3.2 Principal Component Analysis

The Catell's Scree Test results suggested using three components, which cumulatively explained 51% of the total variance (Table 2). The three components explained 26%, 14%, and 11% of the variance, respectively. The first principal component was comprised of seven neurocognitive variables— Running Span Original, Letter Number Sequencing, BACS Processing Speed, Running Span Adaptive, Hopkins Verbal Learning, Change Detection and Change Localization. This component can be viewed as a composite of Working Memory and Episodic Memory (WM-EM). The second principal component was comprised of the four EPILT neurocognitive variables — W80, L90, L80, and W90. This component can be viewed as a composite of positive and negative Reinforcement Learning (PosNegRL). The third principal component was comprised of both Reversal Learning neurocognitive variables — Reversal Learning First Reversal and Reversal Learning Initial Acquisition and EPILT W90. The component scores were used in the following analyses.

3.3 Regression

3.3.1 UPSA

17% of the variance in functional competence was accounted for by age and WM-EM (Table 3, Supplemental Figure 3). A 1 standard deviation unit (SDU) increase in age was associated with a 20% increase in UPSA score, and a 1 SDU increase in WM-EM performance was associated with a 43% increase in UPSA score.

3.3.2 Specific Levels of Functioning Scale: Self-Report

Interpersonal Relationships. 31% of the variance in self-reported interpersonal relationships was accounted for by depression, positive symptoms, anhedonia, blunting, diagnosis, PosNegRL, and the interaction of diagnosis with PosNegRL (Table 3, Supplemental Figure 4). A 1 SDU increase in depression score was associated with a 31% decrease in self-reported interpersonal relationships score, a 1 SDU increase in positive symptoms score was associated with a 15% decrease in self-reported interpersonal relationships score, a 1 SDU increase in anhedonia was associated with a 24% decrease in self-reported interpersonal relationships, and a 1 SDU decrease in blunting was associated with a 14% decrease in self-reported interpersonal relationships. Regarding the significant interaction effect, for SZ, a 1 SDU increase in PosNegRL was associated with a 13% *increase* in self-reported interpersonal relationships holding all other variables at 0. In contrast, for BD, a 1 SDU increase in PosNegRL was associated with a 21% *decrease* in self-reported interpersonal relationships holding all other variables at 0.

Social Acceptability. 18% of the variance in self-reported social acceptability was accounted for by depression, positive symptoms, diagnosis, and the interaction of positive symptoms and diagnosis (Table 3, Supplemental Figure 4). A 1 SDU increase in depression was associated with a 16% decrease in self-reported social acceptability. The significant interaction effect reflects that for SZ, a 1 SDU increase in positive symptoms was associated with a 22% decrease in self-reported social acceptability, but a 114% decrease in self-reported social acceptability for BD holding all other variables at 0.

Activities of Community Living. 7% of the variability in self-reported activities of community living was accounted for by anhedonia and WM-EM (Table 3, Supplemental Figure 4). A 1 SDU increase in anhedonia score was associated with a 17% decrease in self-reported activities of

community living, and a 1 SDU increase in WM-EM was associated with a 18% increase in self-reported activities of community living.

Work Skills. 14% of the variability in self-reported work skills was accounted for by depression and anhedonia (Table 3, Supplemental Figure 4). A 1 SDU increase in depression was associated with a 29% decrease in self-reported work skills, and a 1 SDU increase in anhedonia was associated with a 20% decrease in self-reported work skills.

3.3.3 Specific Levels of Functioning Scale Informant-Report

Interpersonal Relationships. 14% of the variance in informant-reported interpersonal relationships was accounted for by anhedonia and blunting (Table 4, Supplemental Figure 5). A 1 SDU increase in anhedonia was associated with a 26% decrease in informant-reported interpersonal relationships, and a 1 SDU increase in blunting was associated with a 19% decrease in informant-reported interpersonal relationships.

Social Acceptability. 9% of the variance in informant-reported social acceptability was accounted for by age, anhedonia, and diagnosis (Table 4, Supplemental Figure 5). A 1 SDU increase in age was associated with an 18% increase in informant-reported social acceptability, a 1 SDU increase in anhedonia score was associated with a 29% decrease in informant-reported social acceptability, and SZ had on average 50% higher informant-reported social functioning scores than BD holding anhedonia and age constant.

Activities of Community Living. 4% of the variability in informant-reported activities of community living was accounted for by anhedonia (Table 4, Supplemental Figure 5), with a 1 SDU increase in anhedonia associated with a 22% decrease in informant-reported activities of community living.

Work Skills. 18% of the variability in informant-reported work skills was accounted for by anhedonia and WM-EM (Table 4, Supplemental Figure 5). A 1 SDU increase in anhedonia was associated with a 33% decrease in informant-reported work skills, and a 1 SDU increase in WM-EM was associated with a 22% increase in informant-reported work skills.

3.3.4 Depression in Relation to Self- versus Informant-Reported Function

In the analyses reported above, depression was consistently related to self-reported but not informant-reported function. We conducted a series of regressions with both self-and informant reported interpersonal relationships, social acceptability, and work skills predicting depression to test whether this was a significantly different relationship. The linear regression for each of these domains of function indicated that when self and informant are in the same model, only self-report significantly related to depression (Supplemental Table 3).

4 Discussion

We found that two neurocognitive components, one comprised of working and episodic memory and the other comprised of negative and positive reinforcement learning, selectively predicted different domains of function. Additionally, most of the associations were transdiagnostic, except for the relations of positive and negative reinforcement learning to self-reported interpersonal relationships and the relationship of positive symptoms to self-reported social acceptability. Furthermore, our results demonstrated that depression was associated with all self-reported domains of function, except for activities of community living. We also found that positive symptoms predicted a decrease in self-reported interpersonal relationships, and that this effect was stronger for BD than SZ. Lastly, the predictors for each domain of self- and informant-reported function differed in important ways. The most notable differences were that

depression robustly predicted self-reported but not informant-reported function, and anhedonia predicted all domains of informant-reported function.

The literature indicates that traditional domains of neurocognition are robustly associated with occupational functioning.[8–12] In the current study, we found that the neurocognitive component defined as a composite of working and episodic memory was positively associated with informant-reported work skills but was unassociated with self-reported work skills. The lack of association between neurocognition and self-reported work skills is consistent with prior literature suggesting that individuals with psychosis may not accurately self-evaluate their functional capacities.[53] Further, given that self-reported work skills were predicted in part by depression, these results may reflect that depression skews self-reported ratings of work skills functioning,[52,53] as discussed in more detail below.

While the existing literature supports a relationship between work skills and neurocognition, evidence regarding the associations between domains of neurocognition and social functioning is unclear. Our results suggest that social functioning might be associated with reinforcement learning rather than with traditional domains of neurocognition. We found that the working and episodic memory component was not associated with social functioning. However, the component reflecting positive and negative reinforcement learning was associated with self-reported interpersonal relationships, though it interacted with diagnosis. Specifically, we found that better positive and negative reinforcement learning was associated with increased self-reported interpersonal relationships in SZ but decreased self-reported interpersonal relationships in BD. One possible interpretation of these results is that for SZ, reinforcement learning is linked to motivation and apathy, such that poor reinforcement learning may fail to learn about cues predicting positive social engagements. In contrast, for BD, reinforcement learning might be

associated with hyper-reward responsivity, which could be related to socially inappropriate behavior.

As noted above, consistent with some prior literature,[34–36] we found that some aspects of reinforcement learning related to interpersonal function, though not other components of function. Moreover, the component comprised of reversal learning was not significantly associated with any domains of function across modalities of assessment. At this point, it is not clear whether this is due to a construct-related difference (i.e., reversal learning engages differential processes) or different psychometrics of the reversal learning task compared to the other reinforcement learning tasks.

Broadly, the existing literature has yet to come to an agreement on whether the patterns and strength of relationships between domains of neurocognition and function are transdiagnostic.[22,32] Here we found that the neurocognitive component comprised of working and episodic memory was related to self-reported community living, UPSA, and informant-reported work skills similarly across disorders. On the other hand, we found that the relationship of reinforcement learning to self-reported interpersonal relationships differed by diagnosis, suggesting that the pathways linking disrupted reinforcement learning to function might vary as a function of diagnosis. This finding was unexpected and in need of replication, but if confirmed, it suggests potentially different intervention approaches across schizophrenia and bipolar disorder in terms of the role of reward learning in function.

Similar to neurocognition, negative symptoms have been robustly associated with deficits in function.[32,37–42] Our results add support to these prior studies in that anhedonia predicted all informant-reported domains of function and self-reported interpersonal relationships, activities of community living, and work skills. In addition, affective blunting predicted self- and informant-

reported interpersonal relationships. Accordingly, these findings are consistent with prior studies that have highlighted the importance of interventions to target negative symptoms as a mechanism for treating functional impairments.[59]

Additionally, we investigated the impact of depression as a factor independent of negative symptoms. Largely, our results showed that depression plays a critical role in self-reported everyday function across diagnoses. We found that greater depression was significantly associated with worse self-reported function in all domains except activities of community living. However, depression was unassociated with any informant-reported functional domain, with follow-up analyses suggesting a significantly stronger relationship between self-reported function and depression. These results demonstrate that depression impacts self-perceived function and can be contextualized by prior literature that linked depression to introspective inaccuracy in schizophrenia.[53] Additionally, the role of depression in self-reported social acceptability and interpersonal relationships expands upon the prior results that depression is related to the underestimation of interpersonal function.[52] Thus, while targeting depression in psychotic disorders in and of itself may not improve functioning, it may improve accuracy in the perception of functional impairments and could potentially lead to an improved willingness to engage in activities. Ultimately, these results strongly suggest that depression should be further investigated as a contributing factor to function and taken into account when evaluating assessments with patients.

The literature has suggested that positive symptoms are less and differentially associated with function than negative symptoms, though this may reflect the difficulties of recruiting individuals with severe psychotic symptoms and capturing fluctuating positive symptoms at a single time point.[5,50,60] In our study, positive symptoms were negatively related to self-reported

social acceptability across disorders but to a significantly larger degree for BD. This pattern was not found in the model for informant-reported social acceptability. This suggests the possibility that positive symptoms impact an individual's self-perceived social acceptability rather than how others perceive their social acceptability. Ultimately, the key takeaway from these results is that positive symptoms should not be overlooked when considering the predictors of social function, especially for BD.

There are several limitations to this study. First, our study utilized composites of neurocognitive scores rather than individual neurocognitive domains. While this method was used to enhance power and focus on dissociable domains of cognition, it was at the expense of investigating the roles of individual neurocognitive measures. Second, we did not assess introspective accuracy, so we could not formally determine whether it is linked to depression. Third, there were fewer participants with informant- than self-report measures, which might have impacted power in the informant-report analyses. Fourth, the study sample included medicated patients with predominantly nonactive symptoms, so the distribution of positive symptoms was skewed. Fifth, the BD sample was significantly smaller than the SZ sample.

The current study provides evidence that neurocognition and symptoms have comparable associations with functioning in SZ and BD with two notable exceptions. Reinforcement learning had a positive association with interpersonal relationships for SZ and a negative association for BD, and positive symptoms were negatively associated with social acceptability to a larger degree for BD compared to SZ. Overall, these findings imply that traditional domains of neurocognition and symptoms may be effective transdiagnostic targets for future interventions. Additionally, our results suggest that depression impacts self-perceptions of functional ability, highlighting the importance of examining depression in work on function in psychosis

Table 1. Procedure

Name	Reference	Domain	Brief Description	Variable
Symptoms				
Brief Psychiatric Rating Scale (BPRS)	(Overall & Gorham, 1962)[61]	General Psychiatric Symptoms	The depression subscale assesses despondency in mood, sadness. The positive symptom subscale assesses grandiosity, suspiciousness, hallucinations, and unusual thought content.	• Depression Subscale • Positive Symptoms Subscale
Clinical Assessment Interview for Negative Symptoms (CAINS)	(Kring et al., 2013)[62]	Negative Symptoms	The anhedonia subscale measures interest and frequency of motivated behavior, frequency of pleasure and frequency of expected pleasure over the past week. The blunting subscale assesses facial expressivity, vocal expressivity, and body gestures.	• Anhedonia - Motivation and Pleasure (MAP) Subscale • Blunting Subscale
Neurocognition				
BACS Symbol Coding	(Keefe, 2004)[63]	Processing Speed	Participants are asked to quickly write the symbol associated with a given number within 90s.	• T-Score
Hopkins Verbal Learning Test (HVLT)	(Brandt, 1991)[64]	Episodic Memory	Participants are read a list of words and asked to repeat those words across three trials.	• T-Score
Letter Number Sequencing (LNS)	(Gold, 1997)[65]	Working Memory	Participants listen to a string of intermixed letters and numbers and then are asked to restate the sequence in numeric and alphabetical order.	• T-Score
Change Detection	(Gold et al., 2019)[54]	Working Memory	Participants are asked to encode a 5-item array, and after a short delay are presented with a 5-item test with either 0, 1, 2, or 5 items that differ from the original array, then are prompted to indicate whether they detect any changes.	• Percent accuracy
Change Localization	(Gold et al., 2019)[54]	Working Memory	Participants are presented with a single change on the test array and are asked to identify the location of the changed item.	• Percent accuracy
Running Span	(Broadway & Engle, 2010)[66]	Working Memory	Participants are presented with a string of letters and are asked to recall the last X letters.	• Original Operation - # of items remembered in their correct position • Adaptive Operation - # of items remembered in their correct position
Probabilistic Reversal Learning	(MacDonald et al.)[67]	Reversal Learning	Adapted from Cools and colleagues (2002). Participants selected one of two abstract images, with one item reinforced for 80% and 90% of the time, and then were told whether their choice was correct.	• Average Trials to Initial Acquisition • Average Trials to First Reversal
Explicit Probabilistic Incentive Learning Task (E-PILT)	(Gold, 2012)[68]	Reinforcement Learning	Participants are presented with various picture stimuli that are reinforced at different contingencies (80% or 90%) and asked to learn which images are associated with gain or avoiding loss.	• W80 - # of correct responses in gain and 80% condition • W90 - # of correct responses in gain and 90% condition • L80 - # of correct responses in loss and 80% condition • L90 - # of correct responses in loss and 90% condition

Table 2. PCA of Neurocognitive Variables

Variable	First Principle Component (WM-EM)	Second Principle Component (PosNegRL)	Third Principle Component (RevLearn)
Running Span Original	0.791	.	
Letter Number Sequencing	0.784		
BACS Processing Speed	0.741		
Running Span Adaptive	0.730		
Hopkins Verbal Learning	0.638		
Change Detection	0.549		
Change Localization	0.523		
EPILT W80		0.719	
EPILT L90		0.718	
EPILT L80		0.694	
EPILT W90		0.466	0.307
Reversal Learning First Reversal			0.777
Reversal Learning Initial Acquisition			0.674

Note: Only loadings above 0.3 are shown for clarity.

Table 3. UPSA & Self-Report Regression Results: Standardized Beta Coefficients

	UPSA	**Interpersonal Relationships**	**Social Acceptability**	**Activities of Community Living**	**Work Skills**
Age	0.20 *** *[0.08, 0.31]*	-	-	-	-
Depression	-	-0.31 *** *[-0.42, -0.20]*	-0.16 ** *[-0.28, -0.04]*	-	-0.29 *** *[-0.41, -0.18]*
Positive Symptoms	-	-0.15 * *[-0.27, -0.03]*	-0.68 *** *[-0.90, -0.46]*	-	-
Anhedonia	-	-0.24 *** *[-0.36, -0.13]*	-	-0.17 ** *[-0.29, -0.05]*	-0.20 *** *[-0.31, -0.08]*
Blunting	-	-0.14 * *[-0.25, -0.03]*	-	-	-
WM-EM	0.43 *** *[0.31, 0.54]*	-	-	0.18 ** *[0.06, 0.30]*	-
PosNegRL	-	-0.04 *[-0.16, 0.08]*	-	-	-
Diagnosis	-	0.04 *[-0.22, 0.30]*	0.95 *** *[0.59, 1.32]*	-	-
Positive Symptoms x DX	-		0.93 *** *[0.50, 1.35]*	-	-
PosNegRL x DX	-	0.34 ** *[0.10, 0.58]*	-	-	-
Adjusted R-Squared	0.17	0.31	0.18	0.07	0.14
BIC	745.45	719.37	751.51	777.35	754.54
****** p < 0.001; ** p < 0.01; * p < 0.05***					

Table 4. Informant-Report Regression Results: Standardized Beta Coefficients

	Interpersonal Relationships	Social Acceptability	Activities of Community Living	Work Skills
Age	-	0.18 * *[0.03, 0.34]*	-	-
Anhedonia	-0.26 ** *[-0.42, -0.10]*	-0.29 *** *[-0.45, -0.14]*	-0.22 ** *[-0.36, -0.07]*	-0.33 *** *[-0.47, -0.19]*
Blunting	-0.19 * *[-0.34, -0.03]*	-	-	-
WM-EM	-	-	-	0.22 ** *[0.07, 0.36]*
Diagnosis	-	0.49 ** *[0.13, 0.84]*	-	-
Adjusted R-Squared	0.14	0.09	0.04	0.18
BIC	462.69	477.55	477.17	456.19
****** p < 0.001; ** p < 0.01; * p < 0.05***				

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