

Published in final edited form as:

Biol Psychiatry. 2010 July 1; 68(1): 93–99. doi:10.1016/j.biopsych.2010.01.021.

Markers of basal ganglia dysfunction and conversion to psychosis: Neurocognitive deficits and dyskinesias in the prodromal period

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Abstract

Background—Movement abnormalities and cognitive deficits may represent external markers of an underlying neural process linked with the early etiology of psychosis. As basal ganglia function plays a governing role in both movement and cognitive processes, an understanding of the relationship between these phenomena stands to inform etiological conceptualizations of vulnerability and psychotic disorders.

Methods—In this investigation, trained raters coded movement abnormalities in videotapes from structured interviews of adolescents and young adults with a prodromal risk syndrome ($n = 90$). The participants were administered a neuropsychological battery including measures of verbal comprehension, perceptual organization, immediate/delayed auditory memory, and an estimate of full scale intelligence quotient. Diagnostic status was followed for a two-year period utilizing structured clinical interviews, during which time 24 high-risk participants (26.66%) converted to an Axis I psychotic disorder.

Results—Elevated dyskinetic movements in the upper-body region were correlated with deficits in domains of verbal comprehension, perceptual organization and both immediate and delayed auditory memory. Further, discriminant function analyses indicated that baseline movement abnormalities and neurocognitive deficits significantly classified those high-risk participants who would eventually convert to a psychotic disorder (72.3%).

Conclusions—Results support a common cortico-striato-pallido-thalamic circuit irregularity, underlying both movement abnormalities and cognitive deficits in individuals at high-risk for

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The authors report no biomedical financial interests or potential conflicts of interests.

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psychosis. Models incorporating external markers of progressive basal ganglia dysfunction may enhance detection and preventive intervention for those high-risk individuals most in need of treatment.

Keywords

Neuropsychology; Dyskinesia; Biomarker; Psychosis; Prodrome; Conversion

Several lines of evidence point to a role of cortico-striato-pallido-thalamic dysfunction in the early pathogenesis of schizophrenia spectrum disorders (1). A recent study found that one such indicator, hyperkinetic movements (e.g., writhing or flinging movements of the limbs, fingers or face), distinguished those high-risk individuals who would later convert to psychosis (2). In a parallel line of work, researchers have observed neurocognitive deficits during the period preceding formal onset of psychotic disorder, and noted that this dysfunction may differentiate those high-risk individuals who go on to convert to Axis-I psychosis (3-15).

Until now these two domains – movement abnormalities and neurocognitive deficits – have been viewed as largely unrelated in etiological conceptualizations of psychotic disorders. However, a traditional view that the basal ganglia structures are solely involved in the control of movement has been challenged in recent years. Specifically, anatomical studies have revealed discrete connections between the basal ganglia region and the cerebral cortex, reciprocally interconnecting a large and diverse set of cortical areas (16). Within these distinct circuits, dopamine (DA) acts as a regulator (17), and abnormal dopaminergic neurotransmission could contribute to hyperkinetic movements as well as specific cognitive impairments (18-20). Based on these trends, Robbins (21) proposed that the heterogeneous range of core symptoms associated with psychosis, appearing to be associated with a range of structural and functional abnormalities, might be explained by a frontal-striatal hypothesis, where an altered balance in the flow of information between cortico-striatal loops could explain the seemingly disparate symptoms and characteristics of the disorder.

Hyperkinetic movements are commonly observed in patients receiving DA agonists (i.e., l-dopa, stimulants) and in diseases linked with altered striatal DA (e.g., Huntington's Chorea, Parkinson's disease, schizophrenia) (22-24). Evidence also suggests that movement abnormalities manifest in a developmental trajectory that converges with changes posited by neurodevelopmental models of schizophrenia (25-27). These movements are of interest because they are more common in schizophrenia spectrum disorders (28) and occur in medication naïve populations (29), suggesting they may, in part, reflect pathological processes underlying this spectrum of disorders.

Cognitive dysfunction observed in high-risk (3-15) and pre-psychotic populations (30-31) may also reflect an underlying core vulnerability (6). Discrete cortico-striato-pallido-thalamic circuits, moderated by DA, act as powerful regulators of different aspects of neurocognitive function (18,32). It thus seems possible that the pathoetiological processes involved in psychotic symptom development may impinge on the neural regions that both modulate cognition (33) and govern dyskinetic movements (23).

Despite the evidence suggesting that both movement and neurocognitive markers are prominent during the prodromal period, to date no studies have examined the neurocognitive correlates of movement abnormalities in this population. The present investigation tests the prediction that hyperkinesia will be associated with deficient cognitive function among youth with a prodromal risk syndrome. Further, it is predicted that baseline movement-related and cognitive markers will enhance our ability to identify those high-risk participants who will eventually convert to Axis I psychosis.

Method

Recruitment

Participants were recruited for a collaboration of longitudinal prospective studies of adolescents and young adults at high-risk for developing a psychotic disorder. These studies are ongoing at the University of California Los Angeles (UCLA) and Emory University, and the present analysis constitutes the first use of the combined sample, thus affording greater statistical power for detecting predictors. Recruitment of participants was conducted by staff in the Emory University Adolescent Development Program (EADP) and the UCLA Center for Assessment and Prevention of Prodromal States (CAPPS) through psychoeducational talks given to healthcare clinics/hospitals and schools and a website describing prodromal symptoms in layperson terminology. This report presents data on 90 high-risk participants (34), ranging in age from 11 to 29 years, who underwent an initial assessment and ongoing follow-ups for a two-year period (demographic characteristics and baseline movement and neurocognitive scores are presented in Table 1).

Assent and written consent was obtained from all participants and a parent (in the case of minors), in accordance with the guidelines of the Emory and UCLA Biomedical Institutional Review Board (IRB). Exclusion criteria were presence of a neurological disorder, mental retardation (FSIQ score < 70), substance abuse or addiction (by DSM-IV criteria) within 6 months of baseline, and history of significant head injury with the exception of mood, anxiety, attention-deficit, and other disruptive behavior disorders as the latter disorders show a high rate of comorbidity with psychosis (35). In the group of prodromal participants who did not convert, the comorbidity included: conduct disorder+depression (1.5%), conduct disorder+depression+anxiety (1.5%), attention deficit hyperactivity disorder (ADHD) (16.6%), ADHD+anxiety (1.5%), ADHD+depression+anxiety (3%), anxiety (7.5%), depression (15.2%), depression+ADHD (3%), and depression+anxiety (22.7%). Comorbidity in the group of prodromal participants who did convert during the study period included: ADHD (4.1%), ADHD+anxiety (8.3%), anxiety (4.1%), depression (29.2%), and depression+anxiety (25%). The final sample of prodromal subjects was comprised of those who met diagnostic criteria for a prodromal risk syndrome (34), but no Axis I psychotic disorder.

Controlling for Psychotropic Medications Status

Although movement abnormalities have been observed in medication naïve samples of patients with psychosis (29), existing evidence suggests that these medications can affect movement (36-37). Because anti-psychotic medications are dopamine (DA) antagonists, particularly for D2 receptors, they can have motor side effects ranging from hyperkinesia to hypokinetic syndromes (38). Like antipsychotics, antidepressants can also affect movement characteristics (39-41). For example, animal models also indicate that selective serotonin reuptake inhibitors (SSRI) administration decreases extracellular dopamine in the striatum, a region of the basal ganglia that is tied to extra-pyramidal symptoms (42). Finally, evidence also suggests that stimulants affect movement abnormalities. Specifically, stimulant medication increases DA and, therefore, can increase tics and other involuntary movements (43).

Although priority was given to the recruitment of participants who had never received a psychotropic drug, some participants were taking one or more psychotropics. This reflects national pattern, in that there has been an increase in the number of adolescents with adjustment problems, who are prescribed treatment with psychotropic medications, particularly stimulants, antidepressants and, to a lesser extent, antipsychotics (44). A total of 61% of the participants showed a history of treatment with psychotropic medication prior to entering the study: the most common treatment history was antidepressant medication (44%), followed by stimulants (27%) and antipsychotics (23%). A total of 60% of the participants were treated

during the study; the most common psychotropic was antidepressant medication (37%), followed by stimulants (20%) and antipsychotics (14%). Nine (16%) of the 54 medicated subjects were taking two or more medications simultaneously during the study period (antidepressant+stimulant=3; antidepressant+antipsychotic=4; antidepressant+stimulant+antipsychotic=2). Because these potential confounds, medication status was modeled statistically in the analyses.

Procedures

Assessing Symptomatology

The Structured Interview for Prodromal Symptoms (SIPS) (34) was administered at baseline to gauge the presence of prodromal symptoms. The SIPS contains an instrument, the Scale of Prodromal Symptoms (SOPS), which rates the severity of relevant symptoms along a 7-point scale ranging from absent to severe and psychotic. A prodromal or high-risk syndrome was defined by moderate levels of positive symptoms and/or a decline in global functioning accompanying the presence of schizotypal personality disorder and/or a family history of schizophrenia (34).

To assess for the presence of Axis I disorders, the Structured Clinical Interview for Axis-I DSM-IV Disorders (SCID) (45) or the Kiddie Schedule for Affective Disorders and Schizophrenia (for ages 14 and under; K-SADS) (46) was administered during the initial evaluation and at subsequent yearly follow up assessments. Both measures have been demonstrated to have excellent inter-rater reliability in adolescent populations (47). Advanced psychology doctoral students and clinical psychologists conducted the respective interviews.

Neurocognitive Measures

A range of functional domains were assessed using the Wechsler Intelligence Scales for Children, Third Edition (WISC-III) (48) for participants ages 11-15 and the Wechsler Adult Intelligence Scales, Third Edition (WAIS-III) (49) for participants ages 16 and older. Selected subtests included Vocabulary (administered at both sites), Block Design (administered at the EADP site), and Matrix Reasoning (administered at the CAPPS site). The Wechsler Memory Scales, Third Edition (WMS-III) (50) Logical Memory I and II subscales were also used to assess memory function (i.e., immediate/delayed auditory memory) at both sites. Collectively, these measures were chosen because a body of research has indicated neurocognitive dysfunction in these domains in high-risk populations (2-14). These particular cognitive tests were the only common measures utilized across the two high-risk sites and no sub-tests were excluded.

An index of estimated FSIQ was derived using Vocabulary and Block Design subtests of the WAIS and WISC in the EADP site, and with the Wechsler Abbreviated Scale of Intelligence (WASI; Vocabulary and Matrix Reasoning) at the CAPPS site. The estimated FSIQ yielded from these measures correlates very highly with Full Scale IQ (51-52) and FSIQ estimates show excellent reliability between the WISC and WAIS (51-52).

Coding of Movement Abnormalities

Following the procedures used in previous publications (53-54), movement behavior was coded from videotapes of subjects made during the initial clinical interviews (SIPS/SCID). Interviews were conducted in private rooms, and the participants were videotaped while seated in a chair facing a wall-mounted camera behind the interviewer. The participant's feet were not visible for a majority of the videos, and subsequently, movement abnormalities involving the feet were omitted from the present series of analyses. To limit bias, raters were blind to the participants' clinical status, and rating was conducted on muted videotapes.

An empirically developed scale, the Dyskinesia Identification System: Condensed User Scale (DISCUS) was used to code involuntary movements (55). The DISCUS contains 15 items that are rated on a 0-4 (absent to severe) scale (56). Research assistants were trained across sites in the application of the coding procedures using tapes of non-participants. Coding of the subject tapes began after all pairs of raters had achieved a minimum inter-rater reliability of (intraclass correlation coefficients [ICCs]>.80) for coding, independently, for each body region and movement type.

Statistical Analysis

Chi square and t-tests were used to check for demographic differences between groups and sites. Medication use was dummy-coded by class of medication (stimulants, anti-depressant, and anti-psychotics), and this data was entered as covariates. Partial correlations were employed to examine associations of movement abnormalities with neuropsychological test performance. Multiple discriminant function analyses were conducted to determine discriminative ability of neurocognitive and movement variables in predicting conversion.

Results

Of the 90 participants with a prodromal risk syndrome, 24 (26.67%) converted to an Axis I psychotic disorder during the 2-year period of the study. The specific diagnostic outcomes were schizophrenia (N=5), schizoaffective disorder (N=9), mood disorder with psychotic features (N=6), and psychosis not otherwise specified (N=4). The progression of positive, negative, and total prodromal symptoms is presented in Table 2. Analyses were conducted to test for demographic differences between subgroups of the prodromal participants based on subsequent conversion/non-conversion to an Axis I psychotic disorder. Independent t-tests indicated no diagnostic group differences in age [$t(88)=-.56, p=.56$] or parental education [$t(77)=-.84, p=.40$], and Chi Square tests revealed no significant diagnostic differences between the converting and non-converting high risk participants in sex ratio [$\chi^2(1, n=90)=.14, p=.70$] or stimulant [$\chi^2(1, n=90)=.25, p=.61$], antidepressant [$\chi^2(1, n=90)=.33, p=.56$], and antipsychotic [$\chi^2(1, n=90)=2.85, p=.09$] medications (please see Table 1). This finding suggests that differential medication treatment was not a likely source of bias.

A series of analyses was conducted to identify potential demographic differences between the prodromal participants from the EADP (N=41) and CAPPs (N=49) sites. EADP (24%) and CAPPs (28%) sites had comparable rates of prodromal participants who converted to psychosis. There were no significant site differences for gender [$\chi^2(1, n=90)=.01, p=.92$], or parental education [$t(77)=-1.60, p=.11$]. There were significant differences between the EADP (mean=14.14, SD=1.66) and CAPPs (mean=16.95, SD=3.24) sites for age [$t(88)=-4.98, p\leq .01$], where the EADP participants were slightly younger than those at the CAPPs site. To address any potential systematic error, analyses included statistical controls for age.

Associations Between Movement Abnormalities and Neurocognitive Functioning

Partial correlations (controlling for age and medication class) were conducted to test for relationships between movement abnormalities and neurocognitive dysfunction. As seen in Table 3, there were no significant associations in the facial region. In contrast, the results indicated that movements in the upper-body region were associated with several domains of neurocognitive functions. Notably, poorer performance on measures of verbal comprehension (Vocabulary) and perceptual organization (Block Design) were associated with elevated hyperkinetic movements. Similarly, deficit performance on immediate and delayed verbal memory (Logical Memory I & II), and estimated FSIQ was associated with an increased incidence of hyperkinetic movements.

Classification: Prodromal Participants at Highest Risk for Conversion

To maximize statistical power, discriminant function analyses were conducted using those variables that were administered across sites, namely facial and upper-body movement abnormalities and neuropsychological domains including both immediate and delayed verbal memory (Logical Memory I and II) and a composite estimate of FSIQ (the Vocabulary subtest was also administered across sites, but was omitted because it was utilized to index the composite FSIQ score). The Box M test was not significant, indicating that variances and covariances among dependent variables were the same across all levels of the factor, assumptions of homoscedasticity were not violated, and the results of the discriminant function analysis can be reliably interpreted.

The Wilk's lambda was significant $\Lambda=.81$, $\chi^2(5, N=65)=12.48$, $p=.03$, indicating that overall, the predictors differentiated among the converted and non-converted prodromal participants. When the model was run with age and medications included, the significant, direction and magnitude did not change. Table 4 presents the within-group correlations between the predictors and the discriminant functions as well as the standardized weights. These coefficients indicate that the upper-body movement scores have the strongest relationship with the discriminant function, while the neuropsychological test scores each show a strong negative relationship. The converted group ($M=.86$) had the highest mean on the discriminant function scores, while the non-converted group showed the lowest ($M=-.25$). Notably, the discriminant function correctly classified 72.3% (76.0% not converted, 60.0% converted) of the individuals in our sample as converted vs. non-converted. The test characteristic included: sensitivity=76.0%, specificity=60.0%, positive predictive value (PPV)=86.3%, and negative predictive value (NPV)=43.0%. Further, while the combined model (neurocognitive domain and movement abnormality variable les) successfully classified 72.3% of cases, the independent models such as neurocognitive variables alone (57.4%) and movement variables alone (65.5%) classified fewer cases.

Finally, to assess how well this classification program could predict a new sample, we estimated the percent of participants accurately classified using the leave-one-out cross validation technique (57). Results indicated that this classification procedure (including both movement-related and neurocognitive markers) would accurately classify 69.2% (74.0% not converted, 53.3% converted) of cases in a new prodromal sample.

Discussion

To our knowledge, this is the largest study to examine movement abnormalities in a prodromal population, and the first to explore relationships between these movements and neurocognition. As predicted, there were significant negative associations between hyperkinetic movements and neuropsychological performance, and the combined sets of movement and neurocognitive markers showed good discriminative power when classifying those high-risk participants most in need of intervention. Taken together, results suggest that these domains share common neurological underpinnings.

This pattern is consistent with a "two hit" model, suggesting that a disruption of neurodevelopment increases the risk for developing schizophrenia (58-59). As movement abnormalities are observable during early childhood in individuals who later go on to develop schizophrenia (23), they are thought to be indicative of a constitutional vulnerability (60). Specifically, hyperkinetic movements are believed to reflect abnormal striatal dopamine activity, resulting in reduced basal ganglia output to the thalamus and disinhibition of the thalamocortical neurons (16). Indeed, investigators observed that signs of neuromotor impairment are associated with significant grey matter reductions in subcortical structures comprising the basal ganglia (61). Because heightened striatal DA also characterizes

schizophrenia (62), and abnormal movements have been found to increase in severity during prodromal adolescence (63), it is possible that hyperkinetic movements reflect an interaction between early basal ganglia dysfunction and later neural maturational processes (27).

Present results support the idea that movement abnormalities and neurocognitive deficits in high-risk populations may be modulated to some degree by common underlying mechanisms. Notably, movement abnormalities were associated with deficits in several domains of neurocognitive function including verbal comprehension, perceptual organization, and based on these combined variables, the estimated FSIQ. Because the striatum serves as a connection point for pathways leading from the basal ganglia to the cortex (33), dysfunction in this region may contribute to irregular movement behaviors as well as an array of cognitive dysfunction ranging from processes primarily regulated by the striatum (e.g., processing novel stimuli, signal preparation for or initiation of behavioral responses), to those governed by the prefrontal cortex (64-65).

It should be noted that to date, there have only been a small number of studies that report relationships between cognition and movement in psychotic disorders. One possibility to consider is that a file door effect (where non significant findings are not published) may be contributing to the limited published support. Despite the limited extant direct support, there are several converging lines of research that do suggest such a relationship. For example, a study examining motor functioning abnormalities in a sample with schizotypal personality disorder, found that variable motor force was correlated with preservative responses on a card-sorting task (66). D'Reaux and colleagues (67) found that motor function (assessed via finger tapping) was strongly correlated with working memory performance in patients with schizophrenia. Further, researchers have also observed relationships between finger tapping and social cognition (68), as well as basal ganglia volumes (69). In a relevant cohort study, researchers reported that delays in infant motor development were associated with adult cognition in the domains of executive function, verbal learning, and spatial memory in patients who developed schizophrenia in adulthood (70). Finally, there is also evidence to suggest that oculomotor abnormalities (indicative of dysfunction in basal ganglia loops) are correlated with cognitive deficits in patients with schizophrenia (71).

As noted, discrete cortico-striato-pallido-thalamic circuits act as a powerful regulator of different aspects of neurocognitive function (18,32). Within these distinct circuits, DA moderates cognitive function, and altering of transmission could contribute to specific cognitive impairments (18,32). This is supported by recent evidence of an inverse relationship of cognitive functioning (namely, verbal fluency) and the rate of striatal F-dopa uptake among patients with schizophrenia symptoms (1). Researchers have also found that striatal D2 receptor density is associated with both immediate and delayed auditory memory (33). Lichter and Cummings (72) have noted that frontostriatal systems are involved in the integration of sensory and limbic phenomena, and play key roles in a number of functions underlying cognitive functioning such as motivation and goal selection for adaptive processes. Further, researchers have detailed how subcortical motor regions also play an important role in cognitive processes associated with prefrontal activity such as explicit and implicit category learning systems (73), attention/working memory (67) and social cognition (68).

It is noteworthy that only upper-body region movements were associated with neurocognitive deficits. Because of the distinct and segregated cortical-striatal-thalamic circuitry, researchers have argued that orofacial dyskinesias appear to constitute a distinct syndrome when compared to involuntary upper-body movements (74-76). Movement abnormalities in the facial region have been linked with the ventromedial area of the putamen, whereas such movements upper-body are associated with the dorsolateral sector and ventromedial area of the putamen (77).

Thus, the present findings suggest that these respective areas of the putamen may be affected in some individuals who develop psychosis.

Roughly 35% of high-risk participants convert to an Axis-I psychotic disorder in a two-year period (78-79). A major goal of prodromal research is to develop strategies that can enhance detection of those individuals at the highest risk for conversion. While previous studies have examined specific biological markers and compared these to converters and non-converters, few have had the statistical power necessary to test models combining these markers. The results from the present collaborative study indicate that elevated upper-body region movements, and deficits in immediate, and delayed auditory memory, and FSIQ are significant defining factors of a group of high-risk participants who will eventually converted to Axis-I psychosis.

The present findings, suggesting that deficit immediate and delayed auditory memory and estimated FSIQ are significant discriminating factors between converting and non-converting high-risk participants, are consistent with a body of high-risk literature. For example, Simon and colleagues (14) observed deficits in verbal fluency and declarative verbal memory when comparing early stage prodromal and late stage prodromal individuals. In another relevant study, Lencz and colleagues (10) also observed those high-risk participants who converted over a one-year study period had significantly lower verbal memory scores than those prodromal patients who did not convert. Further, in a sizable study examining neuropsychological performance and conversion among a high-risk sample (n = 98), researchers observed that impairments in auditory memory were specific to the high-risk participants who converted (9).

Supplementary analyses suggested that cognitive and movement abnormality variables alone did not correctly classify as many individuals as when both sets of variables were entered in the combined discriminant function analysis. However, the increase in prediction associated with a combined index relative to each domain separately was relatively small and the lack of a significant increase supports a common neurological underpinning underlying both movement and neurocognitive dysfunction. These results support the notion that incorporating susceptibility markers into programs for early identification enhance detection of those individuals at highest risk for conversion to psychotic disorder. Within the context of published high-risk studies, the sample size and number of converters available for study is quite high. However, it should also be noted that in terms of statistical modeling, the number of converters was relatively small, and as a result, the presented predictive model is limited.

A limitation of this study involved the use of videotaped interviews as the sole venue for measuring movement abnormalities. While the method has yielded consistent and important results in past studies (54,58), the inability to measure lower-body movement represents a setback. However, it should be noted that previous examinations following movement abnormalities in schizophrenia-spectrum disorders have found that lower-body movements do not significantly distinguish high-risk individuals (80).

It is also interesting to consider that while the converted group performed below average on both cognitive measures of perceptual organization, movement abnormalities in the upper-body region were significantly associated with the Block Design, but not the Matrix Reasoning task. One potential reason for this apparent phenomenon is that the task-specific cognitive factors for Block Design are particularly associated with the aberrant mechanisms also thought to underlie movement abnormalities. For example, while both measures are reliable and valid measures of perceptual organization (51-52), the Block Design task holds several unique attributes in that it contains a visuoconstructive component, is timed, and is more abstract (48-49). Future studies examining the relationships between movement abnormalities and these

specific cognitive processes will be useful in clarifying this issue. It is also important to consider that because FSIQ estimate is in part contingent on these two measures, the magnitude between upper-body movement abnormalities and FSIQ at the EADP site (which used Block Design) is greater than the at the CAPPS site. As such, the present discriminative function may indeed be a conservative estimate of these potential markers; future studies utilizing FSIQ estimates based solely on Block Design are likely to have greater ability to classify converting from non-converting high-risk individuals.

Although medication was statistically controlled in the present analyses, and found not to be different between converting and non-converting participants, this does not entirely eliminate the potential confound of medication effects. Prescription of psychotropics is expected to be targeted to those with more severe behavioral dysfunction and, perhaps, concomitant movement abnormalities. Thus controlling for medication can affect the variance in ratings of disease progression and movements, thereby attenuating covariance between these two factors. However, it should also be noted that the increased use of psychotropic medication presents an opportunity to study a population less likely to meet the restrictive inclusion criteria of preventive trials, but more likely to represent individuals who are currently being seen in actual practice. Because of these constraints, the present results should be interpreted as preliminary, until advances in methodological design or significantly larger studies can lead to a supplemental analyses on medication-free proportions of the sample.

Acknowledgments

Financial Disclosures This research was supported by National Institute of Mental Health grant MH4062066 to Dr. Walker and by NIH Grants MH65079, MH066286, and P50 MH066286 to Dr. Cannon. V.A.M.'s time was supported by Grant MH14584-33. Additional support was provided by a gift to the UCLA Foundation by Garen and Shari Staglin. Dr. Cannon is a consultant for Rules-Based Medicine on diagnostic biomarkers for mental disorders.

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Table 1

Baseline Characteristics of Prodromal Sample

Demographic Variables	Converted	Not-Converted	Total
Gender			
Males	17	44	61
Females	07	22	29
Total	24	66	90
Age (yrs.) *	15.91(3.67)	15.48(2.70)	15.64(2.97)
Parental Education *	14.28(3.62)	13.38 (4.40)	13.62 (4.21)
Medication			
Stimulants	04	14	18
Antidepressants	08	26	34
Antipsychotics	05	08	13
Movement Abnormalities *			
Facial Region	3.75(2.65)	2.76(3.52)	3.04(3.32)
Upper-body Region	3.95(3.07)	2.28(2.15)	2.74(2.52)
Neurocognition *			
Vocabulary	9.70(3.12)	11.18(3.24)	10.78(3.26)
Matrix Reasoning	8.35 (3.56)	10.17(3.14)	9.64(3.34)
Block Design	9.10(3.69)	9.35(3.49)	9.29(3.50)
Logical Memory I	7.69(3.34)	8.79(3.86)	8.54(3.75)
Logical Memory II	7.94(3.38)	9.33(3.90)	9.00(3.81)
FSIQ	97.54(16.26)	104.64(16.68)	102.74(16.78)

Note: Movement abnormality means reflect scores from the Dyskinesia Identification System (DISCUS); Neurocognition scores are scaled scores (mean = 10, SD = 3) with the exception of FSIQ which represents a composite score (mean = 100, SD =15).

* Mean (Standard Deviation).

Table 2

Symptom Progression of Prodromal Participants Over Three Annual Time Points

Prodromal Groups	Baseline	Year 1	Year 2
Non-Converted			
Positive	2.30(.91)	1.21(.70)	1.26(.62)
Negative	1.94(.99)	1.30(.99)	1.31(.99)
Total	1.93(.71)	1.21(.63)	1.26(.61)
Converted			
Positive	2.50(.95)	2.34(.91)	2.96(1.04)
Negative	2.41(1.32)	2.33(1.35)	2.60(1.35)
Total	2.25(.95)	2.14(.88)	2.60(.94)

Means and standard deviations for symptom scores (Structured Interview for Prodromal Symptoms) over the course of the study.

Table 3

Partial correlations between movement abnormalities and neurocognitive performance for participants with a prodromal syndrome.

Neurocognitive Domains	Facial Region Movements ^a	Upper-Body Region Movements ^a
General		
<u>Verbal Comprehension</u>		
Vocabulary ^a	-.01	-.28**
<u>Perceptual Organization</u>		
Block Design ^b	-.08	-.44**
Matrix Reasoning ^c	.16	.07
Memory		
<u>Immediate Auditory</u>		
Logical Memory I ^a	.14	-.25*
<u>Delayed Auditory</u>		
Logical Memory II ^a	.05	-.23*
Full Scale		
<u>FSIQ</u>		
Full Scale Intelligence ^d	.03	-.29**

Partial correlations control for age and Classes of medication (stimulant, antipsychotic, antidepressant).

** Note: $p < 0.01$

* $p < 0.05$;

† $p < 0.10$;

^a Movement abnormalities, and tests of Vocabulary, Logical Memory I and II were administered at combined sites (n = 90).

^b Block Design was administered at the Emory (EADP) site (n = 41).

^c Matrix Reasoning scores were derived from participants at the UCLA (CAPPS) site (n = 49).

^d Estimated Full Scale IQ (FSIQ) is a derived index based on performance on the Vocabulary and Matrix Reasoning subtest for the CAPPS site and the Vocabulary and Block Design subtests for the EADP site.

Table 4

Correlations of Predictor Variables with the Discriminant Function

Predictor	Correlation Coefficients with discriminant function
	Function 1
Movement Abnormality	
Facial	.16
Upper-body	.93
Neurocognition	
Logical Memory I	-.42
Logical Memory II.	-.34
FSIQ	-.26