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Abnormal movements are associated with poor psychosocial functioning in adolescents at high risk for psychosis

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Abstract

The period immediately preceding the onset of overt psychosis is characterized by a range of symptoms and behaviors including emerging attenuated psychosis, spontaneous movement abnormalities, and a broad decline in role and social functioning. Recent evidence suggests that basal ganglia dysfunction, which is implicated in the development of psychotic symptomatology, may manifest in the form of both movement abnormalities and deficits in processes integral to psychosocial functioning. However, little is known about the relationship between abnormal movement function and the observed psychosocial deficits. In the present study, 40 clinical high-risk participants meeting criteria for a prodromal syndrome were assessed for movement abnormalities and global role and social functioning at baseline. Role and social functioning was then followed up after a one-year period. At baseline, the severity of spontaneous movement abnormalities was associated with poor role functioning. Further, when controlling for baseline functioning, movement abnormalities predicted changes in social functioning one-year later, with a trend in the same direction for role functioning. Exploratory analyses also indicated that elevated baseline movement abnormalities distinguished those at-risk participants who eventually converted to psychosis and that this was also the case for poorer baseline global role functioning (at the trend level). Taken together, the results suggest that movement abnormalities are closely associated with deficits in psychosocial functioning. Elucidating the link between these phenomena may serve to refine etiological models of frontal-subcortical circuit dysfunction and inform understanding of functioning and outcome of these affected youth.

Keywords

Psychosis; Prodrome; Social Functioning; Role Functioning; Dyskinesia

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1. Introduction

The prodromal period immediately preceding onset of psychosis is of interest both as a window for investigating processes involved in disease onset and also as a viable point of intervention. This stage is characterized by the emergence of subthreshold psychotic symptoms (Niendam et al., 2007) as well as substantial impairment in psychosocial functioning (Ballon et al., 2007; Cornblatt et al., 2007). At the same time other signs of progressive neural dysfunction are apparent, including an exacerbation in neuromotor abnormalities (Mittal et al., 2008). Because a drop in functioning often precedes the onset of psychosis (Melle et al., 2005), and spontaneous movement abnormalities become progressively more severe during the prodromal period (Mittal et al., 2007b), it is possible that these two phenomena may reflect a common pathogenesis. Indeed, brain mechanisms underlying movement (i.e., basal ganglia circuits) (Alexander et al., 1990) also govern higher-order functions integral to psychosocial functioning such as cognitive function, decision making, goal planning, and motivation (Chen et al., 2005; Graybiel, 1997; Lichter and Cummings, 2001; Mittal et al., 2010b; Robbins, 1990).

For high-risk individuals, daily role and social functioning are strongly associated with overall quality of life (Addington and Addington, 2008). Further, because greater psychosocial impairment during the prodromal phase of schizophrenia is linked to more severe social and occupational dysfunction later on (Addington and Addington, 2005), functional impairment occurring in adolescence may set the stage for more a severe illness course in the future. Decline in functioning also serves as a significant source of distress among high-risk adolescents. For example, Lencz and colleagues (2004) found changes in functioning were some of the most commonly reported concerns among at-risk participants and their families.

Social and role functioning deficits may also reflect key neural mechanisms underlying the pathophysiology of psychotic disorders. Indeed, a recent study of at-risk adolescents noted an integral link between white matter development and functional outcome over time, suggesting that psychosocial deficits reflect a pervasive neurologically based genesis (Karlsgodt et al., 2009). Consistent with this notion, it has been suggested that psychosocial deficits may reflect a core constitutional vulnerability to schizophrenia (Cornblatt et al., 2003). Further, impairments in social functioning have also been shown to uniquely contribute to the prediction of risk for conversion to psychosis in high-risk individuals (Cannon et al., 2008).

Archival studies have found that neuromotor abnormalities are evident as early as infancy in prepsychotic individuals (Rosso et al., 2000; Walker et al., 1994), suggesting that movement abnormalities may also represent a core underlying vulnerability for psychosis. Recent longitudinal studies have observed that spontaneous dyskinetic movements (e.g., writhing or flinging movements of the limbs, fingers or face) are elevated in schizotypal adolescents when compared with healthy and psychiatric controls (Mittal et al., 2007a). Similar to the pattern of functional deterioration in high-risk adolescents noted above, neuromotor abnormalities have been found to be associated with a broad range of attenuated psychotic symptoms (Mittal et al., 2008), and predictive of eventual conversion to psychosis (Mittal and Walker, 2007). This is particularly noteworthy when considering that dyskinetic movements are believed to reflect abnormal striatal dopamine (DA) activity, a mechanism also proposed to contribute to symptoms and characteristic deficits in psychosis (Kestler et al., 2001).

To date, there have been no empirical studies of the relationship between neuromotor dysfunction and psychosocial function. In the present study, we recruited a sample of

clinical high-risk (CHR) participants who were assessed for global role/social functioning and dyskinesias and then followed clinically over a one-year period. This design was implemented to test the hypothesis that because neuromotor dysfunction reflects basal ganglia dysfunction, and this same system modulates domains integral to psychosocial functioning (e.g., cognitive function, decision making, goal planning, motivation) (Chen et al., 2005; Graybiel, 1997, 2000; Mittal et al., 2010b), baseline movement abnormalities will be associated with concurrent deficits in social and role functioning. Further, it was predicted that neuromotor dysfunction at baseline will predict changes in role and social functioning over the one-year follow-up period.

2. Method

2.1 Recruitment

Participants were recruited for an ongoing longitudinal prospective study of adolescents and young adults at high-risk for developing a psychotic disorder. Recruitment was conducted through psychoeducational talks given to healthcare clinics and a website describing prodromal symptoms in layperson terminology. Of the participants screened for the program, 28% were referred by local school districts, 25% came from outpatient clinical settings, 20% were referred by an adolescent inpatient unit, 13% were referred by psychologists and psychiatrists in private practice, 4% were recruited through advertisements, 1% were referred by the National Alliance for the Mentally Ill (NAMI), and 1% were referred by local community colleges (Meyer et al., 2005). Of the individuals who underwent screening, 27% were found to meet inclusion criteria for a prodromal syndrome), and of this group, 81% provided written assent or consent for participation in the full research program (Meyer et al., 2005). The present study includes those participants who were coded for movement abnormalities (participants were chosen for movement coding based on the presence of a high-quality video-taped interview), and had completed social and role functioning assessments. Taken together, this report presents data on 40 adolescent participants who underwent an initial assessment and a follow-up assessment one-year later (See Table 1).

Written assent/consent was obtained from all participants and a parent (in the case of minors), in accordance with the guidelines of the UCLA Biomedical Institutional Review Board. Exclusion criteria were: the presence of a neurological or tic disorder, psychotic disorder, mental retardation (FSIQ score< 70), substance abuse within the past 6 months, lifetime history of substance dependence, and/or history of significant head injury. The final sample was comprised of those who met diagnostic criteria for a prodromal risk syndrome (Miller et al., 2002; Miller et al., 1999), defined by attenuated positive symptoms and/or a decline in global functioning accompanying the presence of schizotypal personality disorder and/or a family history of psychotic disorder.

2.2 Controlling for Psychotropic Medications

Some participants were taking one or more psychotropic medications at baseline. This reflects national trends in that there has been a significant increase in the number adolescents with adjustment problems, who are prescribed treatment with psychotropic medications (Zito et al., 2003), particularly stimulants, antidepressants and, to a lesser extent, antipsychotics. In most cases in the present sample, psychotropic medications had been prescribed off-label by community-based pediatricians; the most common psychotropic medication was antidepressants (52.5%), followed by antipsychotics (27.5%) and stimulants (5%). It is important to note that in the present sample, results from spearman correlation analyses examining the relationships between total movement abnormalities and classes of stimulant, antidepressant, and antipsychotic medications did not approach statistical

significance. However, because these medications have been widely shown to affect movement (Jimenez-Jimenez et al., 1997; Leo, 1996; Senecky et al., 2002), a conservative approach was adopted and medication status was modeled statistically in each of the following analyses.

2.3 Procedures

2.4 Assessing Symptomatology

The Structured Interview for Prodromal Syndromes (SIPS) (Miller et al., 2002; Miller et al., 1999) was administered at baseline to gauge the presence and severity of at-risk symptoms. The SIPS contains an instrument, the Scale of Prodromal Symptoms (SOPS), which rates the severity of relevant symptoms including positive and negative symptoms along a 6-point scale ranging from absent to severe and psychotic.

To rule out a psychotic disorder diagnosis at baseline, the Structured Clinical Interview for Axis-I DSM-IV Disorders (SCID) (First et al., 1995) or the Kiddie Schedule for Affective Disorders and Schizophrenia (for ages 14 and under; K-SADS) (Kaufman et al., 1996) was also administered. Both measures have been demonstrated to have excellent inter-rater reliability in adolescent populations (Martin et al., 2000) and have been used in several previous studies focusing on adolescent populations with schizophrenia spectrum disorders (Howes et al., 2009).

2.5 Global Role and Social Functioning

Role and social functioning were assessed at both baseline and follow-up with the Global Functioning Scale: Role (GFS-R) (Niendam et al., 2006), and the Global Functioning Scale: Social (GFS-S) (Auther et al., 2006). These inventories provide ratings of functioning on two separate 10-point Likert scales. On the GFS-R, a score of 10 indicates “Superior Role Functioning” (e.g., Independently maintains superior functioning in demanding roles), whereas a low score of 1 reflects “Extreme Role Dysfunction” (e.g., On disability or equivalent non-independent status). A score of 10 on the GFS-S reflects “Superior Social/ Interpersonal Functioning” (e.g., Frequently seeks out others and has multiple satisfying interpersonal relationships including close and casual friends), whereas the lowest score of 1 indicates “Extreme Social Isolation” (e.g., No social or family member contact at all). The scales were designed for adolescents and have been found to be valid and reliable in assessing at-risk populations (Cornblatt et al., 2007).

2.6 Coding of Movement Abnormalities

Following the procedures used in prior reports from other distinct samples (Mittal et al., 2007a), movement behavior was coded from videotapes of subjects made during the initial clinical interviews (SIPS/SCID) at baseline. The participants were videotaped while seated in a chair facing a wall-mounted camera behind the interviewer. The chair was positioned so that the entire face and upper-body are visible on tape. The participant’s feet were not visible for a majority of the videos, and consequently, movement abnormalities involving the feet were omitted from the present series of analyses. A total of 45 minutes of each tape was coded (the same section of the interview was coded for each subject). To limit bias rating was conducted on muted videotapes. The Dyskinesia Identification System: Condensed User Scale (DISCUS) was used to code involuntary movements (Kalachnik and Sprague, 1993). The DISCUS is empirically derived and contains 15 items that are rated on a 0-4 (absent to severe) scale. This scale was chosen because it yields high inter-rater reliability (≥.90) for mentally ill subjects (Sprague et al., 1984). The total movement score consists of the sum of DISCUS items. Coding of the subject tapes for the present study

began after all pairs of raters had achieved a minimum inter-rater reliability of (intraclass correlation coefficients [ICCs]>.80) for coding, independently, for each movement type.

2.7 Data Analysis

Partial correlations, controlling for medication classes (i.e., antidepressant, stimulant, antipsychotic were dummy coded with 0/1) were conducted to examine associations between movement abnormities and measures of role and social functioning at baseline. Two series of hierarchical regression analyses were conducted with role and social functioning at follow-up assessment (time 2) as the dependent variables. For these regression equations, role or social functioning at the initial assessment (time 1) was entered in the first block. In the second block, psychotropic medications (antidepressant, antipsychotic, stimulant) were entered as covariates. The movement abnormality score was entered in the third block. With each respective analysis, the score for movement abnormalities observed during time 1 was entered as a predictor variable, and the magnitude of R^2 change was tested for significance. This analytic approach tests the hypothesis that movement abnormalities will predict a changes in role and social functioning at time 2, when controlling for social and role functioning, respectively, at time 1. Independent t-tests were conducted to examine relationships between baseline movement and functioning scores, and eventual conversion to psychosis.

3. Results

A total of 40 participants meeting criteria for a prodromal syndrome were included in the present study. The sample included 26 males (65%) and 14 females (35%) with a mean age of 16.7 (SD = 3.3). Kolmogorov-Smirnov tests revealed that distributions of movement variables met the assumptions for parametric statistics. A number of participants scored at moderate or more severe scores on DISCUS items indicating spontaneous dyskinesias including: tics (2.5%), grimaces (10%), ocular/blinking (27.5%), chewing/lip smacking (22.5%), puckering/thrusting lower lip (35%), tongue thrusting (37.5%), and lateral tongue (5%), retrocollis/torticollis (7.5%), shoulder/hip torsion (25%), athetoid/myokymic finger-wrist-arm (10%), and pill-rolling (25%).

3.1 Associations

At baseline, elevated dyskinetic movements were associated with more impaired role functioning (r=−.29, p≤.05). However, the relationship between social functioning and neuromotor dysfunction at baseline was not significant (r=.09, *N.S.;* see Table 2).

3.2 Dyskinesias Predict Changes in Psychosocial Functioning

For global role functioning, the average change for the sample was +/− 1.45 points (SD=1.39) over one year. For global social functioning, the average change for the sample over the one-year period was +/− 1.37 points (SD=1.05). To determine if movement abnormalities shown at baseline predicted changes in psychosocial functioning, hierarchical regression analyses were conducted using global role and social functioning at follow-up assessment (time 2) as the dependent variables. As shown in Table 3, movement abnormalities accounted for a significant proportion of the variance in social functioning one year later. Specifically, in predicting global social functioning, there was a significant increment in R^2 for movement abnormalities (R^2change=.10, Beta=−.33, p≤.01). In the analysis predicting longitudinal change in role functioning, there was a trend in the same direction (R^2change=.05, Beta=−.23, p=.07). The negative direction of the betas for both analyses suggests that elevated movements at baseline predicted poorer functioning at the one-year follow-up. Results from the second block from both analyses indicate that

medication status did not affect the relationship between movement abnormalities and measures of role (p=.71) or social (p=.67) functioning.

3.3 Conversion to Psychosis

Supplementary analyses were conducted to determine any potential relationships between the key variables, and conversion to psychosis. Of the 40 participants, 13 (32.5%) converted to psychosis during their participation in the larger study. An independent t-test [$t(38) = -1.72$, $p \leq .05$] indicated that those who converted to psychosis (mean=8.15; SD=3.13) showed greater baseline movement abnormalities when compared to those who did not convert (mean=6.25; SD=3.31). Although there was no detected group difference for baseline global social functioning and conversion, there was a trend to suggest a group difference between global role functioning, [$t(38)=1.28$, $p=.10$], where those who converted (mean=4.77; SD=2.01) showed significantly lower functioning scores than those who did not convert (mean=5.56, SD=1.71).

4. Discussion

To our knowledge, this is the first report to examine the relationship between neuromotor dysfunction and psychosocial functioning in individuals at clinical high-risk for psychosis. Previous studies using a different high-risk sample have observed that at-risk adolescents show elevated dyskinetic movements when compared to healthy and psychiatric controls (Mittal et al., 2008; Mittal et al., 2007b). The present investigation builds upon these results, finding that dyskinesias are associated with impairment in psychosocial functioning and also predictive of a domain specific changes one-year later. Taken together, these findings suggest that pathological processes underlying motor dysfunction may also contribute to the pervasive declines in role and social functioning characteristic of this population.

Both prospective high-risk studies (Dworkin et al., 1994; Hans et al., 2000) and larger birth cohort investigations (Done et al., 1994; Jones et al., 1994) have indicated that early social difficulties are evident in preschizophrenic individuals as early as age seven. Further, it is of interest that the progression of functioning deficits appears to follow what would predict in a two-hit model (Mednick et al., 1998). Specifically, although the deficits are present in childhood, they become progressively worse prior to the onset of schizophrenia, potentially reflecting an underlying vulnerability interacting with maturational processes and environmental stressors. During adolescence, a time characterized by tumultuous environmental stressors and marked neuroendocrine development, these deficits become more severe in those who go on to develop psychosis (Cannon et al., 2008; Yung et al., 2004). In line with these findings, it is also clear that functional decline in clinically at-risk youth is intimately tied with the progression of illness (Yung et al., 2004). Finally, it is noteworthy that functioning appears to be more tied to negative symptoms and other core features such as cognition (Niendam et al., 2007), but not to fluctuations in acute symptoms or medication status (Green et al., 2004). Taken together, these results suggest that psychosocial functioning is reflective of a core underlying pathology.

Results of the present study indicate that elevated dyskinetic movements are associated with deficits in psychosocial functioning, and replicate findings that the presence of baseline movement abnormalities significantly distinguishes those high-risk patients who will eventually convert to psychosis (Mittal and Walker, 2007). Because the striatum serves as a connection point for pathways leading from the basal ganglia to the cortex (Alexander et al., 1990; Nieoullon, 2002), dysfunction in this region may contribute to irregularities in movement behaviors (subsumed by the motor circuit) (Mittal et al., 2010a), as well as disruption in a host of processes integral to psychosocial functioning, ranging from those primarily regulated by the striatum (e.g., processing novel stimuli, initiation of behavioral

responses), to those governed by the prefrontal cortex (e.g., decision making, planning complex cognitive behaviors, moderating correct social behavior) (Clatworthy et al., 2009; Muller et al., 2000). In support of this notion, Lichter and Cummings (2001) have noted that fronto-striatal systems are involved in the integration of sensory and limbic phenomena, and play key roles in both neuromotor processes and psychosocial functioning, (e.g., motivation and goal selection).

The idea of a basal ganglia impairment underlying both movement and role/social functioning is also supported by a birth cohort study which found that delays in infant motor development were associated with poorer adult cognition in the domains of executive function, verbal learning, and spatial memory in patients who developed schizophrenia in adulthood (Murray et al., 2006). In another important study, Schiffman and colleagues (2004) observed a sample of school-age children interacting at lunchtime, many of whom had a parent with schizophrenia. When the authors analyzed the adult psychiatric outcomes for the children, it was found that those who developed schizophrenia as adults evidenced greater social and neuromotor deficits in childhood than those who did not go on to develop a psychotic disorder (Schiffman et al., 2004).

The present findings also suggest that among a group of adolescents at high-risk for developing psychotic disorders, current abnormalities in movement are a prognostic indicator of later course of social functioning and show a strong trend in the same direction for role functioning. Support for this finding comes from a study conducted by Nuechterlein and colleagues (2008), who observed motor deficits in a dual interference task predicted poor occupational outcome in a population of patients with first-onset schizophrenia. It is also interesting that we found evidence to suggest predictive relationships between movement and both longitudinal social and role functioning (albeit at the trend level for role functioning), but that there was not a significant correlation between movement and social functioning at baseline. One possibility to consider is that early basal ganglia dysfunction may impact core aspects underlying more basic role functioning, but also herald more widespread behavioral dysfunction, affecting global social functioning as time progresses. Future research aimed at examining underlying components of social and role functioning, and the relationship of these constructs with neuromotor dysfunction is necessary to untie this complex question.

A limitation of this study involves 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 (Schiffman et al., 2004), the inability to measure lower-body movement is a limitation. 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 youth (Mittal et al., 2007b). Another limitation relates to the modest sized sample; replication with larger samples from multisite collaboration efforts will help to elucidate subtle brain-behavior patterns among at-risk youth. A final limitation relates to the unavoidable use of psychotropic medication in naturalistic designs. Although medication was statistically controlled in the present analyses, and not found to affect the relationship between movement and psychosocial function, 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. Because of these constraints, the present results should be interpreted as preliminary, until larger studies can provide a supplemental analysis on high-risk youth who are medication-free in larger proportions of the sample. Taken together, these findings highlight the need to further understand etiologically factors

underlying psychosocial functioning, which may be an important target for intervention, particularly during a developmental period when social and role functioning behaviors are becoming increasingly central to ones' identity.

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Table 1

Baseline Characteristics of High-risk Sample

Gender	
Males	26(65%)
Females	14(35%)
Total	40
Age (yrs.)	16.67(3.29)
Parental Education	14.55(3.06)
FSIQ [a]	103.73(14.39)
Medication	
Stimulants	02(5%)
Antidepressants	21(52.5%)
Antipsychotics	11(27.5%)
Movement Abnormalities [b]	6.88(3.34)
Psychosocial Function [c]	
GFS-S	5.73(1.69)
GFS-R	5.30(1.82)
Prodromal Symptoms [d]	
Positive	2.57(.83)
Negative	2.23(1.15)

Note: In the present study, 30 participants were taking one or more medications at baseline, and 10 were medication free.

[a] Full Scale IQ (FSIQ) estimate is a derived index based on 2-subtest Wechsler Abbreviated Scale for Intelligence (WASI; Vocabulary and Matrix Reasoning subtests).

[b] Movement symptoms reflect mean scores from the Dyskinesia Identification System (DISCUS)

[c] Psychosocial functioning scores derived from GSF/GRF scales

[d] Means and standard deviations for SIPS symptom scores at baseline.

Table 2

Association between Movement Abnormality and Role and Social Functioning

	Global Role Functioning	Global Social Functioning
Movement Abnormalities	−.29*	.09

Note; presented statistics are partial correlations controlling for psychotropic medication.

** p<0.01;

* p<0.05.

Table 3

Results of regression analyses of the relation of movement abnormality at initial assessment with global social and role functioning at one year follow-up assessment

Predictor	Block I (GSF/GRF Time 1)					Block II (Psychotripic Medication[a])					Block III				
	R^2	df	F	p	β	R^2 change	df	F	p	β	R^2 change	df	F	p	β
Global Social Functioning															
Baseline Movements	.25	(1,38)	12.73	.01**	.50	.03	(3,35)	.51	.67	*NS*	.10	(1,34)	5.75	.01**	−.33
Global Role Functioning															
Baseline Movements	.22	(1,38)	10.60	.01**	.47	.03	(3,35)	.45	.71	*NS*	.05	(1,34)	4.03	.07†	−.23

** p<0.01;

† p< 0.10 (Statistical Trend).

[a] Psychotropic medication class included stimulants, antidepressant, and antipsychotics.