Schizophrenia Research 159 (2014) 263–266

Contents lists available at ScienceDirect

Schizophrenia Research

journal homepage: www.elsevier.com/locate/schres

# Movement abnormalities predict transitioning to psychosis in individuals at clinical high risk for psychosis

Dallas A. Callaway [a,*], Diana O. Perkins [b], Scott W. Woods [c], Lu Liu [a], Jean Addington [a]

[a] Mathison Centre for Mental Health Research & Education, University of Calgary, Calgary, Alberta, Canada
[b] Department of Psychiatry, University of North Carolina, Chapel Hill, NC, USA
[c] Department of Psychiatry, Yale University, New Haven, CT, USA

ARTICLE INFO

*Article history:*
Received 6 August 2014
Received in revised form 18 September 2014
Accepted 21 September 2014
Available online 11 October 2014

*Keywords:*
Psychosis
Schizophrenia
Dyskinesia
Movement abnormality
Conversion
Prodromal

ABSTRACT

Improving upon the predictive validity of determining the transition from high risk to actual psychosis is a primary aim of early intervention research. Previous research has suggested that premorbid spontaneous dyskinesias may be one possible predictor. In this study, dyskinetic movements were assessed with the Abnormal Involuntary Movement Scale (AIMS) at baseline of a longitudinal study of 148 individuals at clinical high risk (CHR) of developing psychosis. Twenty-eight individuals transitioned to a psychotic disorder over the course of the study. Group comparisons between transitioned and non-transitioned individuals indicated that, relative to those that were not observed to transition, participants that developed a psychotic disorder exhibited greater spontaneous dyskinesias at baseline. Moreover, increased dyskinetic movements at baseline resulted in a more than two-fold increase in odds of developing a psychosis for each point increase in AIMS scale score. These findings suggest that individuals with greater premorbid dyskinetic movements may comprise a subset of CHR individuals at inordinate risk to decompensate into psychosis. Future work should employ assessments of spontaneous dyskinesias by instrumentation (e.g., electromyography) and look to ascertain whether specific dyskinesias (e.g., dystonia) or dyskinesias of specific body regions are associated with transitioning to psychosis.


## 1. Introduction

Within the high risk literature, there is a major focus on identifying predictors of the transition to psychosis. Current estimates specify that, among individuals meeting formal operationalized criteria (e.g., Yung et al., 2005; McGlashan et al., 2010) for being at clinical high risk to develop psychosis (CHR), 36% will go on to develop a full-blown psychotic disorder within three years (Fusar-Poli et al., 2012). As part of this effort, premorbid movement abnormalities – namely hyperkinetic movements such as non-drug induced choreoathetoid and ballistic, dystonic, and stereotypic movements – which are collectively referred to as 'spontaneous dyskinesias' have been suggested as potential predictors of psychotic transition. This is largely due to the presence of these behaviors among youth displaying other signs of psychosis-risk (MacManus et al., 2012), the prevalence of these symptoms among CHR individuals (Mittal et al., 2007), evidence from prospective and follow-back studies of motor abnormalities in those who go on to develop psychosis (Rosso et al., 2000; Schiffman et al., 2004; Dickson et al., 2012), and studies in which medication-free individuals with schizophrenia and other psychotic disorders exhibit dyskinetic movements across stages of illness (Whitty et al., 2009). The overlap between the neural substrate thought to underlie both dyskinesias and psychotic symptoms (Walker, 1994) provides further support for dyskinesias as potential predictors of psychosis onset. In particular, and although not definitive, there is evidence that dopaminergic pathways within the striatum including dopamine neurons projecting from the ventral tegmental area to the nucleus accumbens and caudate nucleus as well as cortico-striato-pallido-thalamic pathways more generally are thought to give rise to both dyskinetic movements and psychotic symptomatology (e.g., Walker et al., 1996; DeLong and Wichmann, 2007; Mittal et al., 2008).

Furthermore, Mittal and Walker (2007) evaluated dyskinetic movements as predictors of transition to psychosis within a CHR sample. This study found that dyskinesias of the face and upper body were associated with increased odds of developing a psychotic disorder. To our knowledge, the work by Mittal and Walker represents the only investigation of premorbid movement abnormalities as predictors of transition to psychosis within a CHR sample. Unfortunately, the prospect of confounding pharmacotherapy (i.e., drug-induced movement disorders) within their sample as well as the small subset of participants who transitioned to psychosis ($n = 10$) limits the extent to which the

* Corresponding author at: Mathison Centre for Mental Health Research & Education, University of Calgary, 1D63 TRW Building, 3280 Hospital Drive NW, Calgary, Alberta, Canada, T2N 4Z6. Tel.: +1 403 210 8740; fax: +1 403 210 9304.
*E-mail addresses:* dacallaw@ucalgary.ca (D.A. Callaway), diana_perkins@med.unc.edu (D.O. Perkins), scott.woods@yale.edu (S.W. Woods), luliu@ucalgary.ca (L. Liu), jmadding@ucalgary.ca (J. Addington).

http://dx.doi.org/10.1016/j.schres.2014.09.031
0920-9964/

results of this work may be generalized. The present investigation, therefore, sought to confirm whether premorbid dyskinetic movements predict transition to psychosis using a large, neuroleptic-naïve CHR sample obtained from a multisite longitudinal study.

## 2. Method

### 2.1. Participants

The sample consisted of 148 individuals (86 male, 62 female) at CHR for psychosis. All participants were part of a longitudinal NIMH-funded study entitled "Enhancing the Prospective Prediction of Psychosis" (PREDICT) that was conducted at the Universities of North Carolina at Chapel Hill, Toronto, and Yale to determine predictors of conversion to psychosis in individuals at CHR. All participants met the Criteria of Prodromal States (COPS) based on the Structured Interview for Psychosis-Risk Syndromes (SIPS; McGlashan et al., 2010). The sample had a mean age of 19.77 (4.60) years and the majority were Caucasian (77%). One hundred and forty-five (97.98%) met attenuated positive symptom syndrome (APSS) criteria, one (0.67%) met genetic risk and deterioration (GRD) criteria, and two (1.35%) met both APSS and GRD criteria. APSS includes the onset or worsening of non-psychotic level disturbances in thought content, thought processes, and/or perceptual abnormalities over the past year whereas GRD requires either a first degree relative with a psychotic disorder diagnosis or the participant having schizotypal personality disorder in conjunction with at least a 30% drop in functioning on the General Assessment of Functioning (GAF) scale over the past year.

Participants were excluded if they met criteria for any current or lifetime psychotic disorder, had a measured IQ < 70, had any history of central nervous system disorder or clinically significant head trauma, and if they had any current use of antipsychotic medication at baseline as well as if they received antipsychotic medication at any point during follow-up. Table 1 displays baseline psychotropic medication status for the sample.

### 2.2. Measures

Criteria for a psychosis-risk syndrome and for conversion to psychosis were determined using the SIPS and symptoms were assessed using the Scale of Psychosis-Risk Symptoms (SOPS; McGlashan et al., 2010). The Structured Interview for Axis I DSM-IV Disorders (SCID-I; First et al., 1995) was used to evaluate the presence of any Axis I disorder.

Dyskinetic movements were assessed using the Abnormal Involuntary Movement Scale (AIMS; Guy, 1976). The AIMS is a widely-used 10-item clinician-rated scale that evaluates aberrant movement in three body regions – the orofacial area (items 1–4; e.g., grimacing), extremities (items 5–6; e.g., athetoid movements of the hands), and trunk (item 7; e.g., shoulder rocking) – using a 0 (none/normal) to 4 (severe) scale. The AIMS includes three additional global evaluation items (8–10) that measure global severity of movements, incapacitation due to involuntary movements, and patient awareness of their dyskinesias, respectively. Apart from the individual item scores, the AIMS yields two scale scores: a total score including all 10 items and a non-global score which includes the seven behavior-based ratings of abnormal movements (items 1–7) and excludes the three global evaluation items (8–10).

**Table 1**
Psychotropic medications at baseline.

| Medication | Frequency (%)[a] | |
|---|---|---|
| | Transition to psychosis ($n = 28$) | Non-transition to psychosis ($n = 120$) |
| None | 22 (78.57%) | 74 (61.67%) |
| Sertraline | 3 (10.71%) | 9 (7.50%) |
| Fluoxetine | 1 (3.57%) | 5 (4.17%) |
| Citalopram | 1 (3.57%) | 4 (3.33%) |
| Escitalopram oxalate | 1 (3.57%) | 3 (2.50%) |
| Paroxetine | 0 | 1 (0.83%) |
| Fluvoxamine | 0 | 1 (0.83%) |
| Trazodone | 1 (3.57%) | 0 |
| Venlafaxine | 0 | 2 (1.67%) |
| Mirtazapine | 0 | 2 (1.67%) |
| Bupropion | 0 | 8 (6.67%) |
| Clonazepam | 1 (3.57%) | 4 (3.33%) |
| Lorazepam | 0 | 2 (1.67%) |
| Alprazolam | 0 | 1 (0.83%) |
| Methylphenidate | 0 | 2 (1.67%) |
| Phentermine | 0 | 1 (0.83%) |
| Atomoxetine | 0 | 1 (0.83%) |

[a] Reported frequencies do not distinguish monotherapy and polypharmacy treatments (e.g., one CHR individual that transitioned to psychosis received combined trazodone, sertraline, and clonazepam treatment).

### 2.3. Procedure

The SIPS, SCID-I, and AIMS were administered at in-person baseline sessions. Raters were experienced research clinicians who demonstrated adequate reliability at routine SIPS and SCID-I reliability checks. The AIMS was administered by the same research clinicians and were trained to requisite reliability on the measure by review of a training tape and supervision of the study psychiatrist at each site. Post-training inter-rater agreement on determining initial eligibility and subsequent transition status was excellent ($\kappa = 0.90$). A clinical psychologist or psychiatrist at each site conducted a comprehensive clinical assessment to determine if entry criteria were met. Inter-rater reliability for the SCID-I was determined at the start of the study and evaluated annually by 100% agreement on the diagnosis and at least 80% agreement for symptom presence. J.A. chaired weekly conference calls to review criteria for individuals admitted to the study. The study protocols and informed consents were reviewed and approved by the ethical review boards of all three study sites.

### 2.4. Statistical analyses

None of the AIMS dependent variables satisfied the normality assumption for parametric statistics and were non-transformable by way of square, square root, and log methods. Moreover, there was a preponderance of zero values within the presented sample. Accordingly, nonparametric Mann–Whitney *U* tests were used for group comparisons between transitioned and non-transitioned individuals and the $(x + 0.5)$ correction was applied to all AIMS variables (Yamamura, 1999). To quantify the predictive power of dyskinetic movements, continuous AIMS total and non-global scores were regressed on dichotomous psychosis transition status (non-transitioned vs. transitioned) in independent logistic regression analyses. Significant multicollinearity among several AIMS item scores precluded interpretation of multiple regression analyses. All analyses were conducted using SPSS (IBM Corp., 2012) and Stata/IC 10.0 software (StataCorp., 2007).

## 3. Results

Of the 148 CHR individuals, 28 (18.92%) made the transition to psychosis. Chi-square, *U*, and *t* tests indicated that the groups did not significantly differ in age ($p = .86$), sex ($p = .33$), ethnicity ($p = .42$), or educational attainment ($p = .70$). Further analyses indicated that there were no substantively significant demographic, clinical, or AIMS score difference between participants recruited through the three sites of this study and thus merger of the multisite data was justified.