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Increased postural sway predicts negative symptom progression in youth at ultrahigh risk for psychosis

Derek J. Dean [a,b,*], Jerillyn S. Kent [c,d], Jessica A. Bernard [a], Joseph M. Orr [e], Tina Gupta [a], Andrea Pelletier-Baldelli [a,b], Emily E. Carol [a], Vijay A. Mittal [a,b]

[a] Department of Psychology and Neuroscience, University of Colorado Boulder, Boulder, CO, USA
[b] Center for Neuroscience, University of Colorado Boulder, Boulder, CO, USA
[c] Department of Psychological and Brain Sciences, Indiana University, Bloomington, IN, USA
[d] Minneapolis VA Health Care System, Minneapolis, MN, USA
[e] Institute for Cognitive Science, University of Colorado Boulder, Boulder, CO, USA

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ABSTRACT

Impaired ability to maintain an upright posture may reflect impairment in the cerebellum, a critical structure for the fluid coordination of neural information, thought to be disrupted in psychosis. The current study utilized an instrumental measure of posture in individuals at ultrahigh risk (UHR) for psychosis ($n = 43$) and healthy controls ($n = 44$). Positive and negative symptoms were assessed twice over 12 months. Results showed that increased postural sway in the UHR group predicted changes in negative symptoms. This study provides an important prospective view on the relationship between cerebellar-sensitive behavior and integral symptoms, which until now has received limited biomarker research.

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1. Introduction

A cognitive dysmetria theory of psychosis (Andreasen et al., 1998), which notes impairments in cortico-cerebellar networks, may explain, in part, the heterogeneous symptoms seen in psychosis (Andreasen and Pierson, 2008; Picard et al., 2008). Consistent with this theory, patients with schizophrenia show increased postural sway (Marvel et al., 2004; Kent et al., 2012; Bernard and Mittal, 2014), thought to largely reflect cerebellar abnormalities. While previous cross-sectional research suggests that postural sway is impaired in youth at ultrahigh risk (UHR) for psychosis (Bernard et al., 2014), the potential relationship between postural dysfunction and the progression of attenuated negative and positive symptoms in UHR individuals is currently unknown.

Recent work suggests that impairment in posture may be linked to the pathophysiology of negative symptoms in schizophrenia (Docx et al., 2014). Examining behavioral markers of aberrant neurodevelopment tied to the progression of negative symptoms prior to psychosis may be helpful in understanding etiological conceptions and guide intervention efforts for symptoms that are not traditional targets of treatment (Pelletier and Mittal, 2013). In this study, participants diagnosed with a UHR syndrome, defined by moderate to severe but not psychotic 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 (Miller et al., 1999), as well as healthy controls underwent an instrumental test of postural sway and clinical assessments of negative and positive prodromal symptoms. Diagnostic status was followed for 12-months. We hypothesized that increased postural sway area (i.e., poorer postural control) would be specifically associated with elevated negative and not positive UHR symptoms, and that increased sway area at baseline would predict more severe negative symptoms after 12 months in the UHR group.

2. Materials and methods

2.1. Participants

A total of 87 adolescent UHR and healthy control participants were recruited to the University of Colorado Boulder's Adolescent Development and Preventive Treatment (ADAPT) research program (see Table 1). Exclusion criteria consisted of head injury, the presence of a neurological disorder, lifetime alcohol or substance dependence, and lifetime history of an Axis-I psychotic disorder. The presence of a psychotic disorder in

* Corresponding author at: Department of Psychology and Neuroscience, Center for Neuroscience, University of Colorado at Boulder, 345 UCB, Boulder, CO 80309-0345. Tel.: +1 303 492 4616.
E-mail address: derek.dean@colorado.edu (D.J. Dean).

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Table 1
Demographic characteristics and results of postural sway analysis for baseline and follow-up assessments. NS indicates not significant.

	Baseline				Follow-up			
	UHR	Control	Total	$p\leq$	UHR	Control	Total	$p\leq$
Age								
Mean (SD)	18.49 (1.86)	17.98 (2.63)	18.23 (2.29)	NS	19.43 (1.95)	19.09 (2.93)	19.27 (2.45)	NS
Gender								
Male	24	23	47		14	7	17	
Female	19	21	40		9	15	23	
Total	43	44	87	NS	23	22	45	NS
Education (years)								
Mean (SD)	12.41 (1.94)	12.06 (2.45)	12.23 (2.21)	NS	12.57 (1.72)	11.82 (2.50)	12.20 (2.15)	NS
Parent education								
Mean (SD)	15.96 (2.00)	15.72 (2.84)	15.84 (2.45)	NS	16.33 (2.09)	15.93 (2.37)	16.13 (2.21)	NS
Positive symptoms								
Mean (SD)	12.12 (3.99)	.43 (1.17)	6.14 (6.55)	.001	9.43 (6.96)	.23 (.61)	4.93 (6.79)	.001
Negative symptoms								
Mean (SD)	10.44 (.38)	.38 (.81)	5.36 (6.95)	.001	7.43 (.38)	.82 (1.82)	4.20 (5.92)	.001
BMI								
Mean (SD)	21.65 (3.44)	23.25 (4.97)	22.43 (4.30)	NS	–	–	–	–
Postural sway								
Mean (SD)	42.16 (49.77)	27.49 (19.83)	34.74 (38.22)	.05	–	–	–	–

a 1st degree relative was an exclusion criterion for controls. There were 7 UHR participants who reported taking antipsychotic medication at baseline ($n = 4$) and at follow-up ($n = 3$). The protocol and informed consent procedures were approved by the University of Colorado Boulder Institutional Review Board. (See Table 2.)

The ADAPT study is ongoing, and to date, 12 months have passed for 67 individuals who have completed a baseline assessment. Each of these individuals was invited back, and 45 participants agreed to return to complete clinical interviews. There were no baseline differences in age, gender, education, or parent education between those who did and did not return for follow-up. A subset of the current participants in this study also took part in a previous study examining cortico-cerebellar functional connectivity and postural sway (Bernard et al., 2014). This study focused on the neural correlates of postural dysfunction and did not include a longitudinal component.

2.2. Clinical interviews

The Structured Interview for Prodromal Syndromes (SIPS) (McGlashan et al., 2010) was administered to diagnose a UHR syndrome and track negative and positive symptom progression over time for the subgroup who returned for the 12-month clinical assessment. A total sum score for each domain is used as an indicator of the respective dimensions of symptomatology. The Structured Clinical Interview for Axis-I DSM-IV Disorders (First et al., 1995) was administered to rule out a psychotic disorder diagnosis at baseline. Interviews were conducted by trained advanced doctoral students, and inter-rater reliabilities exceeded the minimum study criterion of Kappa $\geq$ .80.

2.3. Postural sway area

Postural sway was assessed using an Advanced Mechanical Technology Incorporated Accusway force platform (Watertown, MA). Participants stood still while keeping their arms by their sides, their feet shoulder width apart, and their eyes focused on a fixed point on the wall directly across from them. Height and weight was recorded for calculations of participant's body mass index (BMI), which was used to assess group differences in body composition, and by proxy, physical fitness. The center of pressure (COP) was recorded for two minutes with a sample rate of 50 Hz. To isolate the low-frequency postural sway process in the recorded data, we applied a 9th order Butterworth filter with a 20 Hz cutoff frequency. COP and the 95% confidence interval of COP area were measured using principle component analysis (Oliveira et al., 1996).

2.4. Data analysis

Independent *t*-tests and chi-square tests were employed to examine group differences in continuous and categorical demographic variables, respectively. Based on previous work suggesting that UHR and schizophrenia patients show increased postural sway (Bernard et al., 2014), and studies linking cerebellar or posture dysfunction to negative symptoms (Mittal et al., 2014; Morrens et al., 2014), one-tailed independent *t*-tests were used to assess group differences in postural sway, and one tailed bivariate correlations were used to examine predicted relationships between larger sway area and increased negative symptoms within the UHR group. A series of 2 hierarchical regression analyses were conducted within the UHR group alone. Negative and positive symptoms at the follow-up assessment were used as the dependent variables. The respective symptom variable for the baseline assessment was entered in the first block (i.e., time 1 negative and positive symptom total). In the second block, COP area was entered as the predictor variable. With each analysis, the magnitude of R^2 change (ΔR^2) was tested for significance. This analytic approach tests the hypotheses that, while controlling for the variance explained by symptoms at baseline, increased COP area will predict significant changes in respective symptoms 12 months later.

3. Results

3.1. Participants

There were no significant differences between groups on demographic characteristics at baseline assessments including age $t(77.32) = 1.05$, education $t(85) = .74$, gender $\chi^2(1, n = 87) = .11$, parental education $t(85) = .47$, or BMI $t(69.02) = -1.70$ and at follow-up including age $t(43) = 1.03$, education $t(43) = 1.71$, gender $\chi^2(1, n = 45) = 3.81$, or parental education $t(43) = .59$. UHR participants were rated significantly higher than controls on both SIPS symptom domains at baseline and follow-up (see Table 1).