Schizophrenia Research 228 (2021) 319–321

Contents lists available at ScienceDirect

Schizophrenia Research

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

Letter to the Editor

Postural sway in first-degree relatives of individuals with schizophrenia

Motor abnormalities are well-documented in both schizophrenia spectrum disorders and in individuals at clinical or genetic risk for these disorders (Walther and Mittal, 2017). Like motor control generally, postural control relies on key structures including cerebellum, basal ganglia, and parietal and frontal regions (Surgent et al., 2019). Our group (Apthorp et al., 2019; Kent et al., 2012) and others (Marvel et al., 2004) have found increased postural sway in schizophrenia, as well as in schizotypal personality disorder (SPD) (Apthorp et al., 2019) which is characterized by attenuated features of schizophrenia. Moreover, individuals at ultra-high risk of psychosis have increased postural sway which correlated with both clinical symptoms and cerebellar connectivity (Bernard et al., 2014).

The present study tested the hypothesis that first-degree relatives of individuals with schizophrenia without history of psychosis would show impaired postural control by comparing postural sway data from 18 first-degree relatives of individuals with schizophrenia (REL; 9M/9F) and 27 neurotypical controls (CTR; 13M/14F). Potential participants were confirmed as relatives following their proband's schizophrenia or schizoaffective disorder diagnosis as ascertained either using the Structured Clinical Interview for DSM-IV Axis I, Patient Edition (SCID-I-I/P) (First et al., 2002) in our laboratory ($N = 14$), or from detailed information of family history obtained from the Family Interview for Genetic Studies (FIGS; $N = 2$) (Maxwell, 1992). All participants were administered the Wechsler Abbreviated Scale for Intelligence (WASI) (Ryan et al., 2003) and completed the Schizotypal Personality Questionnaire (SPQ; Raine, 1991) self-report scale.

Participants were asked to stand as still as possible with their arms resting comfortably at their sides on an AMTI Accusway (Watertown, MA) force platform, sampling at 200hz, with eyes open and eyes closed, and with feet (base) together or shoulder-width apart, which resulted in 4 separate conditions: Eyes Open, Open Base (EOOB); Eyes Open, Closed Base (EOCB); Eyes Closed, Open Base (ECOB); and Eyes Closed, Closed Base (ECCB). One-minute recordings of center of pressure (COP) were made for each condition for each participant.

The REL group was younger than CTR (M = 39.0 years old vs M = 41.5 years old, respectively; $p = 0.05$). REL had significantly higher SPQ scores compared to CTR (M = 23 vs M = 8, respectively; $p < 0.001$). WASI IQ was significantly lower in the REL group (M = 98 vs M = 111 for CTR; $p < 0.01$). None of these were correlated with sway scores, nor were they significant as covariates in the ANOVAs.

Sway area was larger overall for the REL group, $F(1,43) = 8.65$, $p = 0.005$. There was an Eyes x Group interaction, $F(1,43) = 9.50$, $p = 0.004$, where post-hoc tests indicated that the REL group had significantly increased sway area in the Eyes-Open condition ($p < 0.001$). There was also a Base x Group interaction, $F(1,43) = 4.61$, $p = 0.04$, where REL had larger sway area in the Base-Open condition ($p < 0.001$) and the Base-Closed condition ($p < 0.05$). These interactions appear to be driven by the larger difference between groups in the easier (Eyes- and Base-open) conditions, suggesting that the REL group had difficulty taking advantage of sensory information when it was available (see Fig. 1a).

The REL group had a significantly longer mean sway path overall, $F(1,43) = 4.07$, $p = 0.05$. An Eyes x Group interaction was marginally significant, $F(1,43) = 3.19$, $p = 0.08$, with post-hoc tests demonstrating REL had significantly increased sway path in the Eyes-Open condition only ($p = 0.008$), consistent with the suggestion that REL are less able to utilize available visual information, exemplified by the fact that controls experienced a more dramatic increase in sway area than the REL group in the Eyes-Closed conditions, whereas REL were significantly impaired even in the Eyes-Open conditions (see Fig. 1c).

To contextualize deficits in the REL group, we also present data from our previous work (Apthorp et al., 2019) in which 27 individuals with SPD and 27 with schizophrenia (SZ) were compared to the same 27 CTR individuals. Details of demographic and clinical information for these groups, as well as statistical analyses can be found in the original published report. In addition to differences compared to the CTR group, uncorrected comparisons of the REL group to the SZ and SPD groups revealed REL had both reduced IQ compared to the SPD group ($p < 0.05$) and lower SPQ scores (indicating fewer schizotypal symptoms) compared to the SZ group ($p < 0.001$).

As can be observed from Fig. 1b and d, sway in the REL group was intermediate to the CTR and the schizophrenia spectrum (SPD and SZ) groups, although still significantly impaired. REL, SPD, and SZ all had significantly increased sway area and path compared to CTR but were not statistically different from each other.

The present study found impaired postural sway in first-degree relatives of individuals with schizophrenia, suggesting that genetic risk contributes to motor impairments in SZ. This REL group excluded individuals who met diagnostic criteria for SPD; likewise, the SPD sample (presented in Fig. 1b & d) only included individuals without first-degree relatives with psychotic disorders. Because SPD is associated with deficits in postural sway [as shown here and previously published (Apthorp et al., 2019)], this suggests that in addition to the genetic factors the present findings implicate, environmental and neurodevelopmental factors also contribute to motor abnormalities in schizophrenia spectrum disorders. In addition, the finding that first-degree relatives are impaired on postural sway is consistent with our previous results establishing deficits in first-degree relatives on cerebellar-dependent delay eyeblink conditioning (Bolbecker et al., 2014), and with reports of increased neurological soft signs in this group (Feng et al., 2019; Schappi et al., 2018). Taken together with the critical contribution of the cerebellum to postural stability (Surgent et al., 2019), these findings suggest that functional cerebellar deficits may be risk markers for schizophrenia spectrum disorders.

A limitation of this study is the small sample size of the REL group. Future studies with a larger group of relatives could more definitively characterize postural control deficits in this population. In addition, a study of relatives both with and without SPD would be particularly

https://doi.org/10.1016/j.schres.2020.12.024

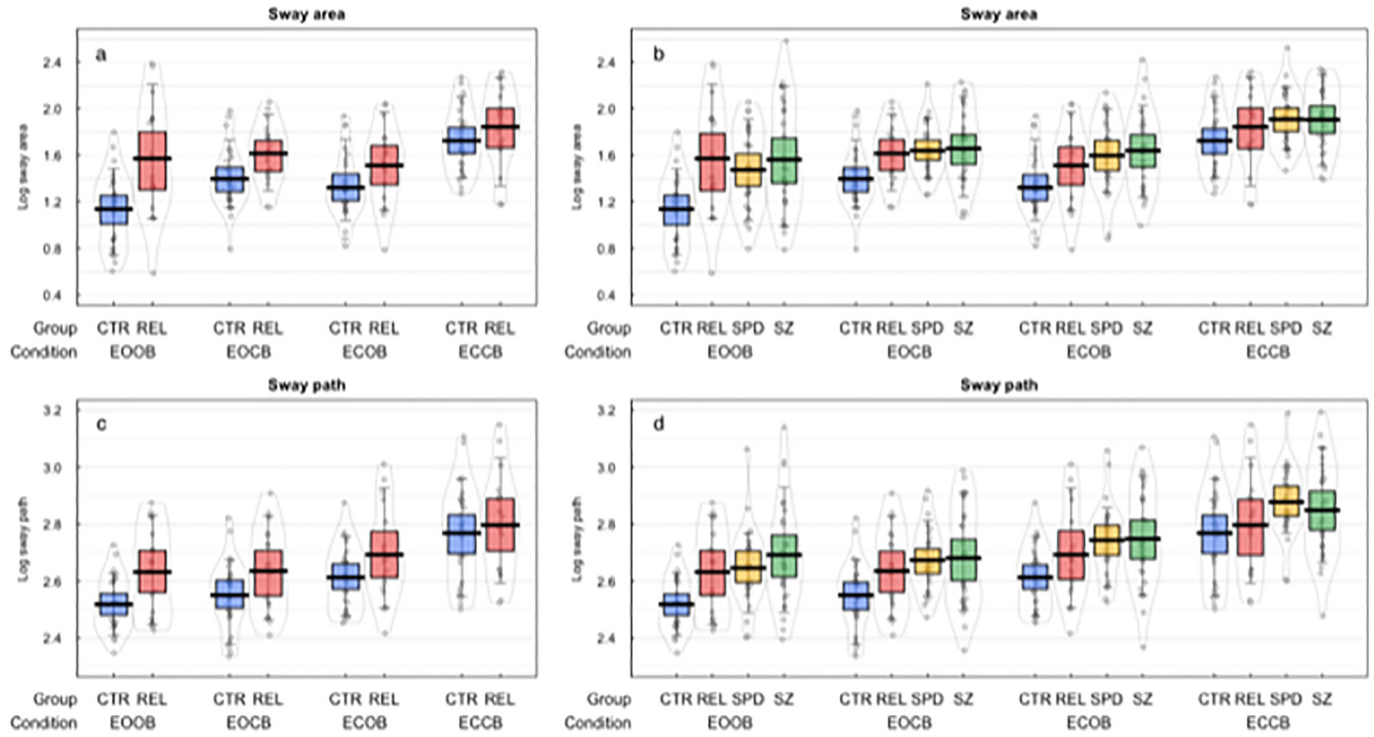

Fig. 1. Shows sway area and sway path for all 4 conditions: Eyes Open, Open Base (EOOB); Eyes Open, Closed Base (EOCB); Eyes Closed, Open Base (ECOB); and Eyes Closed, Closed Base (ECCB). Panel a depicts sway area for all CTR and REL participants for all sway conditions (log transformed to correct skewness). Means are shown by black horizontal bars. Individual scores are represented by black circles, slightly jittered for clarity; colored areas represent 95% Highest Density Intervals (HDIs), calculated using R's BEST (Bayesian Estimation Supersedes the *T*-Test) package, and vertical bars represent the 10th and 90th quantiles. The thin grey lines show the full densities for each group. Panel b includes the same data for CTR and REL, but also includes sway area data displayed in the same way for SPD and SZ groups for comparison. Panels c and d depicts sway path and are formatted in exactly the same way as panels a and b.

informative for understanding the genetic and clinical symptom contributions to SZ motor abnormalities. Finally, future studies should carefully dissociate the effects of shared environmental factors in the form of toxins, stress, poverty, abuse, etc. from genetic contributions to impaired motor coordination.

Funding

This study was supported by the National Institute of Mental Health (R01 MH074983B) and National Institute on Drug Abuse (R01 DA048012-02) to WPH.

The funding source for this research study had no role in the design, implementation, statistical analysis, interpretation of results, or presentation of findings.

CRediT authorship contribution statement

Amanda R. Bolbecker assisted with the study design, contributed to data processing and analysis, and wrote the manuscript. Deborah Apthorp was instrumental in data processing, creating figures depicting results, and the writing and editing of the manuscript. Lisa Bartolomeo assisted with editing the manuscript. Brian F. O'Donnell and William P. Hetrick contributed to study design, statistical analysis, and to writing and editing the manuscript.

Declaration of competing interest

The authors have declared that there are no conflicts of interest in relation to the subject of this study.

Acknowledgments

We wish to thank the patients and their families for participation as well as support from the staff and administration of Larue D. Carter Memorial Hospital.

References

Apthorp, D., Bolbecker, A.R., Bartolomeo, L.A., O'Donnell, B.F., Hetrick, W.P., 2019. Postural sway abnormalities in schizotypal personality disorder. Schizophr. Bull. 45 (3), 512–521.

Bernard, J.A., Dean, D.J., Kent, J.S., Orr, J.M., Pelletier-Baldelli, A., Lunsford-Avery, J.R., Gupta, T., Mittal, V.A., 2014. Cerebellar networks in individuals at ultra high-risk of psychosis: impact on postural sway and symptom severity. Hum. Brain Mapp. 35 (8), 4064–4078.

Bolbecker, A.R., Kent, J.S., Petersen, I.T., Klaunig, M.J., Forsyth, J.K., Howell, J.M., Westfall, D.R., O'Donnell, B.F., Hetrick, W.P., 2014. Impaired cerebellar-dependent eyeblink conditioning in first-degree relatives of individuals with schizophrenia. Schizophr. Bull. 40 (5), 1001–1010.

Feng, Y., Wang, Z., Lin, G., Qian, H., Gao, Z., Wang, X., Li, M., Hu, X., Li, Y., 2019. Neurological soft signs and neurocognitive deficits in remitted patients with schizophrenia, their first-degree unaffected relatives, and healthy controls. Eur. Arch. Psychiatry Clin. Neurosci. 270 (3), 383–391.

First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 2002. Structured Clinical Interview for DSM- IV-TR Axis I Disorders, Research Version, Patient Edition (SCID-I/P). York, New.

Kent, J.S., Hong, S.L., Bolbecker, A.R., Klaunig, M.J., Forsyth, J.K., O'Donnell, B.F., Hetrick, W.P., 2012. Motor deficits in schizophrenia quantified by nonlinear analysis of postural sway. PLoS One 7 (8), e41808.

Marvel, C.L., Schwartz, B.L., Rosse, R.B., 2004. A quantitative measure of postural sway deficits in schizophrenia. Schizophr. Res. 68 (2–3), 363–372.

Maxwell, M.E., 1992. Manual for the Family Interview for Genetic Studies (FIGS), Clinical Neurogeneticsbranch, Intramural Research Program. National Institute of Mental Health, Bethesda MD.

Raine, A., 1991. The SPQ. A scale for the assessment of schizotypal personality based on DSM-III-R criteria. Schizophr. Bull. 17 (4), 555–564.

Ryan, J.J., Carruthers, C.A., Miller, L.J., Souheaver, G.T., Gontkovsky, S.T., Zehr, M.D., 2003. Exploratory factor analysis of the Wechsler abbreviated scale of intelligence (WASI) in adult standardization and clinical samples. Appl. Neuropsychol. 10 (4), 252–256.

Schappi, L., Stegmayer, K., Viher, P.V., Walther, S., 2018. Distinct associations of motor domains in relatives of schizophrenia patients-different pathways to motor abnormalities in schizophrenia? Frontiers in psychiatry 9, 129.

Surgent, O.J., Dadalko, O.I., Pickett, K.A., Travers, B.G., 2019. Balance and the brain: a review of structural brain correlates of postural balance and balance training in humans. Gait Posture 71, 245–252.

Walther, S., Mittal, V.A., 2017. Motor system pathology in psychosis. Curr Psychiatry Rep 19 (12), 97.

Amanda R. Bolbecker
Psychological and Brain Sciences, Indiana University, USA
Larue D. Carter Memorial Hospital, Indianapolis, IN, USA
Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, USA

Deborah Apthorp
Department of Psychology, University of New England, Armidale, New South Wales, Australia

Lisa A. Bartolomeo
Psychological and Brain Sciences, Indiana University, USA
Larue D. Carter Memorial Hospital, Indianapolis, IN, USA

Brian F. O'Donnell
William P. Hetrick*
Psychological and Brain Sciences, Indiana University, USA
Larue D. Carter Memorial Hospital, Indianapolis, IN, USA
Department of Psychiatry, Indiana University School of Medicine, Indianapolis, IN, USA
*Corresponding author at: Dept. of Psychological and Brain Sciences, Indiana University, 1101 E. Tenth St., Bloomington, IN 47405, USA.
E-mail address: whetrick@indiana.edu.

12 December 2019
Available online xxxx