DOI:
10.1016/j.schres.2019.10.018

Document Version
Peer reviewed version

Adolescent trajectories of fine motor and coordination skills and risk for schizophrenia

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Abstract

Premorbid motor dysfunction is one of the earliest of developmental antecedents identified among individuals who develop schizophrenia in adulthood. However, among individuals with schizophrenia, premorbid motor dysfunction is not apparent at all stages of childhood development and may reduce with increasing age. Currently, little is known about the trajectories of motor development during adolescence among youth at-risk for the disorder. One hundred and one participants were assessed repeatedly, at approximately 24-month intervals (time 1, aged 9-12 years; time 2, 11-14 years; and time 3, 13-17 years), on the Purdue Pegboard assessment, comprising four subtests: Dominant Hand (DH), Non-Dominant Hand (NDH), Both Hands (BH), and Assembly. Fine motor and coordination skills development between ages 9-16 years was compared between youth characterized by a triad of developmental antecedents of schizophrenia (ASz, N=32); youth with at least one affected relative with schizophrenia/schizoaffective disorder (FHx; N=26); and typically developing youth without antecedents or family history (TD, N=43). Longitudinal mixed models for repeated measures indicated significant motor skills improvements with age in TD youth on the Assembly subtest only. Relative to TD youth, we found evidence for developmental *deficits* (i.e., dysfunction that emerged early and remained stable) among ASz youth on DH and BH subtests, and among FHx youth on the Assembly subtest. ASz youth were characterised by a developmental *delay* on the Assembly subtest (i.e., initial performance decrement in middle childhood that caught up with peers' performance during adolescence). These divergences from normative motor development may reflect differences in structural and functional neural correlates.

Keywords: psychosis, motor development, psychotic-like experiences, genetic high-risk, pegboard, antecedents

1. Introduction

The neurodevelopmental hypothesis of schizophrenia (Murray and Lewis, 1987; Weinberger, 1987) and the more recent integrated sociodevelopmental-cognitive model (Howes and Murray, 2014) implicate early brain development abnormalities in the aetiology of schizophrenia. Abnormal motor signs may be among the earliest observable indicators of neurological vulnerability to schizophrenia (Fish, 1987; van Harten et al., 2017). Several meta-analyses have evidenced delayed attainment of infant motor milestones and deficits in motor function during childhood among individuals who later develop schizophrenia (Dickson et al., 2012; Filatova et al., 2017). These premorbid abnormalities might signal early opportunities for targeting preventative intervention to children at risk for schizophrenia, but this relies on characterising the evolving neuropathology over time. Motor development is a dynamic process that improves rapidly during infancy and childhood followed by slower skill gains during adolescence (Davies and Rose, 2000), so that deviations in the pace of maturation of neuromotor circuits in children who later develop schizophrenia might be expected to fluctuate over the developmental stages (Walther and Strik, 2012).

In support of this hypothesis, an early study that rated motor skills from childhood home videos of adults with schizophrenia showed a reduction in motor dysfunction from 4-15 years (Walker et al., 1994). Further, a prospective birth cohort study demonstrated poorer performance on standardised tests of basic motor skills at 3, 5 and 9 years, but not 7 years, among individuals who later developed schizophrenia spectrum disorders (SSD) relative to cohort members who did not (Cannon et al., 2002). However, the variation in motor function with age apparent in these studies might reflect the measures of motor skills employed, with these potentially being differentially sensitive to detecting motor dysfunction over the broad

age range included in the former study, or reflecting the use of different measures of motor skills at each age in the latter.

Pegboard tasks are used widely in schizophrenia research because they are thought to measure functioning in brain areas implicated in psychosis-spectrum disorders (Rakhshan et al., 2016). Moreover, there is evidence to indicate that abnormal striatal dopamine activity, which is implicated in aetiology of schizophrenia (Howes and Murray, 2014), impacts on pegboard performance (Bohnen et al., 2007). In a prospective birth cohort (Meier et al., 2014), assessed fine motor performance at 13 years and again at 30 years using the Grooved Pegboard test, which requires finger-tip dexterity and motor coordination (i.e., the combined movements of both hands). They observed a decline in motor performance between the adolescent and adulthood assessments among individuals who later developed schizophrenia, relative to those who did not. These findings raise the possibility that the examination of fine motor skills development using repeated pegboard assessments with younger children might facilitate early identification of at-risk individuals.

Similar deficits in pegboard task performance from younger ages are evidenced in previous cross-sectional investigations of youth who are identified as at-risk for schizophrenia, either by virtue of having a family history of disorder or because they present with psychotic-like experiences (PLEs, an established risk marker for schizophrenia; Fisher et al., 2013). Among children aged 10-13 years with a positive family history, those who later developed a psychosis-spectrum disorder were significantly slower, and less likely to complete, a pegboard task relative to those who did not develop psychosis-spectrum disorder (Rakhshan et al., 2016). Similarly, children aged 11-13 years who reported PLEs at clinical interview had a significantly lower mean number of pins inserted on a pegboard task than children without PLEs (Blanchard et al., 2010).

In a previous study conducted by our team, we used repeated assessments from a battery of standardized neuropsychological measures over the age range 9-16 years to compare trajectories of cognitive development among two groups of youth at-risk for schizophrenia relative to typically developing youth (Dickson et al., 2018). Across different domains of cognitive functioning, we demonstrated that abnormal function in at-risk youth can emerge early in development and remain stable (developmental *deficit*), manifest in a progressive manner (developmental *lag*), or may be transitory and recuperate with increasing age (developmental *delay*). In the present study, we similarly employed longitudinal linear mixed models on repeated measures to examine developmental trajectories of fine motor and coordination skills, assessed by the Purdue Pegboard (Tiffin, 1948) from middle childhood to adolescence (9-16 years). We assessed these skills at approximately 24-month intervals following an initial assessment at 9-12 years of age among three groups of youth. The two at-risk groups were: (i) youth with a family history (FHx) schizophrenia (i.e., at least one first- or second-degree affected relative with schizophrenia or schizoaffective disorder), and (ii) youth characterized by a triad of replicated developmental antecedents of schizophrenia (ASz) which included PLEs, internalizing and/or externalizing psychopathology, and infant speech and/or motor development lags or problems (Laurens et al., 2007). These risk groups were compared with typically developing (TD) youth without antecedents or a family history. Based on evidence from the cross-sectional studies of motor performance among at-risk youth and prospective and retrospective longitudinal studies of individuals with schizophrenia, we hypothesised that, during adolescence, FHx and ASz children would display *deficits* or *delays* in their development of fine motor skills relative to TD youth.

2. Methods

2.1 Sample and recruitment

Children aged 9–12 years were recruited via two methods described in detail elsewhere (Laurens and Cullen, 2016). In brief, ASz and TD children were identified via questionnaire-based community screening conducted at primary schools in the Greater London, U.K. area. FHx children were identified via either the questionnaire screening in schools or by review of medical records of mental health service users within the South London and Maudsley National Health Foundation Service Foundation Trust to identify patients with a diagnosis of schizophrenia or schizoaffective disorder who had a relative aged between 9-12 years. Identified families were approached following liaison with the patient's care worker.

ASz criteria was defined as: (i) a child-reported "certainly-true" response on at least one of nine PLE items assessing hallucination- and delusion-like experiences (Laurens et al., 2012; Laurens et al., 2007); (ii) a score in the clinical range (approximately top tenth percentile on U.K. population norms) on the child-reported emotional symptoms scale or the caregiver-reported conduct problems, hyperactivity-inattention, or peer relationship problems scales of the Strengths and Difficulties Questionnaire (Goodman et al., 2000); and (iii) a caregiver-reported delay or abnormality of motor and/or speech development (Laurens et al., 2007). TD children were those who presented none of the three ASz criteria and who had no first-, second-, or third-degree relative with a schizophrenia spectrum disorder. Family history for all participants was confirmed via the Family Interview for Genetic Studies interview (FIGS) conducted with the child's primary caregiver (Maxwell, 1992).

Among 1343 children and caregivers who completed screening questionnaires, 9.5% of children (n=128) met ASz criteria, 22.5% (n=302) met criteria for the TD group, and 3.4% (n=35) of children were reported by caregivers to have a first- or second-degree relative with

schizophrenia or schizophrenia spectrum disorders. A further 36 FHx children were identified from patient medical records. We approached 182 families to participate in laboratory assessments (58 ASz, 43 FHx, 81 TD), among whom 43% refused participation (26 ASz, 16 FHx, 36 TD) and 104 consented to participate. None of the participants had a diagnosis of autism or Asperger's disorder, neurological disorder, or learning difficulties (general intelligence <70), or had ever taken antipsychotic medication.

Assessments of fine motor skills were completed with 101 children (32 ASz, 26 FHx [three of whom also met ASz criteria], and 43 TD). Among the 26 FHx children, 8 had a first-degree relative (parent) with schizophrenia, 2 had a first-degree relative (parent) with schizoaffective disorder, 2 had two second-degree relatives (grandparent or aunt/uncle) with schizophrenia, and 14 had one second-degree relative with schizophrenia (6 with a grandparent, 8 with an aunt/uncle). Table 1 presents comparisons of demographic characteristics of each group at the initial assessment.

2.1 Measures

Fine motor function. The Purdue Pegboard, a test of fine motor dexterity and bimanual coordination (Tiffin, 1948), was administered by a trained researcher using standardised instructions. The task required participants to: (1) put as many small metal pegs as possible into the pegboard in 30 seconds using their dominant hand (DH), non-dominant hand (NDH), and both hands (BH) simultaneously; and (2) assemble washers, collars, and pegs in a specific sequence (consisting of four separate pieces) within 60 seconds using both hands (Assembly). Dependent variables for analysis were the mean number of pins inserted in 30 seconds by the DH, NDH, and BH (averaged over three trials), and the average number of parts assembled in 60 seconds, averaged over three trials (Assembly). To capture age-related changes in motor skills, we used mean raw scores in statistical analyses.

Demographic covariates. Information on the child's sex and ethnicity was obtained due to their known association with motor development in typically developing children and children at-risk for schizophrenia (Burton et al., 2017; Kelly et al., 2006; Waber et al., 2012). Children's ethnicity was reported by caregivers according to the 2001 UK Census ethnic group categories during the FIGS interview, and recoded for analysis to white, black African/Caribbean, and other (Maxwell, 1992).

2.3 Procedure

Eligible children completed the pegboard task as part of a battery of neurocognitive assessments (and other biological and psychosocial measures), in up to three assessments conducted at approximately two-year intervals. These provided longitudinal data spanning the age range of 9-16 years (i.e., *time 1*, when children were aged 9-12 years; *time 2*, 11-14 years; and *time 3*, 13-16 years). At each assessment, children provided written assent, and caregivers provided written informed consent, for participation in the study. Ethical review of the study was provided by the Joint South London and Maudsley (SLaM) National Health Service (NHS) Foundation Trust and Institute of Psychiatry Research Ethics Committee.

2.4 Statistical analyses

Differences between groups on demographic variables were compared using univariate ANOVA, Fisher's exact test, and chi-square tests. To examine trajectories of fine motor skills development across adolescence, we conducted longitudinal linear mixed models for repeated measures in STATA 14 statistical software (StataCorp., 2015). Exact age at assessment was fitted as a continuous predictor and centred in analyses to 12.53 years (mean age of the sample at first assessment). Predictors in models were group (ASz vs. TD; FHx vs. TD), fixed linear effects of age, and interactions between linear age and group. For each of the four pegboard subtests, a random-intercept model was fitted using maximum likelihood

estimation, with random effect of participant used to account for correlations between measurements over time. All analyses incorporated sex, ethnicity, and practice effects (i.e., assessment wave) as covariates in statistical models to control their known association with motor functioning. As a sensitivity analysis, all analyses were repeated after excluding five ASz children who met the ASz inclusion criteria on the basis of a reported delay/problem in motor development, rather than speech delays/problems.

Results were interpreted in line with our previous work examining cognitive development among ASz and FHx compared to TD youth (Dickson et al., 2018), except that we did not assess *deterioration* in performance on pegboard subtests during adolescence due to the small number of participants with data available from three assessments (which precluded inclusion of quadratic terms in the longitudinal mixed models) (Curran et al., 2010). The resulting three developmental trajectories were determined as follows: one, a developmental *deficit* was indicated by statistically significant estimated between-group differences at 12.53 years of age (mean intercept value), but the absence of between-group differences in change per one year of age (rate of growth, or 'slope'), such that deficits emerged early and remained stable over time. Two, a significant negative slope value indicated a developmental *lag* (a slower rate of growth over development). Three, a significant positive slope value showing a faster rate of growth over development characterised developmental *delay*.

3. Results

As detailed in Table 1, groups did not differ on proportion male [X^2=1.48, (df=2), p=0.48], laterality [Fisher's Exact Test=1.41, p=0.51], number of assessments completed [Fisher's Exact Test=3.92, p=0.43], or age on day of assessment [F(2,98)=1.09, p=0.34], but did differ on ethnicity [X^2=20.32, (df=4), p=<0.001]. Proportionally more TD youth were of white ethnicity.

Insert Table 1 about here

The average number of pins inserted in each subtest at the first motor assessment is reported in Table 1. Table 2 summarises the parameter estimates of fixed effects for longitudinal models by group, adjusting for sex, ethnicity, and practice effects. The corresponding developmental trajectories for each motor measure are illustrated in Figure 1 (panels A-D). As indicated in Table 2, the sensitivity analysis (which excluded five children who met ASz inclusion criteria solely on the basis of a delay/problem in motor, rather than speech, development) indicated no significant change in results.

Among TD youth, significant slope estimates, which indicated growth in abilities between ages 9-16 years, were obtained only for the Assembly subtest. Relative to TD, ASz children demonstrated poorer performance on the DH and BH subtests at 12 years (intercept), but did not differ in slope values, thus indicating a stable developmental *deficit* up to 16 years (Figure 1, panels A & C). ASz and TD youth showed no differences in performance on the NDH subtest from 9-16 years (panel B). At 12 years (intercept), ASz compared to TD children had lower scores on the Assembly subtest, with a statistically significant positive linear slope value demonstrating that the early impairment was followed by improvements with age, thereby indicating a development *delay* (panel D). Conversely, FHx and TD youth showed no differences in performance at 12 years, or in rate of growth of development with age on DH, NDH and BH subtests. On the Assembly subtest, a significant difference in intercept value but not in slope relative to TD youth indicated a developmental *deficit* from 9-16 years among FHx children.

Insert Figure 1 and Table 2 about here

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4. Discussion

Using repeated pegboard assessments of fine motor and coordination skills from middle childhood to adolescence, the present study demonstrated aberrant trajectories of motor development among youth at-risk for schizophrenia relative to typically developing youth. The dysfunctions differed according to risk definition and type of motor skill. As hypothesised, we found evidence for developmental *deficits* (i.e., performance decrements that emerged early and remained stable) among ASz youth on DH and BH subtests, and among FHx youth on Assembly. These findings align with evidence from cross-sectional studies comparing pegboard performance between youth at-risk for schizophrenia aged 10-13 years and typically developing peers (Blanchard et al., 2010; Rakhshan et al., 2016), and imply that pegboard tasks may be sensitive to detecting the presence of motor abnormalities across a wider span of development (9-16 years). We further observed a developmental *delay* for ASz youth on the Assembly subtest (i.e., initial difficulties in middle childhood that lessened with age, such that motor performance caught up with that of peers during adolescence). We previously reported similar *delays* among ASz youth in some aspects of cognitive function implicated in schizophrenia, including measures of verbal and visual memory, and category fluency, a measure of executive function (Dickson et al., 2018). As human development is a dynamic process, different markers of 'risk' for schizophrenia might fluctuate in prominence during the course of development. The findings from the current study, along with our previous investigation of trajectories of cognitive development in this sample (Dickson et al., 2018), highlight the capacity of longitudinal methods that capture within- as well as between-individual differences to identify recuperation of function among at-risk youth during development that cross-sectional investigations may obscure.

Previous research suggests that performance of the dominant hand on a pegboard test is sensitive to cerebellar damage (Stoodley, 2016). Thus, cerebellar dysfunction might

contribute to the *deficit* apparent from 9-16 years on the DH and BH subtests among ASz compared to TD peers. The cerebellum has been implicated in cognitive and affective processing, although how it is involved in these functions is not clearly understood (Barch, 2014; Bernard and Mittal, 2014). ASz youth are characterised also by dyskinetic movement abnormalities and impairments in cognition and facial emotion processing relative to their TD peers (Cullen et al., 2010; Dickson et al., 2014a; Dickson et al., 2018; Dickson et al., 2014b; MacManus et al., 2012). This body of evidence provides some support for the 'cognitive dysmetria' model of schizophrenia, which posits that cognitive, motor, and affective deficits seen among individuals with schizophrenia result from difficulties in mental coordination due to disconnections in the cortico-cerebellar-thalamic-cortical circuits in the brain (Andreasen and Pierson, 2008; Moussa-Tooks et al., 2018). Abnormalities of cerebellar-cortical connectivity have been demonstrated among youth at ultra-high risk (UHR) for psychosis, that is, youth in the putative prodromal phase of illness immediately preceding onset of frank psychosis, compared to a healthy comparison group (Anticevic et al., 2015; Du et al., 2018). The present findings suggest that such mental coordination problems may emerge by middle childhood and remain as stable deficits during adolescence among ASz children. Knowledge of the underlying network dysfunction associated with psychosis risk is critical for developing targeted interventions. For example, improvements in motor learning following cerebellar transcranial direct current stimulation, which might reflect improvements in communication within cortico-cerebellar-thalamic-cortical circuits, have been reported in youth aged 18-22 years presenting with PLEs relative to those who do not (Gupta et al., 2017).

While the DH and BH subtests detected stable fine motor skill abnormalities from middle childhood through adolescence among ASz youth, on the Assembly subtest, which placed the greatest demands of fine motor dexterity and bimanual coordination on

participants, abnormalities were differentially prominent across development. There are a number of possible explanations for this finding. First, this subtest requires attention to be continually switched between hands in order to complete one 'assembly'. Our previous work reported developmental *delay* among ASz youth compared to TD peers on an executive function task involving attentional processes (Dickson et al., 2018). Taken together, these findings align with evidence for the delayed maturation of neural circuitry underlying executive function among individuals at-risk for schizophrenia (Catts et al., 2013). Second, *delay* might reflect divergence in the pace of maturation in brain areas related to motor development among ASz youth relative to TD peers (Walther and Strik, 2012). However, progressive maturational disturbances in brain development, rather than a brain maturational delay that resolves with age, have been widely reported among individuals who later develop schizophrenia in adulthood (Forsyth and Lewis, 2017). It is possible that the early deficit might re-emerge more prominently as ASz youth approach the period in late adolescence or early adulthood typical of psychosis onset. A cross-sectional study reported lower scores in a motor speed domain (consisting of a pegboard and finger tapping task) among youth aged 12-22 years who met UHR criteria for psychosis compared to a healthy comparison group (Carrion et al., 2011). A further study observed poorer performance on the BH and Assembly subtests in a sample of youth aged 15-18 years recruited from an adolescent psychiatric unit who screened positive for prodromal symptoms relative to those who did not (Lindgren et al., 2010). Third, motor abnormalities might reflect functional, rather than structural, abnormalities of development. In the integrated sociodevelopmental-cognitive model of schizophrenia proposed by (Howes and Murray, 2014), developmental alterations, hazards to the brain, and social adversity in childhood, lead to fluctuating dopaminergic dysfunction. Fine motor and coordination skill impairments might be due to fluctuating dopaminergic function in associated brain areas over the adolescent period (Howes et al., 2012). Only

longitudinal follow-up of ASz youth will determine whether a developmental *deficit* and/or *delay* in fine motor and coordination skills is associated with emerging illness or is a marker of disease vulnerability.

Evidence of a stable *deficit* from 9-16 years among FHx youth relative to TD peers was specific to Assembly. A meta-analysis of cross-sectional studies reported impairments (effect sizes of moderate magnitude) in fine motor and coordination skills from infancy through to adolescence among individuals with a family history of schizophrenia relative to those without (Burton et al., 2016). Evidence of impaired motor function at 7 years among offspring of parents with schizophrenia, but not children of parents with bipolar disorder, relative to children with parents with neither disorder (Burton et al., 2017), suggests that childhood motor impairments might be specific to schizophrenia rather than other mental health outcomes. Whether the differences in pattern of findings across subtests for the ASz and FHx groups might reflect distinct pathological processes requires further investigation. Comparisons of developmental trajectories between different at-risk groups can help establish the generalisability of predictors of psychosis (Barch et al., 2014), but may also highlight vulnerability- versus disease-related dysfunctions (Cannon, 2005).

The findings of the current study should also be considered in light of the recent addition of the sensorimotor domain to the Research Domain criteria (RDoC) framework. This domain was added in response to evidence highlighting the role of motor dysfunction in a broad range psychopathology, including psychosis, with the aim of fostering an improved understanding of the role of motor dysfunction in the development of psychiatric illness, and to support the development of new treatments for these dysfunctions, irrespective of diagnostic boundaries (Mittal et al., 2017). We do not yet know the proportion of ASz youth (if any) who will go on to develop schizophrenia. Some of the ASz children are instead likely to develop other mental health disorders, while others will not develop disorder. Further

longitudinal work is needed to identify the role of motor dysfunction in distinguishing these pathways to alternative outcomes among at-risk youth.

The strengths of the present study include the repeated measurement of fine motor and coordination skills from middle childhood into adolescence, in two groups of youth at-risk for schizophrenia, and our use of longitudinal mixed modelling which affords greater statistical power than alternative procedures for analysing longitudinal data (Curran et al., 2010). Several limitations should be noted. First, only a small number of participants completed all three motor assessments. While we did not observe group differences in the number of assessments completed, our findings require replication in larger samples with at least three assessments. Second, it is not currently known whether inclusion of youth with variable familial loading in the FHx group may have obscured our capacity to detect abnormal trajectories of motor function revealed by DH, NDH, or BH subtests. Third, our study employed only a pegboard assessment of fine motor and coordination skills, which was developed in the 1940s to assess dexterity and coordination in applicants for industrial jobs (Tiffin, 1948). It has been used widely in schizophrenia research (Bachman et al., 2012; Blanchard and Neale, 1994; Dickinson et al., 2007; Lin et al., 2015). Among healthy individuals, the Purdue pegboard has demonstrated good validity and reliability (Yancosek and Howell, 2009). In individuals with schizophrenia, it has been shown to have moderate-to-good test-retest reliability (Lee et al., 2013), though, to our knowledge, the specificity/sensitivity of the measure in discriminating premorbid motor dysfunction in individuals who later develop schizophrenia relative to individuals who do not has not been established. Pegboard tasks are quick, inexpensive, and require little training to administer, but the use of alternative measures might reveal distinct trajectories of development for other motor skills, which have been associated with differential perturbations in the brain network supporting motor functioning (Dean et al., 2018). While pegboard performance is sensitive to

cellebellar dysfunction, recent research has shown that objective cerebellar-mediated motor instruments (e.g., measuring postural sway or motor learning) may be better able to capture the relative contributions and interactions of motor, cognitive, and affective domains in schizophrenia (Bernard and Mittal, 2014; Schiffman, 2017). Assessing performance on such tasks at repeated occasions during development in at-risk youth may provide important insight into premorbid motor and cognitive deficits and emerging affective symptomology in the disorder.

In the present study, relative to TD youth, ASz youth showed stable stable deficits in multiple indices of fine motor function, but developmental delay in the Assembly subtest that also required motor coordination. FHx youth showed a stable deficit on Assembly only. Thus, coordination dysfunctions were differentially prominent during adolescence among ASz youth, but not FHx youth. These divergences from normative motor development may reflect differences in structural and functional neural correlates. As this is the first study to use repeated assessments of a pegboard task to examine developmental trajectories of fine motor and coordination skills from middle childhood to adolescence among youth at-risk for schizophrenia, these findings are preliminary and require replication. Such differences in trajectories of fine motor and coordination skills might be used in future to help refine the identification of individuals at-risk for schizophrenia during development.

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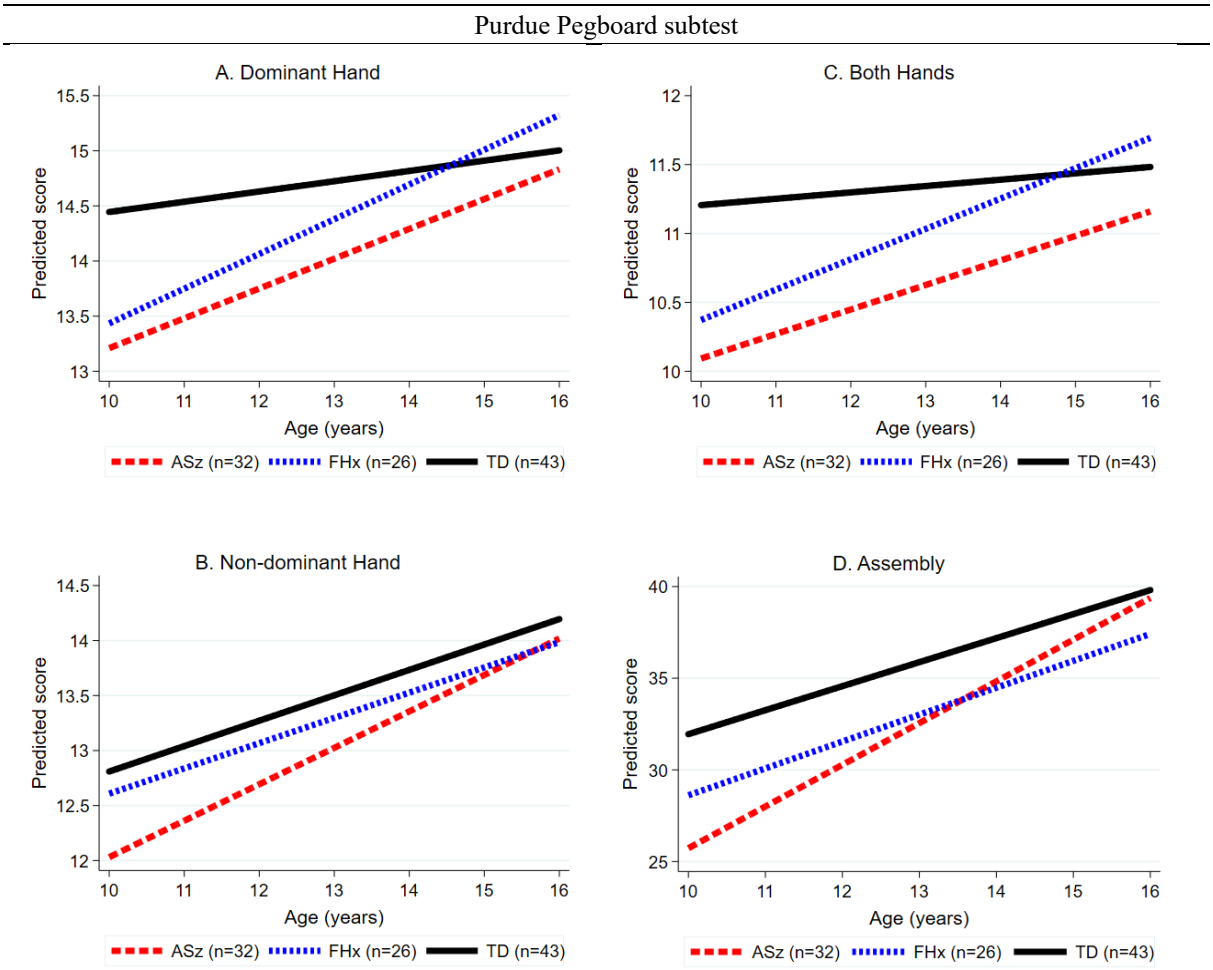
Figure 1. Line graphs of predicted values over age, adjusted for sex, ethnicity, and practice effects, for the Dominant hand (panel A), Non-dominant hand (panel B), Both hands (panel C), and Assembly subtests (panel D) for youth presenting with antecedents of schizophrenia (ASz), youth with a family history of schizophrenia (FHx), and typically developing youth (TD).



Note: Due to the relatively small number of children providing assessments at the extremes of the age distribution in the sample (n = 8 at 9 years and n = 7 at 16 years), *for visualisation purposes only*, the displays have been truncated to illustrate the period from 10.00 to 15.99 years only (all analyses were conducted without truncation).

Table 1: Comparisons of demographic characteristics at first assessment for each participant group

	ASz (n=32)		FHx (n=26)		TD (n=43)	
	n	**(%)**	**n**	**(%)**	**n**	**(%)**
Sex (male)[a]	19	(59)	12	(47)	20	(47)
Laterality [b]						
Right-hand dominance	26	(81)	24	(92)	37	(86)
Mixed- or left-hand dominance	6	(19)	2	(8)	6	(14)
Ethnicity [c, d]						
White	17	(53)	5	(19)	32	(74)
Black African and African-Caribbean	7	(22)	12	(46)	6	(14)
Other	8	(25)	9	(35)	5	(12)
Total number of motor assessments completed [e]						
One	6	(19)	4	(15)	5	(12)
Two	17	(53)	12	(46)	29	(67)
Three	9	(28)	10	(39)	9	(21)
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**
Age on day of first motor assessment [f]	12y, 5m	15m	12y,3m	14m	12y, 8m	14m
Mean number of pins inserted at first motor assessment						
Dominant hand	13.31	1.26	13.48	1.77	14.41	1.72
Non-dominant hand	12.44	1.38	12.68	2.04	13.22	1.51
Both hands	10.10	1.28	10.29	1.60	11.11	1.27
Assembly	29.69	5.44	31.09	5.54	35.04	4.22

Notes: ASz: antecedents of schizophrenia; FHx: family history of schizophrenia; TD: typically developing; y = years, m=months; [a] "Black African and Black African-Caribbean" included children of mixed white-black African/African-Caribbean ethnicity. "Other" included children predominantly of other mixed ethnicities.

Deleted: FE: Fisher's exact test.

Table 2. Parameter estimates of fixed effects within longitudinal mixed models[a] of motor function adjusted for sex, ethnicity and practice effects, describing developmental deficit and developmental delay trajectories.

	Intercept Estimate						Slope estimate			Slope estimate of between group differences per 1 year of age					
	ASz vs. TD			FHx vs. TD			TD			ASz vs. TD			FHx vs. TD		
Purdue Pegboard Subtest	Estimate	(SE)	p value	Estimate	(SE)	p value	Estimate	(SE)	p value	Estimate	(SE)	p value	Estimate	(SE)	p value
Dominant hand															
All participants	-0.88	(0.4)	0.02	-0.58	(0.5)	0.20	-0.07	(0.2)	0.64	0.17	(0.2)	0.28 - *deficit*	0.23	(0.2)	0.25
Motor delay cases excluded*	-0.85	(0.4)	0.03	-0.61	(0.5)	0.18	-0.04	(0.2)	0.79	0.21	(0.2)	0.21 - *deficit*	0.25	(0.2)	0.21
Non-dominant hand															
All participants	-0.58	(0.3)	0.09	-0.22	(0.4)	0.59	0.13	(0.1)	0.37	0.08	(0.2)	0.60	0.01	(0.2)	0.94
Motor delay cases excluded	-0.49	(0.4)	0.17	-0.29	(0.4)	0.49	0.15	(0.1)	0.29	0.11	(0.2)	0.51	0.06	(0.2)	0.78
Both hands															
All participants	-0.84	(0.3)	0.007	-0.50	(0.4)	0.18	-0.05	(0.1)	0.69	0.11	(0.1)	0.33 - *deficit*	0.19	(0.1)	0.20
Motor delay cases excluded*	-0.73	(0.3)	0.02	-0.58	(0.4)	0.11	-0.01	(0.1)	0.96	0.17	(0.1)	0.18 - *deficit*	0.24	(0.1)	0.10
Assembly															
All participants	-4.33	(1.1)	<0.001	-3.04	(1.3)	0.02	1.15	(0.4)	0.005	0.92	(0.4)	0.03 - *delay*	0.18	(0.5)	0.72 - *deficit*
Motor delay cases excluded*	-3.71	(1.2)	0.002	-3.04	(1.4)	0.03	1.25	(0.4)	0.003	0.90	(0.4)	0.04 - *delay*	0.22	(0.5)	0.67 - *deficit*

Notes: [a]Tests for trajectory type show fixed effects estimates with standard errors (SE) and significance values derived from random intercept only models; ASz: antecedents of schizophrenia; FHx: family history of schizophrenia; TD: typically developing; Intercept estimate: Group differences at 12.53 years; Slope estimate: Growth in motor development per 1 year of age; Developmental deficit trajectory type is characterised by a statistically significant intercept estimate and a non-significant slope estimate; Developmental delay is characterised by statistically significant intercept and positive slope estimates.
* Parameter estimates from sensitivity analyses that excluded ASz youth (n=5) who met ASz inclusion criteria on the basis of experiencing infant motor delays/abnormalities only, rather than infant speech delays/abnormalities.