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Collection of developmental history in the evaluation of schizophrenia spectrum disorders

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Abstract

Background*:* Schizophrenia is a heterogeneous disorder that is characterized by varying levels of hallucinations, delusions, negative symptoms, and disorganized features. The presence and severity of neurodevelopmental precursors and premorbid psychopathology also vary among individuals. To fully understand individual patients and to sort out phenotypic heterogeneity for genetic research studies, instruments designed to collect developmental history relevant to schizophrenia may be helpful.
Objective: The goal was to describe a pair of self-report and parent-report instruments developed for the purpose of collecting the developmental history of patients with known or suspected schizophrenia spectrum disorders.
Method: Two developmental history instruments were designed for use in studies of brain morphology and cognition in schizophrenia probands and their unaffected siblings. The instruments focus mainly on motor abnormalities and other features that have been described as schizophrenia precursors.
Results*:* The Motor Skills History Form is a brief self-report form that asks about patients' childhood and adolescent motor abilities as well as their current motor functioning. The Developmental & Motor History Form is a more detailed parent-rated form that covers aspects of patients' early (infant/preschool) development; their childhood and adolescent motor abilities; any childhood behaviors that may be related to later psychosis risk; and their history of any neurological, emotional, or cognitive disorders diagnosed during childhood or adolescence. The instruments can be used either for interviews or as self-administered questionnaires. The parent-rated form has been used for research and for the clinical assessment of children and adolescents with complex neurodevelopmental presentations with or without strong evidence of schizophrenia risk.
Conclusions: The collection of developmental history information is important when evaluating individuals with schizophrenia and related disorders. The Motor Skills History Form and the Developmental & Motor History Form can be used to collect this information for clinical evaluation or research purposes.

Keywords: Schizophrenia; Precursors; Motor; Language; Neurodevelopmental Disorders

Introduction

The collection of a developmental history during the clinical evaluation of patients with schizophrenia and related disorders is important for the following reasons:

1. When evaluating schizophrenia risk states, a history of developmental delays (1-5), abnormal movements (6-9), motor coordination problems (10,11), cognitive dysfunction(2,12,13), and specific psychiatric symptoms or behaviors (14-17) may help to predict the risk of conversion to schizophrenia or another psychotic disorder.

2. A history of premorbid neurodevelopmental disorders such as autism spectrum disorder (ASD), attention-deficit/hyperactivity disorder (ADHD), or learning disorders may require specific interventions or predict an individual's potential level of functioning and the degree of support that he or she will continue to need even after any active psychotic symptoms are under good control.

3. Individuals with a history of social and non-social cognitive problems may benefit from cognitive remediation (18-22).

4. The presence of complex neurodevelopmental problems may suggest a higher likelihood that an

abnormality would be found with genetic testing such as chromosomal microarray or whole exome sequencing (23-33). If a specific genetic cause is found (e.g., 22q11.2 deletion, which is present in 4% of patients with childhood-onset schizophrenia and 0.3% to 1% of patients with adult-onset schizophrenia [23]), this may warrant specific medical monitoring or treatment.

This article describes a set of self-report and parent-report instruments that were originally designed in 2005 for the collection of developmental history information from research assessment participants at the Conte Center for the Neuroscience of Mental Disorders at Washington University School of Medicine. At the Conte Center, the instruments were used in a study of brain morphology and cognition in research subjects with schizophrenia and their unaffected siblings (34-39). Motor abnormalities such as abnormal involuntary movements and poor motor coordination that were present before a schizophrenia diagnosis were of particular interest based on a review of existing literature about neurodevelopment in patients with schizophrenia.

We will now focus on the description of the instruments themselves, and future publications will provide reports of actual research findings as they become available.

Methods

General Description of the Instruments

Self-report and parent-report questionnaires were developed on the basis of the existing literature (as referenced previously) and personal experience working with child, adolescent, and adult patients with schizophrenia or schizophrenia risk states (Table 1). The Motor Skills History Form (MSHF) is a brief self-report instrument that focuses on elements of the developmental history (particularly motor function) that individuals may remember about themselves, even after they have reached adulthood. The Developmental & Motor History Form (DMHF) is a parent-report measure that covers some of the same areas (particularly related to child and adolescent motor abilities) and that also asks about additional childhood and adolescent symptoms, behaviors, and diagnoses. It also covers relevant aspects of early (infant and preschool) development.

There are problems inherent to the collection of retrospective developmental history, particularly related to an individual's poor recall of events that occurred years ago. Child, adolescent, and adult patients are unlikely to know the details of their own early childhood development unless a parent has provided this information to them. However, they may remember aspects of their motor development history, particularly if they experienced poor motor coordination that affected their ability to participate in sports and other activities during childhood or adolescence. They may remember how their abilities compared with those of other children their age, whether they were teased about their poor abilities, whether they avoided physical education classes due to their lack of ability, their degree of participation in organized sports, and perhaps the age at which they learned to ride a bicycle. Individuals can also comment on their perception of their own current motor abilities and any difficulties that they may have had learning complex motor behaviors, such as driving a car. Therefore, the self-report MSHF focuses on these elements. The MSHF focuses on childhood and adolescence, because it is unlikely that individuals will have an accurate recollection of their infancy and preschool years.

Sections A and B of the MSHF focus exclusively on the age range of 5 to 18 years. Section A asks about specific childhood and adolescent motor abilities, while section B focuses on experiences that may have occurred as a consequence of the level of motor ability. Parent-report versions of some of the MSHF Section A and B items are also included in Section C of the DMHF.

Because they ask about current abilities and events, Sections C and D of the MSHF include coverage of adult experiences if the individual completing the questionnaire is an adult. Section C of the MSHF asks about current motor functioning, including the degree of difficulty experienced when learning to drive a car (if applicable), an overall rating of current athletic ability, and current interest in team sports game participation for recreational purposes. Section D of the MSHF asks about any neurological or other medical disorders that may have affected motor skills or athletic ability, the patient's age and sex, and the date of the rating.

The DMHF collects parent-report information about patients' developmental and motor history. Section A addresses infancy and the preschool years, and this is followed by sections B through D, which focus on childhood and adolescence. Parents often have difficulty remembering the details of their children's early developmental history, particularly the exact ages at which their children reached specific developmental milestones. Collecting information about the timing of early developmental milestones (i.e., the ages at which patient first sat, crawled, walked, spoke words, used phrases, and conversed in full sentences) may still be useful in terms of getting a general idea of whether development was seriously delayed, so the DMHF does include questions about these. In the case of motor milestones, there is also an item that asks about the parent's level of certainty regarding the timing. Even if parents do not

remember the exact timing of developmental milestones, they are likely to remember major events such as concerns about development that led to an evaluation of motor or speech delays or to the provision of speech, occupational, or physical therapy to address developmental problems. Thus, questions about the evaluation and treatment of developmental concerns are also included.

TABLE 1. Descriptions and Sections of the Motor Skills History Form and the Developmental & Motor History Form

Motor Skills History Form (MSHF)	Developmental & Motor History Form (DMHF)
Self-report	Parent-report
Focuses on the developmental history, particularly motor function during the age range of 5 to 18 years. Also asks about current motor abilities.	Focuses on the developmental history from infancy through age 18 years, and also asks about additional symptoms, behaviors, and diagnoses during the same time period
Section A: Motor Abilities	Section A: Early Development
Section B: Motor Consequences	Section B: Childhood & Adolescent Behavior
Section C: Current Motor Functioning	Section C: Child & Adolescent Motor Skills
Section D: Untitled section including questions about past and current medical disorders that may have affected motor skills.	Section D: Child & Adolescent Neurological, Emotional, and Cognitive Disorders

Note. Section C of the DMHF includes some items that are also asked in sections A and B of the MSHF. Both instruments also collect information about age, sex, and date of rating at the end of section D.

Studies of infants and children with a high genetic risk for schizophrenia due to parental psychiatric history indicate that these children often show atypical patterns of development and certain types of abnormal movements, even without the presence of clearly abnormal delays in motor milestones (5,6). For this reason, the early childhood section of the DMHF includes an item that asks whether the child walked before learning to crawl. There is also a series of items that ask about any specific motor behaviors, such as atypical activity level, abnormal muscle tone, unusual ways of walking or running, and various abnormal movements that may have been observed during infancy and the preschool years. To help screen for possible ASD, there are some questions about sensory sensitivities, the child's response to being held, and any speech or language delays. There are also questions about any medications taken during early childhood and whether these seemed to affect motor skills or behavior.

Section B of the DMHF contains questions about general childhood behaviors that may indicate some level of increased risk for schizophrenia. Some of these behaviors have been described as characteristics of children with childhood schizophrenia, or they may have been reported as precursor behaviors that appeared in at-risk children who later developed schizophrenia. For example, observations of general unusual behaviors and atypical peer behaviors (e.g., a preference for playing alone, difficulty playing with more than one child at a time) have been made regarding children who have been diagnosed with childhood schizophrenia (40). In addition, teacher-reports of unusual emotional reactions, inappropriate behaviors, and uneasiness about criticism during childhood are some of the unusual behaviors that have predicted the development of adulthood schizophrenia spectrum disorders among high-risk individuals (15,17). Other items within Section B of the DMHF ask about relatively common and non-specific childhood symptoms that may possibly be relevant on the basis of general clinical experience.

Section C of the DMHF focuses on childhood and adolescent motor abilities, beginning with the motor ability items from section A of the MSHF. Since the self-report MSHF has this same set of items, it is possible to compare parent-reports with self-reports. There are also some questions about motor function and sports participation that are similar to items found in Section B of the MSHF.

Section D of the DMHF asks about specific diagnoses that the child was given during childhood or adolescence, any medications that may have affected child or adolescent motor function or behavior, the child's age and sex, and the date of the rating.

Use and Scoring

For clinical use, scoring of the MSHF and DMHF is not essential, but information gathered from the forms can enhance the level of developmental and psychiatric history that is obtained during assessment. Without any need to calculate scores, the information obtained can be used to assist decision making with regard to further diagnostic testing (e.g., to assess the need for detailed autism assessment or genetic testing). The methods of scoring discussed in the following paragraphs may be most important for researchers who seek to compare the levels of

developmental abnormalities among their research participant groups.

Section A of the MSHF is composed of 14 items that ask the individual to rate their own motor skill abilities as compared with peers of the same age on a scale of 1 to 5, with 1 = far below average, 2 = somewhat below average, 3 = average, 4 = somewhat above average, and 5 = excellent. Participants are asked to rate themselves twice: once for childhood (5 to 12 years old) and once for adolescence (13 to 18 years old). If the scale is used for patients who are less than 13 years old, the ratings that apply to adolescent abilities can be skipped. The scores on these items can be averaged to determine a Total Motor Abilities Score, which provides direct information about an individual's perception of his or her ability level. For example, a total score of 2.5 would indicate that, on average, the individual perceives that his or her various motor abilities were somewhere between the average and somewhat below average range during the specified period. Suggested subscales for this section include Gross Motor Abilities (items 1 through 8), Balance (items 9 through 11), and Fine Motor Abilities (items 12 through 14). These can be calculated by averaging the scores of the relevant items. Separate scores for childhood and adolescence can be calculated, or overall child and adolescent scores can be calculated by averaging the childhood and adolescence items together. It may also be useful to develop alternate subscales on the basis of factor analysis after an adequate amount of research data has been collected.

Section C of the DMHF includes 14 questions about motor abilities that are identical to those of Section A of the MSHF. This allows for easy comparison between parent-report and self-report perceptions.

Section B of the MSHF focuses on behaviors or experiences that may have occurred as a result of poor motor coordination, such as a dislike of physical education classes, teasing about poor physical abilities, being clumsy or accident-prone, learning to ride a bicycle at a later age (item C15 of the DMHF asks the same bicycle information), and the order in which the participant was asked to participate in sports teams. Items B1 through B5 can be averaged to get a score, or they may be examined individually. This section also contains items that ask about participation in organized sports (MSHF items B6 through B8) and any history of receiving physical or occupational therapy (B9 and B9a). The number of sports listed may be useful as a variable for analysis. DMHF items C16 through C20a also cover sports participation and therapy history.

The items in sections C and D of the MSHF (see earlier description) may be best considered as individual items rather than being combined into any subscales.

Section A of the DMHF requires parents to recall information about their children's infant and preschool years. As in some other sections of these instruments, respondents are asked to give their best guesses if they are unsure about the answers. This instruction may minimize the tendency for some respondents to skip items due to minor uncertainties and thus allow a greater amount of data to be collected. However, when interpreting this particular section, evaluators should keep in mind that there may be a higher potential for inaccurate responses when parents are trying to recall their children's earliest years. Because it is expected that many parents will not accurately recall the exact dates of developmental milestones, caution is warranted when using and interpreting any scores that are based on the ages at which milestones were met. The comparison of these values among subject groups may still be useful, especially for cases in which baby books or medical records have been used to confirm the exact timing of developmental milestones. The endorsement of dichotomous yes/no answers regarding specific behaviors and problems, early life evaluation for developmental concerns, or specific treatment interventions can be compared among research subject groups as appropriate. The questions that ask about the presence or absence of specific early childhood motor behaviors (items A4 through A24) can be used to create a score by counting the number of positive responses. Because such behaviors may or may not be noticed even if they are present, a "yes" response can be considered to indicate that the behavior was frequent or obvious enough for the parent to recall seeing it, and a "no" or blank response may indicate that the behavior was either not present or not obvious or frequent enough for the parent to clearly remember it. As long as most items in the section are answered, it may be appropriate to recode any missing responses as "no" responses.

Items on Section B of the DMHF, which address childhood and adolescent behavior, can either be considered separately or coded such that each "yes" answer contributes a point to a total symptom count score. Section D items about childhood and adolescent disorders can be scored in a similar manner, and subscales can be created to separately indicate the number of neurodevelopmental disorders (items D1 through D4 and D6 through D13) and other psychiatric disorders (items D14 through D16) that were diagnosed.

The MSHF and the DMHF were first used in the previously mentioned Conte Center research study, which focused on individuals with schizophrenia and

their unaffected siblings. Subjects in that study were mainly adolescents and young adults who were in the range of 14 to 30 years old. The measures were later used in a separate study of child, adolescent, and adult sibling pairs that were discordant for ADHD. Research use of the instruments for both projects was approved by the Washington University Human Research Protection Office.

Results

The original full versions of the MSHF and DMHF are provided along with this report; see the associated Supplemental Materials. The analysis of collected MSHF and DMHF research data is ongoing and will be reported in the future. In addition to being used in the previously discussed research studies, the DMHF has been used in non-research clinical diagnostic evaluations of children and adolescents with complex neurodevelopmental problems or with features that suggest high risk for the development of a schizophrenia spectrum disorder. These instruments have mainly been used as self-administered questionnaires, but they can also be used as interview-based measures. Any questions regarding instructions for the use of these instruments, future updated versions, or progress toward normative data collection can be directed to the author.

Discussion

Assessment of the developmental history is appropriate as part of clinical or research evaluations of children, adolescents, and adults with schizophrenia or with risk factors for the development of a schizophrenia spectrum disorder. A developmental history is often a key component of the standard clinical evaluations performed by child and adolescent psychiatrists, whether or not schizophrenia is part of the differential diagnosis. However, because schizophrenia is often diagnosed during late adolescence or early adulthood, individuals with schizophrenia may first be evaluated and treated by general psychiatrists, who may or may not routinely ask many questions about developmental history as part of their assessments. Even if an evaluating psychiatrist or psychologist does ask about the patient's developmental history, the questions asked may not be tailored toward the collection of information that is particularly relevant to the developmental course of schizophrenia.

The MSHF and the DMHF are presented here as one method for the collection of developmental history information, with an emphasis on aspects that are relevant to the natural developmental course of schizophrenia spectrum disorders. These questionnaires are particularly appropriate for use in individuals with known or suspected schizophrenia spectrum disorders, but they can also be useful for the evaluation of children, adolescents, and adults with complex forms of psychopathology that do not necessarily indicate schizophrenia risk, such as the co-occurrence of multiple neurodevelopmental problems or behavioral disturbances in young patients who do not have any known family genetic or other risk factors for psychosis.

In clinical practice, when evaluating children with symptoms that are suggestive of psychosis, the developmental history may contribute to the making of decisions about whether to order genetic testing. One study found disease-related copy-number variants (CNVs) in 11.9% of patients with childhood-onset schizophrenia, and a few of these individuals (4 out of the 15 with CNV findings) actually had a second neuropsychiatric-disorder–associated CNV (23). These CNV rates were significantly higher than those of the two adult schizophrenia samples that were used for comparison, which were 1.4% and 4.9%. One well-established genetic cause of schizophrenia is 22q11.2 deletion syndrome, which is estimated to be present in 0.3% to 1% of patients with adult-onset schizophrenia and in 4% of patients with childhood-onset schizophrenia (23). Individuals with 22q11.2 deletion have about a 30% chance of developing schizophrenia or another psychotic disorder during their lifetimes (41). These individuals also frequently show signs of ADHD, ASD, and cognitive or learning problems during childhood (28;42-44). Therefore, the co-occurrence of psychotic symptoms with ADHD, ASD, or other childhood-onset neurodevelopmental symptoms may prompt chromosomal microarray testing to evaluate for 22q11.2 deletion and any other CNVs that may be present. Recent studies of CNVs have suggested that various specific genetic duplications and deletions can increase an individual's risk for a broad array of neurodevelopmental disorders, including ASD, ADHD, various movement disorders, intellectual disability, and schizophrenia (24-26;29-33). Thus, the presence of a higher number of these problems may indicate an increased need for genetic testing.

The collection of detailed developmental history information is also important for research studies, particularly those that focus on diagnostic nosology, genetics, and individualized treatment. Recent research suggests that there are several subtypes of schizophrenia, which can be classified according to genotypic networks of interacting single-nucleotide polymorphisms or specific patterns of schizophrenia symptoms (45). Phenotypic subgroups of patients with schizophrenia also were found to have distinct patterns of fractional anisotropy in a diffusion tensor

imaging study of brain white matter (46). Defining more genetically homogeneous phenotypic subtypes of schizophrenia may need to go beyond the examination of schizophrenia symptom patterns to include the presence or absence of motor abnormalities, specific cognitive deficits, learning problems, atypical development patterns, and other co-occurring problems. Future research may reveal that individuals with distinct patterns of developmental history tend to have specific genetic abnormalities that lead to the dysfunction of specific brain systems. If this is the case, then the evaluation of a patient's developmental history in addition to his or her current symptoms may ultimately provide information about that patient's likely responses to specific treatments.

When using the MSHF, the DMHF, or any method of collecting a patient's developmental and psychiatric history, several limitations should be kept in mind. Memory is not perfect, so retrospective reports are not always accurate. There may also be a tendency for recall bias to arise from parents or from the affected individuals themselves as they think back to try to come up with any early risk or causal factors that may help to explain the development of a severe mental illness. This recall bias can be a particular problem in research studies that compare patients with severe mental illnesses to healthy individuals. Reviewing physical records (e.g., baby books, school reports, medical records) rather than relying on an individual's retrospective recall of events may help to reduce error, but some behaviors and symptoms of interest may not be captured in such records, and these additional types of data are not always available.

Since the creation of the DMHF and the MSHF, there have been some advances in the diagnostic nomenclature of childhood-onset psychiatric disorders. Although the 2005 versions of the forms are still appropriate for picking up the problems and diagnoses of interest, some modifications may be helpful to clarify the types of past diagnoses that were present. For example, the term *mental retardation* has now fallen out of favor in the United States, and the *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition* (DSM-5) instead uses the terms *intellectual disability* or *intellectual developmental disorder.* Clinicians and researchers in other countries may use different terminology, so other appropriate adjustments may need to be considered for studies outside of the United States. Although a revised version of the DMHF will include updated terminology, the older term *mental retardation* may be worth mentioning parenthetically for the benefit of parents who were told in the past (before the DSM-5) that their child had this condition and who may not be aware of the updated terminology.

On the basis of experience with the use of this instrument, it has also become evident that parents sometimes have difficulty distinguishing between the terms *speech disorder* and *learning disorder in communication or language.* Additional questioning by the examiner or the inclusion of updated items to help distinguish among the various DSM-5 communication disorders may be helpful. This could include questions to try to determine the presence or absence of a childhood language disorder, a speech sound disorder, a childhood-onset fluency disorder (e.g., stuttering), or a social (pragmatic) communication disorder. In some cases, the parent still may not be able to provide full information to confirm the specific communication disorder diagnosis (e.g., if the parent only knows that the child was given a diagnosis of "speech/language impairment" by the school), but further questions about the specific types of speech/language issues observed may provide some clarification.

Since the creation of these instruments, an association between obsessive-compulsive disorder (OCD) and a future risk of schizophrenia has been reported (47). Although the DMHF includes items about preoccupation with one's own thoughts and certain repetitive behaviors, these symptoms are not specific for OCD, and there is no specific question about past OCD diagnosis. Therefore, asking additional questions about OCD symptoms may be helpful during the course of clinical evaluation.

Despite the limitations and current lack of normative data, the MSHF and DMHF instruments can be used to collect valuable developmental history information that, according to the existing literature, has known relevance to schizophrenia spectrum disorders. Future reports of normative and psychometric data as well as studies that compare scores among various high-risk and diagnostic groups may greatly increase the usefulness of these instruments for both clinical and research purposes.

Clinical Significance

When evaluating a patient with a known or suspected schizophrenia spectrum disorder, obtaining an appropriate developmental history may provide information relevant to the patient's prognosis and to decisions about the further diagnostic testing and treatment intervention needs of the patient. The self-report MSHF and parent-report DMHF can be used as interviews or self-administered questionnaires to collect this developmental history information.

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References

1. Sorensen HJ, Mortensen EL, Schiffman J, Reinisch JM, Maeda J, Mednick SA. Early developmental milestones and risk of schizophrenia: a 45-year follow-up of the Copenhagen Perinatal Cohort. Schizophr Research 2010;118(1-3):41-7.

2. Cannon M, Caspi A, Moffitt TE, et al. Evidence for early-childhood, pan-developmental impairment specific to schizophreniform disorder: results from a longitudinal birth cohort. Arch Gen Psychiatry 2002;59(5):449-56.

3. Isohanni M, Jones PB, Moilanen K, et al. Early developmental milestones in adult schizophrenia and other psychoses. A 31-year follow-up of the Northern Finland 1966 Birth Cohort. Schizophr Research 2001;52(1-2):1-19.

4. Jones P, Rodgers B, Murray R, Marmot M. Child development risk factors for adult schizophrenia in the British 1946 birth cohort. Lancet 1994;344(8934):1398-402.

5. Fish B. Neurobiologic antecedents of schizophrenia in children. Evidence for an inherited, congenital neurointegrative defect. Arch Gen Psychiatry 1977;34(11):1297-313.

6. Schiffman J, Walker E, Ekstrom M, Schulsinger F, Sorensen H, Mednick S. Childhood videotaped social and neuromotor precursors of schizophrenia: a prospective investigation. Am J Psychiatry 2004;161(11):2021-7.

7. Rosso IM, Bearden CE, Hollister JM, et al. Childhood neuromotor dysfunction in schizophrenia patients and their unaffected siblings: a prospective cohort study. Schizophr Bull 2000;26(2):367-78.

8. Mittal VA, Neumann C, Saczawa M, Walker EF. Longitudinal progression of movement abnormalities in relation to psychotic symptoms in adolescents at high risk of schizophrenia. Arch Gen Psychiatry 2008;65(2):165-71.

9. Mittal VA, Walker EF, Bearden CE, et al. Markers of basal ganglia dysfunction and conversion to psychosis: neurocognitive deficits and dyskinesias in the prodromal period. Biol Psychiatry 2010;68(1):93-9.

10. Schiffman J, Sorensen HJ, Maeda J, et al. Childhood motor coordination and adult schizophrenia spectrum disorders. Am J Psychiatry 2009;166(9):1041-7.

11. Cannon M, Jones P, Huttunen MO, et al. School performance in Finnish children and later development of schizophrenia: a population-based longitudinal study. Arch Gen Psychiatry 1999;56(5):457-63.

12. Cannon TD, Bearden CE, Hollister JM, Rosso IM, Sanchez LE, Hadley T. Childhood cognitive functioning in schizophrenia patients and their unaffected siblings: a prospective cohort study. Schizophr Bull 2000;26(2):379-93.

13. Vorstman JA, Breetvelt EJ, Duijff SN, et al. Cognitive decline preceding the onset of psychosis in patients with 22q11.2 deletion syndrome. JAMA Psychiatry 2015;72(4):377-85.

14. Bearden CE, Rosso IM, Hollister JM, Sanchez LE, Hadley T, Cannon TD. A prospective cohort study of childhood behavioral deviance and language abnormalities as predictors of adult schizophrenia. Schizophr Bull 2000;26(2):395-410.

15. Olin SC, Mednick SA, Cannon T, et al. School teacher ratings predictive of psychiatric outcome 25 years later. Br J Psychiatry Suppl 1998;172(33):7-13.

16. Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R. Prior juvenile diagnoses in adults with mental disorder: developmental follow-back of a prospective-longitudinal cohort. Arch Gen Psychiatry 2003;60(7):709-17.

17. Olin SS, John RS, Mednick SA. Assessing the predictive value of teacher reports in a high risk sample for schizophrenia: a ROC analysis. Schizophr Res 1995;16(1):53-66.

18. Eack SM, Greenwald DP, Hogarty SS, et al. Cognitive enhancement therapy for adults with autism spectrum disorder: results of an 18-month feasibility study. J Autism Dev Disord 2013;43(12):2866-77.

19. Eack SM, Hogarty GE, Greenwald DP, Hogarty SS, Keshavan MS. Effects of cognitive enhancement therapy on employment outcomes in early schizophrenia: Results from a two-year randomized trial. Res Soc Work Pract 2011;21(1):32-42.

20. Eack SM, Mesholam-Gately RI, Greenwald DP, Hogarty SS, Keshavan MS. Negative symptom improvement during cognitive rehabilitation: results from a 2-year trial of Cognitive Enhancement Therapy. Psychiatry Res 2013;209(1):21-6.

21. Eack SM, Pogue-Geile MF, Greenwald DP, Hogarty SS, Keshavan MS. Mechanisms of functional improvement in a 2-year trial of cognitive enhancement therapy for early schizophrenia. Psychol Med 2011;41(6):1253-61.

22. Revell ER, Neill JC, Harte M, Khan Z, Drake RJ. A systematic review and meta-analysis of cognitive remediation in early schizophrenia. Schizophr Res 2015;168(1-2):213-22.

23. Ahn K, Gotay N, Andersen TM, et al. High rate of disease-related copy number variations in childhood onset schizophrenia. Molecular Psychiatry 2014;19(5):568-72.

24. Addington AM, Rapoport JL. Annual research review: impact of advances in genetics in understanding developmental psychopathology. J Child Psychol Psychiatry 2012;53(5):510-8.

25. Elia J, Gai X, Xie HM, et al. Rare structural variants found in attention-deficit hyperactivity disorder are preferentially associated with neurodevelopmental genes. Molecular Psychiatry 2010;15(6):637-46.

26. Malherbe PJ, Roos JL, Jr., Ehlers R, Karayiorgou M, Roos JL. Phenotypic features of patients with schizophrenia carrying de novo gene mutations: a pilot study. Psychiatry Res 2015;225(1-2):108-14.

27. Szatkiewicz JP, O'Dushlaine C, Chen G, et al. Copy number variation in schizophrenia in Sweden. Molecular Psychiatry 2014;19(7):762-73.

28. Vorstman JA, Breetvelt EJ, Thode KI, Chow EW, Bassett AS. Expression of autism spectrum and schizophrenia in patients with a 22q11.2 deletion. Schizophr Res 2013;143(1):55-9.

29. Cellini E, Vignoli A, Pisano T, et al. The hyperkinetic movement disorder of FOXG1-related epileptic-dyskinetic encephalopathy. Dev Med Child Neurol 2016;58(1):93-97.

30. Dale RC, Grattan-Smith P, Nicholson M, Peters GB. Microdeletions detected using chromosome microarray in children with suspected genetic movement disorders: a single-centre study. Dev Med Child Neurol 2012;54(7):618-23.

31. Peall KJ, Kurian MA, Wardle M, et al. SGCE and myoclonus dystonia: motor characteristics, diagnostic criteria and clinical predictors of genotype. J Neurol 2014;261(12):2296-304.

32. McGrath LM, Yu D, Marshall C, et al. Copy number variation in obsessive-compulsive disorder and tourette syndrome: a cross-disorder study. J Am Acad Child Adolesc Psychiatry 2014;53(8):910-9.

33. Tomiyasu A, Nakamura M, Ichiba M, et al. Novel pathogenic mutations and copy number variations in the VPS13A gene in patients with chorea-acanthocytosis. Am J Med Genet B Neuropsychiatr Genet 2011;156B(5):620-31.

34. Delawalla Z, Barch DM, Fisher Eastep JL, et al. Factors mediating cognitive deficits and psychopathology among siblings of individuals with schizophrenia. Schizophr Bull 2006;32(3):525-37.

35. Delawalla Z, Csernansky JG, Barch DM. Prefrontal cortex function in nonpsychotic siblings of individuals with schizophrenia. Biol Psychiatry 2008;63(5):490-7.

36. Harms MP, Wang L, Mamah D, Barch DM, Thompson PA, Csernansky JG. Thalamic shape abnormalities in individuals with schizophrenia and their nonpsychotic siblings. J Neurosci 2007;27(50):13835-42.

37. Harms MP, Wang L, Campanella C, et al. Structural abnormalities in gyri of the prefrontal cortex in individuals with schizophrenia and their unaffected siblings. Br J Psychiatry 2010;196(2):150-7.

38. Harms MP, Wang L, Csernansky JG, Barch DM. Structure-function relationship of working memory activity with hippocampal and prefrontal cortex volumes. Brain Struct Funct.2013;218(1):173-86.

39. Barch DM, Cohen R, Csernansky J. Altered cognitive development in the siblings of individuals with schizophrenia. Clin Psychol Sci 2014;2(2):138-51.

40. Cantor S. About normal children. In: Cantor S. Childhood Schizophrenia. New York: The Guilford Press; 1988. p. 57-74.

41. Murphy KC. Annotation: velo-cardio-facial syndrome. J Child Psychol Psychiatry 2005;46(6):563-71.

42. Hidding E, Swaab H, de Sonneville LM, et al. Intellectual functioning in relation to autism and ADHD symptomatology in children and adolescents with 22q11.2 deletion syndrome. J Intellect Disabil Res 2015;59(9):803-15.

43. Schneider M, Debbane M, Bassett AS, et al. Psychiatric disorders from childhood to adulthood in 22q11.2 deletion syndrome: results from the International Consortium on Brain and Behavior in 22q11.2 Deletion Syndrome. Am J Psychiatry 2014;171(6):627-39.

44. Vorstman JA, Morcus ME, Duijff SN, et al. The 22q11.2 deletion in children: high rate of autistic disorders and early onset of psychotic symptoms. J Am Acad Child Adolesc Psychiatry 2006;45(9):1104-13.

45. Arnedo J, Svrakic DM, Del Val C, et al. Uncovering the hidden risk architecture of the schizophrenias: confirmation in three independent genome-wide association studies. Am J Psychiatry 2015;172(2):139-53.

46. Arnedo J, Mamah D, Baranger DA, et al. Decomposition of brain diffusion imaging data uncovers latent schizophrenias with distinct patterns of white matter anisotropy. NeuroImage 2015;120:43-54.

47. Meier SM, Petersen L, Pedersen MG, et al. Obsessive-compulsive disorder as a risk factor for schizophrenia: a nationwide study. JAMA Psychiatry 2014;71(11):1215-21.

Supplementary files

1) Motor Skills History Form
2) Developmental & Motor History Form