Parental ADHD Status and its Association with Proband ADHD Subtype and Severity

Toshinobu Takeda, MD, PhD, Kory Stotesbery, DO, Thomas Power, PhD, Paul J. Ambrosini, MD, Wade Berrettini, MD, PhD, Hakon Hakonarson, MD, PhD, and Josephine Elia, MD

Objective To better understand the familial transmission of attention deficit hyperactivity disorder (ADHD), a highly heritable disorder, the effects of paternal and maternal ADHD status on probands' ADHD symptoms and subtypes were investigated.

Study design In 323 trios with ADHD, data from a structured interview and a self-report scale (score of >21) were used to determine ADHD probands' diagnostic status and parental ADHD status, respectively. Parental ADHD status on proband ADHD severity and subtypes was investigated.

Results ADHD criteria were endorsed by 23% of fathers and 27% of mothers, and by at least one parent in 41% of the cases. ADHD severity was higher for children whose parents had ADHD versus those whose parents were without it. Paternal ADHD was associated with an increased likelihood of ADHD combined subtype (odds ratio = 3.56) and a decreased likelihood of the inattentive subtype (odds ratio = 0.34) in male children.

Conclusions Parental ADHD status appears to confer different risks for the severity of hyperactive-impulsive and inattentive symptoms depending on parental sex; however, parental ADHD self-report scale score has low to negligible correlation with proband's ADHD severity. Biparental ADHD does not appear to have an additive or synergistic effect on the proband's ADHD severity. *(J Pediatr 2010;157:995-1000)*.

Attention deficit hyperactivity disorder (ADHD) is highly heritable, but familial transmission is not well understood. Familial aggregation was observed in early ADHD studies, with higher rates reported in siblings of ADHD probands (20.8% vs 5.6% in control subjects),[1] among first-degree family members of male[2] and female probands[3,4] with ADHD and in second-degree relatives.[5] Shared genes rather than shared environment were suggested to be primarily responsible for transmitting ADHD according to adoption studies of children with ADHD, with reports of 18% ADHD in biologic versus 6% in adoptive parents.[6]

ADHD in siblings has been widely investigated through numerous studies that assessed heritability (estimated at 51% to 90%),[7] as well as the role of proband sex.[8-13] Adult ADHD has been investigated as well;[14-16] however, the relationship between parental ADHD and proband's ADHD has not been widely explored. In a study of boys and girls with ADHD and a maternal history of ADHD compared with children with ADHD and a paternal history of ADHD, the maternal history group had greater levels of impairment than the paternal group, and girls' scores were lower than boys' scores in the paternal history group and equaled or exceeded boys' scores in the maternal history group.[17] In another study of families with multiple members affected with ADHD, female probands were more likely to have at least one parent with ADHD than male probands.[18] These findings differ from other reports in which the prevalence of ADHD in families did not differ in female and male cohorts.[19] Subtyping, however, may be important as indicated by a recent study in which higher parental psychopathology was reported in families of girls but not of boys with combined ADHD compared with the inattentive subtype.[20]

In this report, data from 323 trios were used to investigate the association between parental ADHD and ADHD proband severity and subtypes. We hypothesized that ADHD severity and subtype membership differs in ADHD probands depending on parental ADHD status.

Methods

This study included 323 trios (ADHD proband and both biologic parents), a subset of families from 500 trios with ADHD who were enrolled in a genetic ADHD

ADHD	Attention deficit hyperactivity disorder
ANOVA	Analysis of variance
ASRS	ADHD Self-Report Scale
IQ	Intelligence quotient
K-SADS	Kiddie-Schedule for Affective Disorders and Schizophrenia
SES	Socioeconomic status

From the Ryukoku University, Kyoto, Japan (T.T.); Children's Hospital of Philadelphia (T.T., T.P., H.H., J.E.), Jefferson University (K.S.), Drexel University (P.A.), and the University of Pennsylvania (W.B., H.H., J.E.), Philadelphia, PA

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study. ADHD proband age ranged from 6 to 18 years, and all families were North American of European descent. Individuals of other ancestries were not included because this was a genetic study, and haplotype frequencies vary substantially across major world populations, lowering the power of the study to detect genetic association if multiple ethnic groups were included.

The 500 families with ADHD included 39 families with two siblings and 8 families with 3 siblings. In families with more than one sibling, only the first child (case A) evaluated was included, irrespective of age, leaving a total of 449 trios. Among 449 trios, complete adult ADHD Self-Report Scale (ASRS) data for both parents was available in 323 trios, and these are the data used for the analyses in this report.

The study was approved by the Institutional Review Boards of The Children's Hospital of Philadelphia and the University of Pennsylvania School of Medicine. Parents provided consent and children assent.

Families were recruited from pediatric and behavioral health clinics in the Philadelphia area. Phone screenings were conducted to determine age range of 6 to 18 years, presence of ADHD symptoms, ancestry, availability and willingness to participate in a genetic study from both biological parents. Exclusionary criteria included gestational age <36 weeks, IQ scores <75, major medical diagnoses (excluding asthma), and neurologic issues (eg, seizures, fetal alcohol syndrome, plumbism). Some neuropsychiatric disorders, namely pervasive developmental disorders, bipolar disorder, major depressive disorder with symptoms starting before ADHD, or ADHD symptoms occurring primarily during depressed or psychotic episodes were also grounds for exclusion. Subjects with disruptive behavior disorders, other mood disorders, and anxiety disorders were not excluded. Siblings meeting inclusion and exclusion criteria were also invited to participate in the study, but their participation was not required.

The cohort of 500 trios was enrolled and completed the study from 2003–2008. Thirty-six subjects who had signed consent/assent were excluded from the study. Twenty subjects passed the phone screen but did not meet ADHD criteria on Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS). Five subjects met criteria for ADHD; however, in 3 subjects these symptoms were considered to be due to a major depression, and in two subjects anxiety symptoms significantly contributed to the ADHD. Three other subjects who also met criteria for ADHD were excluded, one meeting criteria for cyclothymia, one for bipolar disorder, and one for psychotic symptoms. Five subjects were excluded because of medical history that became evident during the office visit and included one subject each for sleep apnea, intelligence quotient (IQ) <70, severe hypoglycemia at birth, absence seizures, and febrile seizures. Two children agreed to participate and signed assent but then did not want to answer K-SADS questions; this was interpreted as their way of retracting assent. One additional child had severe social anxiety that prevented him from completing the interview.

ADHD and psychiatric comorbidity were assessed by a semistructured interview, the Schedule for Affective Disorders and Schizophrenia for School Age Children (K-SADS-IVR) administered by a child psychiatrist (J.E.) to the parents and child separately. This semistructured interview provides diagnoses occurring within the previous 12 months and for the previous week. This version of the K-SADS rates each symptom on a graded Likert-type severity scale (from 1 to 4; thus summing up inattention or hyperactivity-impulsivity score in ADHD may range from 9 to 36) thus allowing for a composite severity rating score.[21] All ADHD symptoms are scored from 0 (no information) to 4 (severe/extreme). Scores of >3 are considered clinically significant. Intraclass correlations between the primary diagnostician and a clinician with extensive experience with this semistructured interview (P.J.A.) for the diagnostic symptoms of the major disorders were assessed through videotape reviews. All intraclass correlations values were highly significant with the following ranges: ADHD: 0.82; oppositional defiant disorder: 0.80; affective disorders 0.74-0.85; and anxiety disorders 0.75-0.92; ADHD: 0.82; oppositional defiant disorder: 0.80.

Available reports of IQ assessments for subjects tested before participation in the genetics study were reviewed. The Wechsler Abbreviated Scale of Intelligence IQ assessment was administered to a subset of children without previous IQ testing. Other children, included but not formally tested, were able to understand and complete the K-SADS. Data from the Wechsler Abbreviated Scale of Intelligence were available in 232 of the cases. Socioeconomic status (SES) was measured by the Hollingshead 4-Factor Scale.[22]

Parents were given the 18-question World Health Organization ADHD Self-Report Scale (ASRS). This screener assesses the presence of ADHD symptoms in the subjects' parents on the basis of a numerical rating of 18 symptoms on a scale of 0-4 (0 = Never, 4 = Very Often). The questions are divided in two parts, Part A assessing symptoms of inattention and Part B assessing hyperactivity and impulsivity. The scale has been validated,[23,24] and a score of >21 on Part A or B was accepted as criteria for positive parental ADHD because it is associated with a high (94.5%) rate of classification accuracy. Patients were asked to answer the questions using a 6-month recall period.

Analysis

ADHD probands were divided into 4 groups according to parental ADHD status (maternal and paternal affected; maternal and paternal not affected; paternal affected but maternal not affected; maternal affected but paternal not affected).

Probands' age was compared between two sexes with a non-paired *t*-test. Association between parental ADHD and proband sex was tested by chi-square analysis. Proband demographic characteristics (age, IQ, SES) were compared among parental ADHD status groups by χ^2 or analysis of variance (ANOVA). Then, parental age at proband birth and parental ASRS total score as well as proband ADHD severity (K-SADS ADHD total symptoms score; Inattention symptoms score; and hyperactivity/impulsivity symptoms score) were compared among parental ADHD status groups with