

Conscientiousness as a mediator of the association between masculinized finger-length ratios and attention-deficit/hyperactivity disorder (ADHD)

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Background: One often-overlooked biological risk factor that may help explain sex-biased prevalence rates in psychopathology is sex hormones. Personality traits, which also show sex differences, may mediate relations between biological risk factors like hormones and childhood psychopathology such as ADHD (or, alternatively, be independent risk factors). **Methods:** Three hundred and twelve children/adolescents (178 boys, 134 girls) between the ages of 8 and 17 completed a comprehensive, multistage, clinical diagnostic procedure; 168 children were diagnosed with ADHD and 144 were classified as non-ADHD comparison controls. Primary caregivers completed the California Q-sort in order to provide a measure of conscientiousness. Finger-length ratios (specifically right 2D:4D) served as a proxy of prenatal testosterone exposure (relative to estrogen). **Results:** Lower levels of conscientiousness statistically mediated the relationship between more masculine right 2D:4D (i.e., increased prenatal testosterone exposure) and increased ADHD inattentive symptoms. **Conclusion:** More masculinized finger-length ratios show associations with ADHD symptoms, possibly acting through the trait mechanism of conscientiousness. **Keywords:** ADHD, hormones, personality, mediation.

Sex differences in the prevalence rates of developmental psychopathology are a well-established fact (Zahn-Waxler, Shirtcliff, & Marceau, 2008). Common childhood-onset disorders such as attention-deficit/hyperactivity disorder (ADHD), oppositional-defiant disorder (ODD), conduct disorder (CD), and autism exhibit male-biased prevalence rates (APA, 2000). Although these sex differences are well established, the mechanisms of sex-biased prevalence rates of childhood psychopathology have yet to be elucidated. Personality traits may help to explain the sex-biased prevalence rates of common forms of developmental psychopathology since traits also exhibit sex differences early in development and may be more proximal to etiological biological factors such as genetic risk alleles and hormones, potentially mediating relations between biological risk factors and psychopathology (Else-Quest, Hyde, Goldsmith, & Van Hulle, 2006).

One often-overlooked biological risk factor that may help explain sex-biased prevalence rates in psychopathology is sex hormones. The organizational hypothesis of hormonal effects states that prenatal exposure to hormones during a critical period of development affects the developing brain, altering behavior even into adulthood (Breedlove & Hampson, 2002; Phoenix, Goy, Gerall, & Young, 1959). Organizational hormonal effects may influence the development of childhood neurobiology, traits, and behavior related to psychopathology (e.g., Voracek, 2008). ADHD may be a disorder

particularly suited to the exploration of these effects since it is a common childhood disorder with a sex-biased prevalence rate (3 boys: 1 girl) that has often been described as trait-like (Braaten & Rosen, 1997).

Well-established sex differences have been noted in developing neurobiology and traits and behavior associated with childhood psychopathology. Such sex differences are complex and shift over time. Boys have greater brain volume than girls, particularly in the bilateral frontal and occipital lobes, whereas girls exhibit thicker cortices in right inferior parietal and posterior temporal regions (Sowell et al., 2007). Females exhibit higher whole blood serotonin levels and slower serotonin synthesis, as well as enhanced dopaminergic function, including increased dopamine transporter availability (Cosgrove, Mazure, & Staley, 2007). The pattern of striatal dopaminergic development is also different for males and females (Andersen & Teicher, 2000). Young children exhibit sex differences in traits that may be relevant to the development of disruptive behavior disorders. Boys exhibit lower levels of effortful control (i.e., deliberate control including attention focusing and shifting) and higher levels of surgency (i.e., high-intensity pleasure, activity, and sociability) compared to girls (Else-Quest et al., 2006).

Although sex differences in hormone exposure, neurobiology, traits, and psychopathology are well established, little work has directly assessed hormonal associations with these sex differences. Within human populations, this question has most frequently been addressed indirectly using a proxy of prenatal hormone exposure: sexually dimorphic

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finger-length ratios, particularly those on the right hand. Smaller ratios of finger length, particularly that of the index finger to ring finger (2D:4D), are associated with relatively higher prenatal testosterone exposure (Cohen-Bendahan, van de Beek, & Berenbaum, 2005), as assessed in one study looking at amniotic fluid in humans (Lutchmaya, Baron-Cohen, Raggett, Knickmeyer, & Manning, 2004) and in other studies of girls with congenital adrenal hyperplasia, a disorder in which girls are exposed to abnormally high levels of androgen prenatally and exhibit smaller right 2D:4D ratios that are comparable with typically developing boys (Brown, Hines, Fane, & Breedlove, 2002; Okten, Kalyoncu, & Yaris, 2002).

Finger-length ratios have just recently begun to be examined in relation to childhood disorders like ADHD. Boys with autism/Asperger syndrome and ADHD/oppositional defiant disorder (comorbid groups) had lower finger-length ratios than boys with anxiety disorders, and boys with autistic spectrum disorders had lower finger-length ratios than boys without psychiatric disorders (De Bruin, Verhiej, Wiegman, & Ferdinand, 2006). In another study of clinically-diagnosed children, boys and girls (ages 7–15) with the Inattentive subtype of ADHD had smaller finger-length ratios than those with the Combined subtype of ADHD or typically developing control children (McFadden, Westhafer, Pasanen, Carlson, & Tucker, 2005). Martel and colleagues (Martel, Gobrogge, Breedlove, & Nigg, 2008) examined associations between finger-length ratios (2D:4D) and ADHD in a larger and clinically well-characterized sample of community-recruited boys and girls aged 6 to 18 years and found that ADHD, particularly inattention, was associated with more masculinized finger-length ratios in boys but not in girls. Overall, studies found relations between more masculine finger-length ratios, or relatively increased prenatal testosterone exposure, and behaviors and symptoms relevant to ADHD (De Bruin et al., 2006; Fink, Manning, Williams, & Podmore-Nappin, 2007; Martel et al., 2008; McFadden et al., 2005; Stevenson et al., 2007; Williams Greenhalgh, & Manning, 2003).

The mechanisms of these effects are not well understood, although one study may shed light on possible mechanisms of hormone-psychopathology relations. Low 2D:4D and high concurrent levels of testosterone were related to increased sensation-seeking (Fink, Neave, Laughton, & Manning, 2006), a trait that shows sex differences that favor boys and that has been related to externalizing disorders (Zuckerman, 2005). Trait-psychopathology relations are well established, although the etiology of these relations is not understood. To date, there is some evidence to support both the vulnerability and spectrum hypotheses of trait-psychopathology relations, suggesting that traits may increase risk for psychopathology or lie on the same spectrum

(Eisenberg et al., 2001; Krueger & Tackett, 2003; Van Leeuwen, Mervielde, De Clercq, & De Fruyt, 2007; Watson, Kotov, & Gamez, 2006).

Regardless of the mechanism of relations between traits and psychopathology, traits may serve as more proximal indicators of biological risk factors for psychopathology since they can be more reliably measured at earlier ages (Aksan & Kochanska, 2004). The examination of traits as mediators of relations between biological risk factors and later-developing childhood psychopathology may shed light on the manner in which these biological risk factors have their influence on childhood psychopathology and on subsequent developing adolescent and adult psychopathology (Maughan & Kim-Cohen, 2005). Hormonal associations with psychopathology are arguably one of the areas most in need of this kind of exploration. Although many studies have documented associations between prenatal hormone exposure and childhood psychopathology, no work to date has examined potential mechanisms or mediators of these relations.

Based on previous work on associations between prenatal hormone exposure, measured via finger-length ratios, and childhood ADHD (Martel et al., 2008), conscientiousness is currently examined as a potential mediator of this relationship. ADHD has commonly been associated with low levels of effortful control like conscientiousness (Martel & Nigg, 2006; Parker, Majeski, & Collin, 2004), as well as with more masculine finger-length ratios, with some evidence to suggest that potential hormonal effects may be more specific to inattention than hyperactivity-impulsivity (McFadden et al., 2005). In addition, recent dual-pathway models of ADHD suggest that inattentive symptoms may be more related to effortful traits such as executive function and possibly conscientiousness (Sonuga-Barke, 2005). In the current study, it was hypothesized that conscientiousness would mediate the relationship between finger-length ratios as a proxy of prenatal testosterone exposure and inattentive ADHD symptoms. This effect was hypothesized to be stronger in boys than in girls due to relatively higher exposure to prenatal testosterone.

Method

Participants

The current study reports on 312 participants (ages 8–17; $M = 13.31$, $SD = 2.96$) from 274 families who provided informed consent for participation. Participants were recruited into two groups: ADHD ($n = 168$; 89 ADHD-Combined type [ADHD-C], 78 ADHD-Inattentive type [ADHD-PI], 1 ADHD-Hyperactive/Impulsive type [ADHD-PHI]) and control ($n = 144$). Within the whole group, there were 178 boys (106 boys with ADHD and 72 boys in control group). As shown in Table 1, there were significantly more boys in the ADHD group than in the control group, and the ADHD group was younger

Table 1 Sample demographics

	ADHD	Controls	Total
	<i>n</i> = 168	<i>n</i> = 144	<i>N</i> = 312
<i>N</i> (%)			
Males	106 (63.1%)	72 (50%)	178 (57.1%)*
Ethnic minority	40 (23.81%)	38 (26.39%)	78 (25%)
<i>M</i> (SD)			
Age	12.71 (3.01)	14.01 (2.76)	13.31 (2.96)**
Family Income	71173.91 (83045.01)	77306.52 (55531.69)	74051.52 (71400.45)
Full Scale IQ	103.09 (12.66)	111.55 (14.34)	106.98 (14.08)
Inattention Symptoms ¹	8.54 (.72)	1.86 (1.91)	5.42 (3.62)**
Hyperactive Symptoms ¹	6.19 (2.90)	1.17 (1.44)	3.85 (3.43)**
ODD Symptoms	2.41 (2.48)	.51 (1.21)	1.59 (2.23)**
CD Symptoms	.35 (.73)	.05 (.22)	.23 (.58)**
Conners' Cognitive Problems (P)	71.08 (10.64)	47.66 (6.97)	60.37 (14.83)**
Conners' Hyperactivity (P)	67.42 (15.80)	49.17 (7.57)	58.93 (15.58)**
Conners' ADHD T-score (P)	72.27 (9.33)	48.11 (7.05)	61.18 (14.67)**
Conners' Cognitive Problems (T)	60.15 (11.47)	48.63 (7.39)	54.58 (11.28)**
Conners' Hyperactivity (T)	61.84 (14.80)	50.60 (10.53)	56.37 (14.05)**
Conners' ADHD T-score (T)	66.43 (12.78)	50.03 (9.58)	58.42 (13.98)**

Note: * $p < .05$. ** $p < .01$. (P) = parent-report. (T) = teacher-report. ¹ = parent+teacher OR algorithm ADHD symptoms based on K-SADS. Significant group differences tested by *t*-tests or chi-square statistics.

($p < .05$). Children with ADHD had more ADHD symptoms, higher Conners' *t*-scores, and more ODD and CD symptoms ($p < .01$). Forty-eight children were diagnosed with ODD. Four children were diagnosed with CD.

Multistage recruitment and diagnostic assignment process. All participants were recruited from mid-Michigan schools, clinics, and community through public advertisements and announcements, mass mailings, and outreach to schools and clinics in order to recruit a broad and representative sample. The first stage was a screen that precluded any children who took slow-acting psychotropic medication (i.e., prednisone, antidepressant, anti-psychotic, anticonvulsant medications), had major medical or neurological conditions, including genetic, gonadal, or hormonal abnormalities as reported by the parent, and who did not speak English as their first language.

At the second stage, parents and teachers completed normative behavior rating scales: School and Home versions of the ADHD Rating Scales (DuPaul, Power, Anastopolous, & Reid, 1998), the Parent and Teacher Behavior Assessment System for Children (BASC; Reynolds & Kamphaus, 1992), and the Conners (1997) Parent and Teacher Rating Scales-Revised-Short Forms. These scales were chosen based on their empirically-validated cut-offs, thorough coverage of symptoms, and adequate reliability and validity. Further, these scales are among the most widely-accepted rating scales currently used and were judged to have the best cut score data for screening (Ostrander, Weinfurt, Yarnold, & August, 1998; Power et al., 1998). Test-retest reliability for these scales ranged from .62 to .95. Internal reliability in this study ranged from .84 to .96, and validity coefficients ranged from .78 to .98 (Conners, 1997; DuPaul et al., 1998; Reynolds & Kamphaus, 1992).

For the third stage, participants completed an individual, semi-structured, clinical interview (i.e., Schedule for Affective Disorder and Schizophrenia – School Age Version; KSADS-E; Puig-Antich & Ryan, 1986). The

KSADS-E was chosen because its structure is clinically sensitive, and it provides a thorough coverage of childhood disorders (Biederman, Faraone, Keenan, Knee, & Tsuang, 1990; Biederman et al., 1992). The data from the interviews and parent and teacher rating scales were then presented to a clinical diagnostic team consisting of a social worker, board certified child psychiatrist, and licensed clinical child psychologist. A best estimate diagnostic process was implemented, in which the psychiatrist and psychologist independently arrived at a clinical decision regarding ADHD diagnosis, subtype, and presence of comorbid disorders; following their decisions, their answers were compared. Their agreement rates were acceptable for ADHD, its subtypes, and current ODD and CD (all kappas $\geq .89$). In the event of a disagreement, they conferred and easily arrived at consensus. Inattentive and hyperactive-impulsive symptom counts based on parent and teacher report using the 'or' algorithm (Lahey et al., 1994) were used in the current study and ranged from zero to nine.

Comorbid psychiatric problems. For both samples, comorbid symptoms and diagnoses (i.e., anxiety disorders, mood disorders, Post-Traumatic Stress Disorder, Obsessive-Compulsive Disorder, Tic disorders, ODD, and CD) were assessed via modules of the relevant parent semi-structured or structured interview and behavioral rating scales. Autistic Disorder, Mental Retardation, Schizophrenia, Bipolar Disorder, Fetal Alcohol syndrome, known neurological disorder, Cerebral Palsy, Tourette's disorder, and genetic, gonadal, and hormonal abnormalities were exclusionary criteria.

Measures

Temperament traits. The mother (or primary caregiver) completed the common language version of the California Child Q-Sort (CCQ; Caspi et al., 1992). The CCQ is a typical Q-Sort consisting of 100 cards which must be placed in a forced-choice, 9-category, rectangular distribution. The rater describes the child by

placing descriptive cards in one of the categories, ranging from 1 (least descriptive) to 9 (most descriptive). To measure conscientiousness, a scale developed by John and colleagues (John, Caspi, Robins, Moffitt, & Stouthamer-Loeber, 1994) was used, consisting of nine items (e.g., does not give up easily; has high standards for self) with internal reliability of .87. Two items could be argued to overlap with ADHD symptoms: pays attention (item 66) and plans ahead (item 67). Analyses were also conducted using a scale that had these items removed (internal reliability remained .87).

Prenatal levels of testosterone via finger-length ratios. Finger-length ratio was used as a proxy for prenatal testosterone (for discussion of validity of this procedure, see McFadden et al., 2005). This approach is a relatively established procedure for measuring prenatal androgen exposure; however, it remains debated (Cohen-Bendahan et al., 2005). Child finger-length images were obtained using a photocopier,¹ and measurements were taken using a ruler. Two raters then independently recorded measurements of the finger-length of index, middle, ring, and little fingers. The measurements between raters were reliable ($n = 20$; all r above .91; all $p < .01$) with an average correlation between the two raters' measurement of finger-lengths of .97. Ratios were then computed between each of the pairs of fingers on both hands. Ratios are typically less reliable, with established intraclass correlation coefficients of around .75 (Voracek, Manning, & Dressler, 2007). The ratio exhibiting large sex differences and most often used in prior research was the right 2D:4D (Fink et al., 2007; Martel et al., 2008; Stevenson et al., 2007) so primary analyses emphasize this ratio. It should be noted that finger-length ratios show ethnic, as well as sex, differences (Cohen-Bendahan et al., 2005).

Data analysis

Non-normality, outliers, and missingness were addressed in Mplus with robust maximum likelihood estimation, a method of directly fitting models to raw data without imputing values (Curran, West, & Finch, 1996; McCartney, Burchinal, & Bub, 2006; Muthén & Muthén, 2007). The presence of siblings and the result-

ing non-independence of data points were addressed using the clustering feature of Mplus. For analyses utilizing all children, sex was covaried to control for the greater number of boys in the ADHD group, compared to the control group. For analyses examining finger-length ratio, ethnicity was covaried (Manning, Churchill, & Peters, 2007). All analyses were conducted with and without covariates. Results reported below include covariates, and any changes in results due to removal of covariates are detailed. In addition, a data analytic check was conducted in which main study analyses were rerun using age as a covariate, and any changes in results are noted in the text below. Due to the number of statistical tests conducted, results were considered significant if they had a p -value at or below .01.

Results

Descriptive statistics and preliminary data checks

Descriptive statistics. Descriptive statistics on the sample, broken into ADHD, control, and total groups, are shown in Table 2. As shown in Table 2, the right 2D:4D and 3D:4D were marginally more masculine (i.e., smaller) in the ADHD group as compared to the control group ($p < .05$). In addition, children with ADHD, as compared to controls, exhibited significantly less conscientiousness ($p < .01$). These results were as expected.

Preliminary data check I: Subtype differences in finger-length ratios or personality traits in children with ADHD and controls. A MANCOVA, covarying sex and ethnicity, was conducted to examine subtype differences in three finger-length ratios (i.e., right 2D:4D, 2D:5D, and 3D:4D). There were no significant differences between subtypes in finger-length ratios ($F[3, 119] = 1.71, \eta^2 = .04, p > .05$). An ANCOVA, covarying sex, was conducted to examine subtype differences in conscientiousness. The combined subtype had lower conscientiousness than did the inattentive subtype ($F[1, 164] = 4.45, \eta^2 = .03, p < .05$). Sex by subtype interactions were not significant ($p > .05$ for all). Since no subtype differences were noted in hormone measures and in order to maximize statistical power, the two subtypes were pooled in subsequent analyses.

Preliminary data check II: Sex and diagnostic differences in finger-length ratios or personality

Table 2 Descriptive statistics by diagnostic group

	ADHD $n = 168$	Control $n = 144$
R 2D:4D	.94 (.06)	.96 (.07)*
R 2D:5D	1.50 (.19)	1.54 (.21)
R 3D:4D	1.12 (.04)	1.14 (.05)*
Conscientiousness	4.05 (1.25)	6.40 (1.19)

Note: * $p < .05$. ** $p < .01$. Significant group differences tested by t -tests.

¹ Photocopies of finger length may introduce some distortion into the calculation of finger-length ratios (Manning, Fink, Neave, & Caswell, 2005). Such effects were not a major focus because they presumably would not be able to explain ADHD-specific effects. However, as a precaution, calipers were also used in addition to photocopies and rulers for a subset of children to enable comparison between these two different measures of finger length. For the subset of the sample ($n = 57$) who had photocopied image and caliper measurements available, correlations between raw finger lengths were large and significant (average $r = .84, p < .01$). However, correlations between finger-length ratios, computed from photocopied images and caliper measurements, were relatively low and marginally significant (average $r = .26$, average $p = .13$) consistent with the literature on lower reliability of ratio scores than raw scores (Manning et al., 2005). For main study analyses, photocopies of finger-length ratios were analyzed, and this potential unreliability is noted as a limitation in the discussion.

Table 3 Descriptive statistics by sex within diagnostic group

	ADHD (n = 168)		Control (n = 144)	
	Boys	Girls	Boys	Girls
	n = 106	n = 62	n = 72	n = 72
R 2D:4D	.93 (.06)	.97 (.05)**	.95 (.07)	.98 (.06)+
R 2D:5D	1.46 (.18)	1.57 (.17)	1.51 (.20)	1.57 (.22)
R 3D:4D	1.11 (.05)	1.14 (.03)	1.14 (.05)	1.14 (.04)
Conscientiousness	4.02 (1.13)	4.11 (1.44)	6.12 (1.26)	6.68 (1.04)**

Note: + $p < .10$. * $p < .05$. ** $p < .01$. Significant group differences for boys vs. girls within diagnosis were tested by t -tests.

traits in children with ADHD and controls. Descriptive statistics, broken into four groups by sex and diagnostic group, are shown in Table 3. A MANCOVA examined sex and diagnostic differences, controlling for ethnicity, in right 2D:4D, 2D:5D, and 3D:4D. There was a significant multivariate main effect for sex ($F[3, 214] = 4.99$, $\lambda = .94$, $\eta^2 = .07$, $p < .01$) in the expected direction (i.e., boys had more masculine finger-length ratios), but not for diagnostic status ($F[3, 214] = 1.80$, $\lambda = .98$, $\eta^2 = .03$, $p > .05$). The interaction between sex and diagnostic status was not significant ($F[3, 214] = .74$, $\eta^2 = .01$, $p > .05$).

ANCOVA was conducted to examine sex and diagnostic differences in right 2D:4D (i.e., the most widely validated finger-length ratio), controlling for ethnicity. Sex and ADHD main effects were significant in the expected direction: boys and children with ADHD had more masculine finger-length ratios ($F = 13.96$, $\eta^2 = .06$, $p < .01$ for sex; $F = 4.13$, $\eta^2 = .02$, $p < .05$ for ADHD). When ethnicity was not covaried, the diagnostic effect dropped to non-significant ($p = .06$). The interaction between sex and diagnostic status was not significant ($p = .34$). The ADHD effect held in a single-factor ANCOVA with sex and ethnicity covaried ($F = 4.79$, $\eta^2 = .02$, $p < .05$).

Another ANCOVA examined sex and diagnostic differences in conscientiousness. An interaction between sex and ADHD diagnosis was marginally significant ($F[1, 308] = 4.14$, $\eta^2 = .01$, $p < .10$). Sex and diagnostic differences were significant ($F[1, 308] = 8.01$, $\eta^2 = .02$, $p < .05$; $F[1, 308] = 409.39$, $\eta^2 = .48$, $p < .01$). Girls had higher levels of conscientiousness than boys in the non-ADHD group (Table 3). Bivariate correlations were conducted between finger-length ratios, symptoms, and traits in the full sample, shown in Table 4. As can be seen, right 2D:4D was significantly related to inattention, hyperactivity-impulsivity, and conscientiousness, in the expected direction (i.e., more masculine finger-length ratios related to more symptoms and less conscientiousness).

Overall, finger-length ratios showed expected sex differences, supporting the validity of the supposition that the ratios are indexing prenatal testosterone exposure (relative to estrogen) and providing a minimal necessary condition for proceeding to the main analyses. Significant sex differences were apparent for trait measures, also consistent with the

Table 4 Correlations among finger-length ratios, clinical symptoms, and trait and cognitive control

	R 2D:4D	2D:5D	3D:4D
Inatt Sx	-.21**	-.11	-.19**
Hyper Sx	-.20**	-.09	-.19**
Cog Probs (T)	-.08	.03	-.09
Hyper (T)	-.09	-.01	-.06
Cog Probs (P)	-.11	-.05	-.12
Hyper (P)	-.16*	-.11	-.14*
ODD sx	-.14	-.08	-.08
CD sx	.03	.03	-.04
Consc	.22**	.07	.17*

Note: + $p < .10$. * $p < .05$. ** $p < .01$. Inatt Sx = Inattentive symptoms. Hyper Sx = Hyperactive-impulsive symptoms. Cog Probs (T) = teacher-rated Cognitive Problems. Hyper (T) = teacher-rated Hyperactivity. Cog Probs (P) = parent-rated Cognitive Problems. Hyper (P) = parent-rated Hyperactivity. ODD Sx = Oppositional-Defiant symptoms. CD Sx = Conduct Disorder symptoms. Consc = Conscientiousness.

literature. Correlational analyses in the combined group of boys and girls provide preliminary support and justification for formally testing the hypothesized mediation analyses, which now follow.

Question 1: Is more masculinized right 2D:4D associated with (a) more inattentive symptoms and (b) decreased conscientiousness in boys?

In boys, lower (i.e., more masculine) right 2D:4D predicted more inattentive symptoms ($\beta = -.23$, $z = -2.70$, $R^2 = .05$, $p < .01$), controlling for ethnicity (covaried in all subsequent analyses involving finger-length ratios). Lower right 2D:4D also significantly predicted less conscientiousness ($\beta = .25$, $z = 3.20$, $R^2 = .08$, $p < .01$). Low conscientiousness significantly predicted inattentive symptoms ($\beta = -.70$, $z = -11.74$, $R^2 = .48$, $p < .01$), even controlling for item overlap between conscientiousness and inattentive ADHD symptoms ($\beta = -.62$, $z = -9.54$, $R^2 = .42$, $p < .01$). Right 2D:4D was significantly related to hyperactive-impulsive ADHD symptoms ($\beta = -.20$, $z = -2.29$, $R^2 = .06$, $p < .05$). Right 2D:4D was not significantly related to ODD or CD symptoms ($\beta = -.16$, $z = -1.66$, $R^2 = .04$ for ODD symptoms; $\beta = .04$, $z = .64$, $R^2 = .01$ for CD symptoms; both $p > .05$).

For completeness, results were checked in the full sample (boys and girls combined; without covarying sex), with the same results, as follows. Lower right

2D:4D again predicted more inattentive symptoms ($\beta = -.21$, $z = -3.26$, $R^2 = .05$, $p < .01$) and less conscientiousness ($\beta = .22$, $z = 3.76$, $R^2 = .05$, $p < .01$).² Low conscientiousness significantly predicted inattentive symptoms ($\beta = -.74$, $z = 19.73$, $R^2 = .55$, $p < .01$), even controlling for item overlap between conscientiousness and inattentive ADHD symptoms ($\beta = -.67$, $z = -16.56$, $R^2 = .48$, $p < .01$). In the full group, lower right 2D:4D was significantly related to more hyperactive-impulsive symptoms ($\beta = -.19$, $z = -2.82$, $R^2 = .04$, $p < .01$). Right 2D:4D was not significantly related to ODD ($\beta = -.15$, $z = -1.79$, $R^2 = .03$, $p > .05$) or CD symptoms ($\beta = .02$, $z = .29$, $R^2 = .01$, $p > .05$).

Sex was examined as a possible moderator of the relationship between right 2D:4D and conscientiousness and between right 2D:4D and inattentive symptoms. These interactions were not significant, in line with our previous work. In summary, conscientiousness emerged as a possible mediator of prenatal testosterone effects on inattentive ADHD symptoms, because it was related to both ADHD symptom and right 2D:4D. This was next tested formally.

Question 2: Does low conscientiousness mediate the association between more masculinized right 2D:4D and inattentive ADHD symptoms in boys?

Within boys, when right 2D:4D and conscientiousness were both entered as predictors of inattentive symptoms, right 2D:4D no longer significantly predicted inattentive symptoms ($\beta = -.06$, $z = -.84$, $p > .05$), but conscientiousness remained a significant predictor ($\beta = -.69$, $z = -10.86$, R^2 for full model = .49, $p < .01$). The mediation model was significant ($z = -2.85$, $p < .01$; estimate = -8.63; 95% c.i.: -14.57 to -2.7), supporting the mediation model in that the indirect path was significant. The indirect path remained significant when using a conscientiousness scale that eliminated overlap with inattentive ADHD symptoms ($z = -2.36$, $p < .05$; estimate = -6.54; 95% c.i.: -11.95 to -1.12). Thus, low conscientiousness mediated the relationship between right 2D:4D and inattentive ADHD symptoms in boys (Figure 1).

Again for completeness, the same effects were tested in boys and girls combined. Once again, the same result held: When right 2D:4D and conscientiousness were both entered as predictors of inattentive symptoms, right 2D:4D no longer significantly predicted inattentive symptoms ($\beta = -.05$, $z = -1.13$, $p > .05$), but conscientiousness remained a significant predictor ($\beta = -.74$, $z = -19.73$, R^2 for full model = .55, $p < .01$). The mediation model was again significant ($z = -3.66$, $p < .01$; estimate =

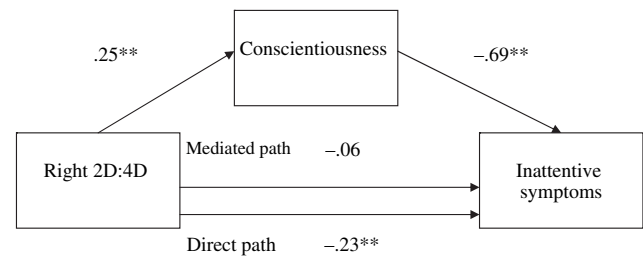


Figure 1 Conscientiousness mediates the relationship between more masculinized right 2D:4D and inattentive ADHD symptoms in boys

-9.11; 95% c.i.: -13.98 to -4.23), even when controlling for overlap between conscientiousness and inattentive ADHD symptoms ($z = -3.27$, $p < .01$; estimate = -7.41; 95% c.i.: -11.86 to -2.96).

Discussion

Hormonal effects are often touted, but less frequently empirically examined, as biological risk factors for childhood psychopathology and for ADHD specifically. The current study examined sex differences in ADHD and related personality traits. It also examined whether a key personality trait might mediate relations between masculinized finger-length ratios and childhood ADHD symptoms. Normative sex differences in conscientiousness found in the control group were not evident in children with ADHD. More masculine finger-length ratios, which are a proxy for relatively higher exposure to prenatal testosterone, were related to lower levels of conscientiousness and more inattentive ADHD symptoms in boys, in line with recent multiple pathway models of ADHD (Sonuga-Barke, 2005). Lower conscientiousness mediated the association between right 2D:4D and inattentive ADHD symptoms. Overall, results are consistent with study hypotheses that more masculinized finger-length ratios are associated with lower levels of conscientiousness and increased inattentive symptoms of ADHD.

Sex differences in traits

This was the first study to examine sex differences in conscientiousness, comparing across control and ADHD groups. Sex differences in conscientiousness varied between the ADHD and control groups, manifested in a marginally significant interaction. While girls had higher levels of conscientiousness than boys within the control group, girls and boys in the ADHD group had comparable, low levels of conscientiousness. The sex difference in conscientiousness found in the control group is in keeping with past research. In childhood, girls typically exhibit higher levels of conscientiousness (i.e., are more planful) than boys (e.g., Else-Quest et al., 2006). This sex difference may not be due entirely to sex, but rather may be due to prenatal hormonal exposure

² Finger-length ratios, measured by calipers, were not significantly related to inattentive ADHD symptoms ($\beta = -.26$, $p > .05$) or conscientiousness ($\beta = .16$, $p > .05$) in boys and girls, although the direction of effects was the same as for hand scan measurements.

that occurs in sex-specific patterns. Further, boys may be at increased risk for ADHD due to their lower levels of conscientiousness, a finding in line with the vulnerability or spectrum hypotheses of personality–psychopathology relations (Watson et al., 2006). This interpretation would also be consistent with the polygenic multiple threshold model of ADHD, which states that girls have a higher threshold for the disorder, or require a greater liability in order to manifest the disorder (Rhee, Waldman, Hay, & Levy, 2001). For example, girls may be relatively protected from the development of ADHD due to their higher levels of conscientiousness in childhood.

More masculinized finger-length ratios and ADHD

Lower (i.e., more masculine) finger-length ratios, particularly the right 2D:4D, were associated with more inattentive ADHD symptoms. This finding replicates other research studies that have found that more masculine finger-length ratios are related to more externalizing problems and more ADHD symptoms (De Bruin et al., 2006; Fink et al., 2007; Martel et al., 2008; McFadden et al., 2005; Stevenson et al., 2007; Williams et al., 2003). More masculinized right 2D:4D was related to trait dysregulation more generally, in that it was associated with lower levels of conscientiousness and increased ADHD symptoms. In the current study, more masculine finger-length ratios (i.e., right 2D:4D) were related to lower conscientiousness, which statistically mediated the relationship between those ratios and inattentive ADHD symptoms in boys.

More masculinized finger-length ratios (i.e., the right 2D:4D), rather than male sex per se, were associated with ADHD and some forms of trait dysregulation. Current results are consistent with the idea that higher prenatal testosterone exposure increases inattention and does so via its association with conscientiousness in childhood. Children (i.e., both boys and girls) with ADHD had more masculine finger-length ratios and lower levels of conscientiousness than children in the control group. In contrast, girls in the control group were characterized by higher levels of conscientiousness than boys

in the control group and also had higher (i.e., more feminine) finger-length ratios.

Limitations

Because the design was cross-sectional and non-experimental, causality cannot be addressed. The study had a relatively small sample of girls, limiting power to detect some sex effects; future work might replicate these findings in a larger sample with equal numbers of boys and girls. Future work might examine observational measures of traits in addition to parental ratings (Rothbart & Goldsmith, 1985). Questions remain about the reliability and validity of photocopy and ruler measurement of finger-length ratios (Voracek et al., 2007). Future work might examine correlations between finger-length ratios, measured via photocopies/rulers and calipers, and actual prenatal testosterone exposure.

Summary

Sex differences in conscientiousness are apparent. More masculinized right 2D:4D was related to inattentive symptoms of ADHD in boys, and this relationship was mediated by low conscientiousness.

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Key points

- Prenatal hormone exposure, childhood personality traits, and psychopathology such as attention-deficit/hyperactivity disorder (ADHD) show sex differences.
- Personality traits like conscientiousness may mediate associations between biological risk factors like prenatal hormone exposure and ADHD symptoms.
- Lower levels of conscientiousness statistically mediated the relationship between more masculine right 2D:4D (i.e., a proxy for increased prenatal testosterone exposure) and increased ADHD inattentive symptoms.
- Results are consistent with the idea that prenatal testosterone exposure may increase general risk for ADHD symptoms acting through the trait mechanism of conscientiousness.

References

- Aksan, N., & Kochanska, G. (2004). Links between systems of inhibition from infancy to preschool years. *Child Development*, 75, 1477–1490.
- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed., text rev.). Washington, DC: American Psychiatric Association.
- Andersen, S.L., & Teicher, M.H. (2000). Sex differences in dopamine receptors and their relevance to ADHD. *Neuroscience and Biobehavioral Reviews*, 24, 137–141.
- Biederman, J., Faraone, S.V., Keenan, K., Benjamin, J., Krifcher, B., Moore, C., Sprich-Buckminster, S., Ugaglia, K., Jellinek, M.S., Steingard, R., Spencer, T., Norman, D., Kolodny, R., Kraus, I., Perrin, J., Keller, M.B., & Tsuang, M.T. (1992). Further evidence for family-genetic risk factors in attention deficit hyperactivity disorder. Patterns of comorbidity in probands and relatives in psychiatrically and pediatrically referred samples. *Archives of General Psychiatry*, 49, 728–738.
- Biederman, J., Faraone, S.V., Keenan, K., Knee, D., & Tsuang, M.T. (1990). Family-genetic and psychosocial risk factors in DSM-III attention deficit disorder. *Journal of the American Academy of Child and Adolescent Psychiatry*, 29, 526–533.
- Braaten, E.B., & Rosen, L.A. (1997). Emotional reactions in adults with symptoms of attention deficit hyperactivity disorder. *Personality and Individual Differences*, 22, 355–361.
- Breedlove, S.M., & Hampson, E. (2002). Sexual differentiation of the brain and behavior. In J.B. Becker, S.M. Breedlove, D. Crews, & M.M. McCarthy (Eds.), *Behavioral endocrinology* (2nd edn, pp. 75–114). Cambridge, MA: MIT Press.
- Brown, W.M., Hines, M., Fane, B.A., & Breedlove, S.M. (2002). Masculinized finger length patterns in human males and females with congenital adrenal hyperplasia. *Hormones and Behavior*, 42, 380–386.
- Caspi, A., Block, J., Block, J.H., Klopp, B., Lynam, D., Moffitt, T.E., & Stouthamer-Loeber, M. (1992). A 'common-language' version of the California Child Q-Set for personality assessment. *Psychological Assessment*, 4, 512–523.
- Cohen-Bendahan, C.C.C., van de Beek, C., & Berenbaum, S.A. (2005). Prenatal sex hormone effects on child and adult sex-typed behavior: Methods and findings. *Neuroscience and Biobehavioral Reviews*, 29, 353–384.
- Conners, C. K. (1997). *Conners Rating Scales-Revised*. Toronto: Multi-Health Systems, Inc.
- Cosgrove, K.P., Mazure, C.M., & Staley, J.K. (2007). Evolving knowledge of sex differences in brain structure, function, and chemistry. *Biological Psychiatry*, 62, 847–855.
- Curran, S.G., West, S.G., & Finch, J.F. (1996). The robustness of test statistics to nonnormality and specification error in confirmatory factor analysis. *Psychological Methods*, 1, 16–29.
- De Bruin, E.I., Verhij, F., Wiegman, T., & Ferdinand, R.F. (2006). Differences in finger length ratio between males with autism, pervasive developmental disorder – not otherwise specified, ADHD, and anxiety disorders. *Developmental Medicine and Child Neurology*, 48, 962–965.
- DuPaul, G.J., Power, T.J., Anastopoulos, A.D., & Reid, R. (1998). *ADHD Rating Scale – IV: Checklists, norms, and clinical interpretation*. New York: Guilford Press.
- Eisenberg, N., Cumberland, A., Spinrad, T.L., Fabes, R.A., Shepard, S.A., Reiser, M., Murphy, B.C., Losoya, S.H., & Guthrie, I.K. (2001). The relations of regulation and emotionality to children's externalizing and internalizing problem behavior. *Child Development*, 72, 1112–1134.
- Else-Quest, N.M., Hyde, J.S., Goldsmith, H.H., & Van Hulle, C.A. (2006). Gender differences in temperament: A meta-analysis. *Psychological Bulletin*, 132, 33–72.
- Fink, B., Manning, J.T., Williams, J.H.G., & Podmore-Nappin, C. (2007). The 2nd to 4th digit ratio and developmental psychopathology in school-aged children. *Personality and Individual Differences*, 42, 369–379.
- Fink, B., Neave, N., Laughton, K., & Manning, J.T. (2006). Second to fourth digit ratio and sensation seeking. *Personality and Individual Differences*, 41, 1253–1262.
- John, O.P., Caspi, A., Robins, R.W., Moffitt, T.E., & Stouthamer-Loeber, M. (1994). The Little-Five: Exploring the nomological network of the five-factor model of personality in adolescent boys. *Child Development*, 65, 160–178.
- Krueger, R.F., & Tackett, J.L. (2003). Personality and psychopathology: Working toward the bigger picture. *Journal of Personality Disorders*, 17, 109–128.
- Lahey, B.B., Applegate, B., McBurnett, K., Biederman, J., et al. (1994). DSM-IV field trials for attention deficit hyperactivity disorder in children and adolescents. *American Journal of Psychiatry*, 151, 1673–1685.
- Lutchmaya, S., Baron-Cohen, S., Raggett, P., Knickmeyer, R., & Manning, J.T. (2004). 2nd to 4th digit ratios, fetal testosterone and estradiol. *Early Human Development*, 77, 23–28.
- Manning, J.T., Churchill, A.J., & Peters, M. (2007). The effects of sex, ethnicity, and sexual orientation on self-measured digit ratio (2D:4D). *Archives of Sexual Behavior*, 36, 223–233.
- Manning, J.T., Fink, B., Neave, N., & Caswell, N. (2005). Photocopies yield lower digit ratios (2D:4D) than direct finger measurements. *Archives of Sexual Behavior*, 34, 329–333.
- Martel, M.M., Gobrogge, K.L., Breedlove, S.M., & Nigg, J.T. (2008). Masculinized finger-length ratios of boys, but not girls, are associated with attention-deficit/hyperactivity disorder. *Behavioral Neuroscience*, 122, 273–281.
- Martel, M.M., & Nigg, J.T. (2006). Child ADHD and personality/temperament traits of reactive and effortful control, resiliency, and emotionality. *Journal of Child Psychology and Psychiatry*, 47, 1175–1183.
- Maughan, B., & Kim-Cohen, J. (2005). Continuities between childhood and adult life. *British Journal of Psychiatry*, 187, 301–303.
- McCartney, K., Burchinal, M.R., & Bub, K.L. (2006). Best practices in quantitative methods for developmentalists. *Monographs of the Society for Research in Child Development*, 71(3).
- McFadden, D., Westhafer, J.G., Pasanen, E.G., Carlson, C., & Tucker, D.M. (2005). Physiological evidence of hypermasculinization in boys with

- the inattentive type of attention-deficit/hyperactivity disorder (ADHD). *Clinical Neuroscience Research*, 5, 233–245.
- Muthén, L.K., & Muthén, B.O. (1998–2007). *Mplus user's guide, fourth edition*. Los Angeles, CA: Muthén & Muthén.
- Okten, A., Kalyoncu, M., & Yaris, N. (2002). The ratio of second- and fourth-digit lengths and congenital adrenal hyperplasia due to 21-hydroxylase deficiency. *Early Human Development*, 70, 47–54.
- Ostrander, R., Weinfurt, K.P., Yarnold, P.R., & August, G.J. (1998). Diagnosing attention deficit disorders with the Behavioral Assessment System for Children and the Child Behavior Checklist: Test and construct validity analyses using optimal discriminant classification trees. *Journal of Consulting and Clinical Psychology*, 66, 660–672.
- Parker, J.D.A., Majeski, S.A., & Collin, V.T. (2004). ADHD symptoms and personality: Relationships with the five-factor model. *Personality and Individual Differences*, 36, 977–987.
- Phoenix, C.H., Goy, R.W., Gerall, A.A., & Young, W.C. (1959). Organizing action of prenatally administered testosterone propionate on the tissues mediating mating behavior in the female guinea pig. *Endocrinology*, 65, 369–382.
- Power, T.J., Andrews, T.J., Eiraldi, R.B., Doherty, B.J., Ikeda, M.J., DuPaul, G.J., & Landau, S. (1998). Evaluating attention deficit hyperactivity disorder using multiple informants: The incremental utility of combining teacher with parent reports. *Psychological Assessment*, 10, 250–260.
- Puig-Antich, J., & Ryan, N. (1986). *Kiddie Schedule for Affective Disorders and Schizophrenia*. Pittsburgh, PA: Western Psychiatric Institute.
- Reynolds, C.R., & Kamphaus, R.W. (1992). *Behavioral Assessment System for Children manual*. Circle Pines, MN: American Guidance Service.
- Rhee, S.H., Waldman, I.D., Hay, D.A., & Levy, F. (2001). Aetiology of the sex difference in the prevalence of DSM-III-R ADHD: A comparison of two models. In F. Levy, & D. Hay (Eds.), *Attention, genes, and ADHD*. Philadelphia: Brumer-Routledge.
- Rothbart, M.K., & Goldsmith, H.H. (1985). Three approaches to the study of infant temperament. *Developmental Review*, 5, 237–260.
- Sonuga-Barke, E.J.S. (2005). Causal models of attention-deficit/hyperactivity disorder: From common simple deficits to multiple developmental pathways. *Biological Psychiatry*, 57, 1231–1238.
- Sowell, E.R., Peterson, B.S., Kan, E., Woods, R.P., Yoshii, J., Bansal, R., Xu, D., Zhu, H., Thompson, P.M., & Toga, A.W. (2007). Sex differences in cortical thickness mapped in 176 healthy individuals between 7 and 87 years of age. *Cerebral Cortex*, 17, 1550–1560.
- Stevenson, J.C., Everson, P.M., Williams, D.C., Hipkind, G., Grimes, M., & Mahoney, E.R. (2007). Attention deficit/hyperactivity disorder (ADHD) symptoms and digit ratios in a college sample. *American Journal of Human Biology*, 19, 41–50.
- Van Leeuwen, K.G., Mervielde, I., De Clercq, B.J., & De Fruyt, F. (2007). Extending the spectrum idea: Child personality, parenting and psychopathology. *European Journal of Personality*, 21, 63–89.
- Voracek, M. (2008). Digit ratio (2D:4D) as a marker for mental disorders: Low (masculinized) 2D:4D in autism-spectrum disorders, high (feminized) 2D:4D in schizophrenic-spectrum disorders. *Behavioral and Brain Sciences*, 31, 283–284.
- Voracek, M., Manning, J.T., & Dressler, S.G. (2007). Repeatability and interobserver error of digit ratio (2D:4D) measurements made by experts. *American Journal of Human Biology*, 19, 142–146.
- Watson, D., Kotov, R., & Gamez, W. (2006). Basic dimensions of temperament in relation to personality and psychopathology. In R.F. Krueger, & J.L. Tackett (Eds.), *Personality and psychopathology* (pp. 7–38). New York: Guilford Press.
- Williams, J.H.G., Greenhalgh, K.D., & Manning, J.T. (2003). Second to fourth finger ratio and possible precursors of developmental psychopathology in preschool children. *Early Human Development*, 72, 57–65.
- Zahn-Waxler, C., Shirtcliff, E.A., & Marceau, K. (2008). Disorders of childhood and adolescence: Gender and psychopathology. *Annual Review of Clinical Psychology*, 4, 275–303.
- Zuckerman, M. (2005). *Psychobiology of Personality* (2nd edn). Cambridge: Cambridge University Press.

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