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Age of pubertal onset and 2nd to 4th digit ratios: Preliminary findings

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ABSTRACT

Background: The second to fourth digit ratio (2D:4D) is used as a marker of prenatal sex hormone exposure. The aim of this study was to evaluate the possible relation between digit ratio and age of pubertal onset.
Methods: Participants were 321 men and 202 women aged between 18 and 28 at the time of assessment who self-reported their onset of puberty (i.e., age at first conscious ejaculation or menarche). Participants' right and left digit lengths were measured from hand scans.
Results: All groups of males, i.e., early, average, and late pubertal onset, had lower mean 2D:4D than the comparable female groups, regardless of the relative timing of their pubertal onset. Among the males, there was a significant difference in digit ratios between individuals who experienced early, average, and late onset of puberty. In the males, we observed a positive relationship between 2D:4D and age of pubertal onset for both right and left hands. There were no significant differences in 2D:4D among the three groups of female maturers. We observed no significant association between digit ratios and age at menarche.
Conclusions: These data lend further support for using 2D:4D as a measure of prenatal androgen exposure.

1. Introduction

The ratio of the second digit to fourth digit (2D:4D) of the hand is a sexually dimorphic trait marker of prenatal hormone exposure. The 2D:4D ratio appears as early as the 2nd trimester of gestation and is stable by age two [1–3]. Overall, the ratio between the second and fourth digit is associated with the estimated ratio of prenatal testosterone relative to prenatal estradiol; as the 2D:4D ratio increases, the estimated ratio of testosterone to estradiol decreases [4,5]. Various lines of evidence link prenatal hormone levels and digit ratios: genital development and digit development are both controlled by the HoxA and HoxD genes [6]; 2D:4D ratios correlate with prenatal sex steroid levels [3,4]; and smaller digit ratios are associated with a marker of greater androgen sensitivity, namely, androgen receptor alleles with fewer CAG repeats [7,8]; but see [9]. Indeed, using a mouse model, Zheng and Cohn [10] provide experimental evidence that the sexually dimorphic 2D:4D ratio is caused by relative levels of androgen to estrogen signaling in utero. Additional support for an association between androgen sensitivity and 2D:4D comes from studies of children with congenital adrenal hyperplasia (CAH), a condition characterized by very high prenatal androgen level as well as studies of males with Klinefelter's syndrome (KS). Most studies of male and female children with congenital adrenal hyperplasia (CAH) report smaller, more “masculinized” digit ratios than age-matched controls (see, for example, [11,12]). KS males have shown digit ratios similar to those displayed by female populations [13].

In typically developing humans, the 2D:4D is significantly higher in females than in males [3,14], whether measured directly in vivo [15] or indirectly from hand photocopies [16]. The sex difference in digit ratios is significantly larger in the right hand than in the left hand [17,18]. Both cross-sectional [3] and longitudinal data [19,20] suggest that sex differences in 2D:4D are unaffected by pubertal onset. Moreover, a recent study [16] of 1656 adults demonstrated that 2D:4D is not strongly associated with adult hormone concentrations. However, to date, relatively few investigators have examined whether there was an association between digit ratios and age of onset of puberty.

Thus far, all the investigations have focused on the association between digit ratios and timing of pubertal onset (menarche) in females. To date, there have been three findings of a significant association between 2D:4D and age at menarche. Matchock [21] found evidence for a negative relationship between right 2D:4D and age at menarche, with lower, more masculinized digit ratios being observed among females who reported a later age of menarche. Using a different methodology, Manning and Fink [22] also observed a significant and negative association between right 2D:4D and age at menarche. A later group [23] observed a significantly negative relationship between digit ratios and age at menarche in both left and right hands. It is noteworthy that for all three of the studies that yielded positive findings, the females represented a large age range, typically from 18 through 70 years old. In contrast, the studies finding no significant relationship between either

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left or right hand digit ratio and age at menarche both drew from older samples of females; the Helle [24] investigation focused on females in their post-reproductive stages and the Muller et al. [25] investigation examined females between the ages of 47 and 62. For example, Helle's Finnish sample may not have been representative of contemporary females due to secular trends [22]. Given that food scarcity and other environmental factors may also influence age at menarche, it is possible that cohort effects may have contributed to the negative findings.

The purpose of the present investigation was to examine the association between 2D:4D and pubertal onset in the general population. We hoped to reconcile the discrepant findings regarding the relationship between digit ratio and pubertal timing in females, and to extend extant knowledge by investigating the relationship between 2D:4D and age of pubertal onset in males. To our knowledge, this is the first such investigation in males. First, we hypothesized that we would see the well-replicated sex difference in 2D:4D, whereby males displayed smaller digit ratios. Second, we predicted that there would be an association between 2D:4D ratios and age of pubertal onset. Given the evidence linking prenatal hormones, genital development, and digit development, we speculated that amount and duration of intrauterine exposure to hormones, particularly androgens, might affect pubertal onset as well as digit ratios in both males and females. We predicted that 2D:4D would be negatively correlated to age at puberty in females, such that later age at menarche would be associated with lower digit ratios. We also predicted that in males, 2D:4D would be positively correlated to age at pubertal onset. That is, we hypothesized that males with earlier age at puberty would display lower digit ratios relative to the males with later pubertal onset.

2. Materials and methods

2.1. Participants

This was a nonclinical university sample of undergraduates enrolled in an undergraduate Psychology class at a large Midwestern university. None of these individuals had been participants in any prior investigation of digit ratios from this lab [15,26].

2.2. Procedure

After the experimenters described the study procedures, the participants gave their written informed consent. Ethics approval was obtained from the Educational and Social and Behavioral Sciences Institutional Review Board. Participants received course credit for completion of the study.

2.3. Digit ratios

The assessment of 2D:4D followed the procedure as outlined in [2] and described in [26]. Briefly, each hand was scanned individually using a photo scanner. Participants placed a hand on the glass of the flatbed scanner with fingers lightly touching. A 5 lb weight was used to apply even pressure to all digits to prevent bending, decrease shadows and provide a contrasting background to assist in scoring. Vernier calipers measuring to 0.01 mm were used to measure the distance between the most basal crease on each finger and the most distal point on the fingertip. If the basal crease or the fingertip was not visible, measurements were not included in analyses. Digit ratios were calculated for each hand by dividing the length of the second digit by that of the fourth digit. Digit ratio asymmetry was calculated as the difference between right 2D:4D and left 2D:4D (Dr-l).

Two independent raters who were unaware of group membership measured digit lengths. Interrater reliability in digit ratio measurements was calculated using intra-class correlation coefficients. Interrater reliability for the right and left hands was 0.970 and 0.965 respectively.

2.4. Age of pubertal onset

All participants were administered a medical history questionnaire as part of their laboratory experience. Embedded in a list of questions regarding their health status, current and past medications and inoculations, participants were queried about their age of pubertal onset. Females were asked to report their onset of menstruation, because the major landmark of puberty for females is menarche. Investigators (such as (27) have used the first conscious ejaculation as a marker of pubertal criterion for males; accordingly, males were asked to report the age at which they experienced this event.

We classified participants as being early, average, or late to attain puberty, according to national averages. We used the average age at menarche from a nationally representative sample of U.S. females [28] and Canadian females [29], approximately 12.54 and 12.72 years, respectively. Moreover, the National Longitudinal Survey of Children and Youth [29] operationally defined early maturation as onset before 11.53 years, average maturation as occurring between 11.53 and 13.91 years, and late maturation as onset > 13.91 years. Thus, based on these published norms, we operationally defined early maturation as menarche beginning prior to age 12, and late maturation as menarche occurring after age 14. We defined average maturation as occurring between the ages of 12 and 13 years of age. In our sample, the mean ages of onset for the females in each of the groups are as follows: early (10.68), average (12.47), and late (14.50).

The largest cross-sectional study of over 6000 boys [27] indicated a mean age of 13.27 ± 1.08 years as the average age of pubertal onset; this age appeared comparable to other estimates from other countries, despite ethnic and geographic differences. Based on the Tomova et al. findings [27], we operationally defined early maturation as pubertal onset before age 12 and late maturation as pubertal onset after age 14. The mean ages of the males in each of the groups are as follows: early (10.78), average (13.09), and late (15.60). The three groups will be referred to as average maturers, early maturers, and late maturers.

3. Results

The sample included 321 males and 202 females. Overall, this was a young group; the mean age at the time of assessment was 18.90 ± 1.18 years (range, 18–28). The males did not differ from the females in terms of age at the time of testing, $t(521) = 0.81$, n.s. Injured or missing digits excluded some measurements, so that scans were not available for all the participants. However, the groups did not differ significantly in terms of missing data. Scans were available for nearly all participants (514 right hands and 519 left hands).[1]

3.1. Comparison of 2D:4D ratio among average maturers

We first compared the male and female average maturers in terms of their digit ratios. *t*-Tests for right 2D:4D revealed a significant sex difference, whereby males displayed smaller right digit ratios than females, $t(432) = -6.33$, $p < 0.001$. Similarly, males displayed smaller left digit ratios than the females, $t(311) = -6.17$, $p < 0.001$. Table 1 provides digit ratios for the left and right hands for early, average, and late maturers in both males and females.

3.2. Effect of pubertal onset on digit ratios

We conducted a two-factor analysis of variance in order to examine the effect of pubertal onset on digit ratios. A 2 (male/female) × 3 (early, average, or late pubertal onset) ANOVA for right digit ratios revealed a significant main effect of sex [$F(1, 508) = 33.13$,

[1] We were missing data from one hand from thirteen participants (11 males and 2 females).