Does early androgen exposure moderate developmental plasticity?

A thesis presented to the faculty of the University of Missouri, Columbia

In partial fulfillment of the requirements for the degree of Master of Arts

By

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Under the advisement of

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The undersigned, appointed by the dean of the Graduate School, have examined the master's thesis entitled

Does early androgen exposure moderate developmental plasticity?

presented by Joseph LaMendola V, a candidate for the degree of Master of Arts, Psychology, and hereby certify that, in their opinion, it is worthy of acceptance.

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Abstract

Little is known about what mechanisms allow some individuals more than others to flexibly develop cognitive competencies and behavioral biases while growing up to better meet the demands of their ecology, a phenomenon known as developmental plasticity. Since many traits are found to be more variable in men than women and because men tend to exhibit greater developmental plasticity than women, Del Giudice et al. (2018) proposed that early androgen exposure may moderate developmental plasticity in both sexes in traits that vary more in men. The associated hypothesis that higher perinatal androgen exposure will enhance responsivity to the environment was tested. Using digit ratio (a well-known measure of perinatal androgen exposure) to predict how strongly early spatial experiences impacted the development of adult spatial ability and sensory processing sensitivity, four separate tests failed to support the hypothesis. Limitations of the tests are discussed.

Introduction

Organisms capable of developmentally adapting their emerging cognitive and behavioral biases to better meet the demands of their local ecology have a significant advantage over their less developmentally flexible peers (for a review, see Snell-Rood, 2013). Developmental plasticity refers to a genotype's ability to express a range of permanent or semi-permanent phenotypes, depending on its early environment (Schlichting & Pigliucci, 1998; West-Eberhard, 2003; Boyce & Ellis, 2005). For example, the bulb mite can express one of two known reproductive strategies, and whether it grows to become a "fighter" or a "scrambler" is primarily determined by the quality of their diet in juvenility (Smallegange, 2011). Natural variation in an organism's level of developmental plasticity has been studied in humans as differential susceptibility to the environment; individuals vary in their responsiveness to both harsh and accommodating environmental influences (Belsky, 1997; Belsky, 2005; Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011; Belsky & Pluess, 2009). The exact mechanisms underlying individual differences in differential susceptibility are not yet known, however a recent proposal suggested that early androgen exposure may be one such mechanism (Del Giudice et al., 2018).

Del Giudice et al. (2018) proposed that early androgen exposure moderates developmental plasticity, and their argument can be summarized as follows: men exhibit greater variability than women in many phenotypes regardless of mean levels, especially in traits that are sexually selected, that is, related to competition for mates or by influencing mate choice (Lehre, Lehre, Laake, & Danbolt, 2009; Geary, 2016, 2017). Greater phenotypic variances in men are not likely to be entirely genetic due to their

higher levels of variation but lower levels of heritability (at least for some traits) when compared to women (see e.g., Ge et al., 2017). As a result, the environment or gene x environment interactions could account for the higher variability among men than women for many traits, especially those related to sexual selection (e.g. Geary, 2016, 2017). Therefore, men's greater trait variability may be due at least partially to enhanced developmental plasticity. Due to the consistent male bias in trait variability and the fact that androgen exposure is sex-differentiated and subject to both genetic and environmental factors, the authors hypothesized that early androgen exposure moderates individual differences in developmental plasticity for those traits that exhibit greater variance in men. These two predictions (that greater male variability may be the consequence of greater male plasticity and that this plasticity may be moderated by early androgen exposure) have yet to be tested. In the following sections, I describe a proxy measure of prenatal and early postnatal androgen exposure, visual-spatial skills, and how the above hypothesis concerning developmental plasticity may be tested.

Perinatal Androgen Exposure

Digit ratio, typically the length of the second (index) finger divided by the length of the fourth (ring) finger on the same hand, has been widely used as a measure of fetal androgen exposure (for a concise review, see McIntyre, 2006) reflecting "total androgenic stimulation, proportional to both the level of circulating androgens and the individual's sensitivity to those hormones" (Breedlove, 2010). The fourth digit inherently has more sex hormone receptors affecting its growth than does the second digit, causing absolute and relative amounts of sex hormones to moderate its rate of growth (Zheng & Cohn, 2011). The effect of increased early androgen exposure decreasing digit ratio has

been experimentally demonstrated across taxa in rats (Zheng & Cohn, 2011) and in rhesus macaques (Abbott, Colman, Tiefenthaler, Dumesic, & Abbott, 2012). A consistent sex difference in digit ratio (lower in men than women; e.g. Berenbaum, Bryk, Nowak, Quigley, & Moffat, 2009) indicates that the effect is present in humans as well, although studies investigating the link between early androgen exposure and digit ratio in women with congenital adrenal hyperplasia (that results in excess prenatal exposure to androgens) and in men with complete androgen insensitivity syndrome have yielded mixed results (Buck, Williams, Hughes, & Acerini, 2003; Brown, Hines, Fane, & Breedlove, 2002; Okten, Kalyoncu, & Yaris, 2002).

Digit ratio has not been found to covary with adult hormone levels, suggesting that digit ratio is determined largely in early fetal and postnatal development and remains mostly stable throughout the lifespan (Hönekopp, Bartholdt, Beier, & Liebert, 2007), though digit ratio may marginally increase with age (Buck et al., 2003) contributing to an increasing sex difference in the ratio with age (Manning, 2010). Digit ratio is likely established within the first two years of life (Manning, Scutt, Wilson, & Lewis-Jones, 1998). Newborns boys tend to have lower mean digit ratios than newborn girls, though whether this effect is more pronounced in the left hand or the right is inconsistent (Ventura, Gomes, Pita, Neto, & Taylor, 2013; Breedlove, 2010; Berenbaum et al., 2009). Interestingly, the digit ratios of newborn girls tend to be more indicative of fetal testosterone than for boys (Ventura et al., 2013; McIntyre, 2006). That the sex difference in digit ratio tends to be greater in the right hand than the left suggests that righthand digit ratio may be more sensitive to early hormones than the left in adulthood (Manning et al.,

1998). However, in adults, digit ratio tends to be lower in men and lower in the dominant hand (e.g. Jaiswal, Kaushik, & Singh, 2017).

Other measures of early androgen exposure such as measuring testosterone levels in amniotic fluid or the anogential distance in newborns covary with digit ratio. Anogenital distance and digit ratio covary with increased masculinization of male traits such as size of genitals (Thankamony, Ong, Dunger, Acerini, & Hughes, 2009). Although digit ratio is a comparatively weaker predictor of early androgen exposure, it is a more reliable measure across experimenters since there is no standardized measure of anogenital distance that has been widely used (Dean & Sharpe, 2013). Another more direct way of assessing early androgen exposure would be to perform a hormonal assay on the mother's amniotic fluid at one or more times during pregnancy. Lower digit ratios for newborn females were significantly related to greater levels of testosterone in the amniotic fluid obtained via amniocentesis typically performed between 14 and 16 weeks (Ventura et al., 2013). Moreover, compared to other methods, digit ratio is a simpler and less invasive means of measuring early androgen exposure. However, it is a relatively noisy measure that may vary by ethnicity (Manning, Stewart, Bundred, & Trivers, 2004; Manning, et al., 2000), though latitude has been weakly implicated (Loehlin, Mcfadden, Medl, & Martin, 2006; but see Xu & Zheng, 2015). Due to its inherent variability, the use of digit ratio to gauge individual differences in prenatal androgen has been discouraged (e.g. Berenbaum et al., 2009; Wallen, 2009), but abundant evidence shows that digit ratio works well to characterize intergroup differences or intragroup correlations in larger samples (Breedlove, 2010).

Visual-spatial Ability

Testing the above hypothesis requires measuring a phenotype whose adult expression is dependent on early environmental conditions. Sex differences are reliably found in measures of visual-spatial processing, and mental rotation tasks produce one of the largest sex differences found in cognitive studies (Lauer, Yhang, & Lourenco, 2019). Beyond mean differences, the variances in spatial abilities significantly differ between the sexes also (e.g. Hedges & Nowell, 1995). The sex differences in both mean levels of performance and variances in performance may be driven by differences in spatial experiences (Gaulin & Hoffman, 1988). This is because, relative to girls and women, boys and men tend to engage more frequently in activities that appear to further the development of spatial abilities (Baenninger & Newcombe, 1989; Newcombe, Bandura, & Taylor, 1983; Greenfield, Brannon, & Lohr, 1994; Subrahmnaym & Greenfield, 1994; Matthews, 1986; Webley, 1981). Even when they engage in the same activities, boys' spatial learning often proceeds more rapidly than that of girls, suggesting a sex difference in sensitivity to spatial-related activities (Herman & Siegel, 1978; Levine, Foley, Lourenco, Ehrlich, & Ratliff, 2016; Nazareth, Herrera, & Pruden, 2013). More directly, early engagement in highly spatial activities was found to moderate the relationship between sex and mental rotation skill (Nazareth, Herrera, & Pruden, 2013). The development of boys' spatial skills also appears to be sensitive to early stressors such as exposure to toxins, disease, or low socioeconomic status (Venkataramani, 2012; Levine, Vasilyeva, Lourenco, Newcombe, & Huttenlocher, 2005; Rosado et al., 2007; Geary, 2016). Since all spatial experiences contribute to a cumulative spatial skillset, one's proportion of high-spatial to low-spatial experiences in childhood can be used to gauge

how beneficial one's early experiences were to the development of adult spatial abilities. Due to the sex difference in the variances of mental rotation scores and spatial skills' general sensitivity to early experiences and environmental conditions, mental rotation is thus an ideal candidate for testing the hypothesized effect of early androgen exposure on developmental plasticity.

Current Study

The hypothesis in question was proposed with two immediate predictions. First, "androgens increase variability by [partially] amplifying plasticity to environmental factors," partly explaining why males tend to be more variable than females (Del Giudice et al., 2018, p. 168). Second, "differences in androgen exposure contribute to individual differences in plasticity in addition to sex differences" (p. 168). The authors sometimes qualify this prediction by expecting this effect to be found primarily in traits that exhibit greater variance in males than females. The authors also suggested three potential tests of their hypothesis: (1) "higher [early] exposure to androgens … should correlate with greater phenotypic variability in traits that show greater male variance" (p. 170), (2) the two-way interaction between early androgen exposure and environmental factors in predicting sensitive developmental outcomes, and (3) testing for group differences in susceptibility between males and females (a two-way interaction between sex and environmental influences, p. 170). If early androgen exposure does promote developmental plasticity in traits that exhibit greater variance in men, then digit ratio is predicted to positively correlate with variance in mental rotation skills, interact with early spatial experiences when predicting mental rotation skills, and interact with sex in predicting mental rotation skills.

Suspecting that greater male phenotypic variance may be due to a causal relation between androgen exposure and increased sensitivity to environmental influences, the authors stated that should their hypothesis be correct, “being exposed to higher levels of androgens during early development should lead to increased susceptibility to the environment for a number of traits..." (p 168). Further, they speculate that, “androgens could affect temperament through a wide range of pathways, including through their interactions with dopamine, serotonin, oxytocin, and other neurotransmitters/neuromodulators that contribute to regulate an individual’s sensitivity to external inputs..." (p 169). So, a fourth prediction was tested: digit ratio should predict sensory processing sensitivity over and above the influence of sex.

Methods

Participants and Procedure

Data from 351 participants was collected between October 2019 and March 2020 from the University of Missouri's pool of undergraduate psychology students and screened for developmental conditions or injuries which affect the length of the fingers or sex determination. Participants were invited to the laboratory where, upon providing informed consent, a researcher scanned their hands to produce a digital image. Next, the participant was escorted to a computer testing station where they were asked to provide anonymized demographic information and complete the tests and survey. Upon completion, the participant was debriefed and compensated with course credit.

Materials and Measures

Digit ratio (2D:4D). Digit ratio was measured using digital software, which provides more consistent measurements than those based on commonly used calipers or a ruler (Kemper & Schwerdtfeger, 2009). Each participant's right hand was scanned on a Canon CanoScan LiDE 400 office document scanner, and the image was imported into Adobe Photoshop 2019. Measurements of digit length were made according to the best practices outlined by the Kiel Institute for the World Economy (Levent & Brañas-Garza, 2014).

Mental rotation task (MRT). The MRT assessed participants' ability to mentally rotate an image of a 3D figure and match it to rotated figures from a set of candidate images. (Peters et al., 1995; Vandenburg & Kuse, 1978; 20 items, Kuder-Richardson 20 = .88). For each item, two of the four candidate images were correct, rotated images and two were incorrect, rotated and reversed images. Responses were scored as correct only if

both correct options were selected.

Childhood Activities Questionnaire (CAQ). Participants indicated their engagement in many common childhood activities such as playing with building blocks or dancing. They indicated their degree of participation on a continuous scale ranging from 0 -"NEVER" to 100 -"ALWAYS" (Cherney & Voyer, 2010; Doyle, Voyer, & Cherney, 2012; spatial subscale $\alpha = .77$, 13 items; nonspatial subscale $\alpha = .87$, 14 items). The assessed spatial activities and other similar ones have previously been shown to predict performance on the MRT and other tests of spatial skills (Newcombe, Bandura, & Taylor, 1983; Doyle, Voyer, & Cherney, 2012; Nazareth, Herrera, & Pruden, 2013; Iwanowska & Voyer, 2013). In order to capture early rather than later spatial experience, participants were instructed to restrict their responses on the CAQ by considering whether they participated in those activities between three and 12 years of age. Following Doyle, Voyer, and Cherney (2012), the natural logarithm of participants' ratios between their mean scores for spatial activities and their mean scores for non-spatial activities was used as a spatial-activity composite score. Composite scores on the CAQ were mean centered with low scores corresponding to the participant having fewer spatial experiences than average based on overall childhood activities and high scores corresponding to more spatial experiences than average.

Vocabulary test. This measure is an 18 item, 4-choice synonym test designed to assess college students' vocabularies (Ekstrom, French, Harman, & Dermon, 1976; $\alpha = .83$). The measure provided a control for general intelligence, providing an assessment of the relation between early spatial activities and MRT that was less dependent on intelligence. This also provided a contrast for the MRT to assess whether early spatial

activities are uniquely related to visuospatial abilities.

Highly Sensitive Child scale (HSC). This is an extension of the narrower Highly Sensitive Person scale previously developed to assess sensory processing sensitivity. The HSC more specifically measures three previously identified factors: aesthetic sensitivity, low sensory threshold, and ease of excitation. Over the course of five studies, the HSC was found to be reliable in child and adolescent samples from eight to 19 years of age, asking respondents to rate their agreement to statements such as "I notice it when small things have changed in my environment," "I don't like loud noises," and "I find it unpleasant to have a lot going on at once (12 items; $\alpha > .7$; Pluess et al., 2018). As described by the scale's authors, "The total score of the [HSC] may capture general sensitivity as described in the Differential Susceptibility model combining both Diathesis-Stress … and Vantage Sensitivity" (p. 66).

Analyses

Four tests of the hypothesis were performed. First, digit ratio was correlated with the squared deviation (i.e., the individual's contribution to the variance) in individual MRT scores. Next, linear models were created for men and women, each predicting MRT scores from scores on CAQ, right-hand digit ratio, their interaction, and vocabulary scores. A Box-Cox transformation was performed to satisfy the assumptions of the general linear model. MRT was not corrected for guessing in order to prevent obtaining negative scores from participants who scored below chance on the task, thus permitting a Box-Cox transformation. The strength of the interaction was compared between the sexes by way of a multigroup regression through structural equation modeling. A partial metric invariance was specified such that the fit of two models could be compared: one model

fixing the interaction path to be equivalent between the two sexes and an alternative model freely estimating the interaction path for each sex. Separately, MRT was regressed onto CAQ, sex, and their interaction to probe for group differences in susceptibility. Lastly, HSC was regressed onto digit ratio and sex.

Results

Data from five participants were omitted from the analyses due to poor quality hand scans, 24 for not following study directions (not reading instructions, not obeying time limits, etc.), three outliers for large studentized deleted residuals, four influential points with comparatively large leverage, and three influential points with a comparatively large Cook's D (per Judd, McClelland, & Ryan, 2017). The final analyses included 313 observations (137 males, 176 females). Seventy-seven percent of the sample identified as White/ European, 11% identified as Black/African/African American, 5% identifying as Asian/Pacific Islander, and 3% identifying as Hispanic/Latinx. The remaining 4% identified as Native American, Middle Eastern, or Other. Digit ratio did not significantly differ between ethnicities ($F(5, 310) = 0.93$, $p = .461$), so ethnicity was omitted as a control from the analyses. All analyses were performed in RStudio 1.1.453 (RStudio Team, 2015; R Core Team, 2018). The Brown-Forsythe test confirmed a greater male (M = 7.47, SD = 3.95) than female (M = 5.12, SD = 3.00) variance on the MRT as required by the hypothesis ($F(1, 314) = 11.47$, $p < .001$, $lnVR = 0.27$, though $lnCVR = -0.10$). As expected, males exhibited a lower digit ratio (M = 0.95, SD = 0.03) than females (M = 0.96, SD = 0.03; $t(289.65) = -3.45$, $p < .001$; see Table 1).

Test 1. Digit ratio did not significantly correlate with the squared deviation of untransformed individual MRT scores ($r = .02$, $p = .673$).

Test 2. Data collection was cut short due to social distancing and isolation measures taken in response to the spread of COVID-19, resulting in an estimated power of approximately 60% for the males and approximately 70% for the females for Test 2.

Replicating previous findings (Doyle, Voyer, & Cherney, 2012), preliminary analyses confirmed CAQ significantly predicted MRT in a simple regression ($t(314) = 3.21$, $p = .001$, $ß = 0.18$), but did not significantly predict MRT scores over and above sex, once sex was added to the model ($t(313) = -0.21$, $p = .836$; model comparison $F(1, 313) = 24.97$, $p < .001$). CAQ was not found to significantly predict MRT within either sex ($ßs < 0.10$, $ps > .193$).

MRT was regressed on CAQ, right hand digit ratio, their interaction, and vocabulary scores. The interaction was not significant across all participants ($t(311) = 0.56$, $p = .577$; Table 2), and neither in males ($t(132) = -1.16$, $p = .250$), nor females ($t(171) = 1.35$, $p = .180$). The interaction between CAQ and right-hand digit ratio was not found to differ between the sexes; the structural equation model freely estimating the strength of the interaction across the sexes did not fit significantly better than the model fixing the strength of the interaction to be equivalent across the sexes ($\chi^2_{diff}(1) = 2.66$, $p = .103$, see Figure 1).

Test 3. MRT was regressed onto CAQ, sex, and their interaction. The interaction between CAQ and sex was not significant ($t(312) = -1.11$, $p = .267$; Table 3). Similar to the results mentioned above, CAQ was not found to predict MRT over and above sex or their interaction.

Test 4. HSC was regressed onto digit ratio and sex. Sex significantly predicted HSC ($t(313) = -2.93$, $p = .004$, $ß = 0.16$) with females (M = 6.64, SD = 9.27) scoring higher than males (M = 3.07, SD = 9.32). Digit ratio did not significantly predict HSC over and above the contribution of sex ($t(313) = 1.68$, $p = .094$).

Discussion

Early androgen exposure was hypothesized to promote developmental plasticity (Del Giudice et al., 2018). On the basis of this hypothesis, we would expect (1) digit ratio to negatively correlate with greater variability in MRT scores, (2) digit ratio to interact with childhood spatial activity when predicting adult MRT scores, (3) males as a group to demonstrate greater susceptibility to childhood spatial activity, and (4) for digit ratio to negatively correlate with sensory processing sensitivity. None of these predictions were found in this study; digit ratio was not found to correlate with phenotypic variance in spatial abilities nor did it interact with childhood spatial activity when predicting adult spatial skills (with no evidence that the interaction differed between the sexes). Additionally, sex and not digit ratio predicted sensory processing sensitivity and did so in the opposite direction than expected under the hypothesis.

In accordance with previous research (Berenbaum, Bryk, Nowak, Quigley, & Moffat, 2009; Lauer, Yhang, & Lourenco, 2019; Doyle, Voyer, & Cherney, 2012), men exhibited lower digit ratios, scored higher on the MRT, reported engaging in more spatial activities during childhood than did women, and engagement in these activities was correlated with MRT scores when the sexes were combined. However, the finding that CAQ predicted MRT overall was only a consequence of the sex difference in the means; CAQ failed to predict MRT *within* sex. Previous research had found that CAQ scores predicted performance on both the MRT and the Water Level Task over and above sex in a hierarchical model comparison of multivariate multiple regressions (Doyle, Voyer, & Cherney, 2012). However, subsequent univariate multiple regressions in that same study found that CAQ scores significantly predicted performance on the Water Level Task over

and above the inclusion of sex ($p < .01$, $\eta^2_p = .06$), but were not significant when MRT was treated as the sole criterion ($p > .3$). If early spatial activities as measured by the CAQ are not contributing to the adult spatial abilities measured by the MRT in a causal manner, then this study may have failed to adequately test the hypothesis that early testosterone exposure is moderating the plastic responses to the environment. Tests 2 and 3 were predicated on the assumption that early spatial activity is causally related to adult spatial skills. Given that no significant correlation was found between childhood spatial activities and adult spatial skills as operationalized, the internal validity of those tests concerning two-way interactions is compromised. However, Tests 1 and 4 correlating digit ratio directly with trait variance and environmental sensitivity also found no relationship, failing to support the hypothesis in conjunction with Tests 2 and 3. Test 4 actually found a female advantage in sensory processing sensitivity rather than the predicted male advantage.

Limitations and Future Directions

There were two important limitations to this study. First, Test 2 was underpowered. Data collection was cut short due to social distancing precautions and the stay-at-home orders issued by the state in the wake of COVID-19 in the spring of 2020. Low statistical power by definition increases the probability of type II errors; the likelihood that the results reported above are false negatives is not negligible. However, power analyses were performed on the assumption that the effect size in question was small to medium in size. If there is an effect that this study failed to detect, that effect size is very unlikely to be large.

The second limitation facing this study was the failure of the CAQ to predict MRT within sex. Further inquiry into the scale found that none of the spatial items correlated with MRT above .2 and only five of the 13 did so above .1 (see Appendix C). As mentioned above, this and other similar measures of childhood spatial activity have been found to correlate with adult MRT in the past (Newcombe, Bandura, & Taylor, 1983; Doyle, Voyer, & Cherney, 2012; Nazareth, Herrera, & Pruden, 2013). That the independent test of the relationship between CAQ and MRT was sufficiently powered indicates that the failure to predict adult spatial ability from childhood activity is more likely due to the properties of the scale than to power. In what way the CAQ qualitatively differs from other similar scales remains to be determined.

Future studies investigating the potential role of early androgen exposure on developmental plasticity are advised to consider selecting scales measuring early experiences and adult traits relevant to the hypothesis that have robust and well-replicated, causal relationships. Large sample sizes are also crucial for the tests of interactions, especially the three-way interaction of sex, early androgen exposure, and environment proposed by Del Giudice et al. (2018). Given large sample sizes, further use of digit ratio to characterize early androgen exposure is not discouraged, though more precise (albeit, more invasive) measures are available.

Should this or any further tests of the hypothesis be taken as conclusive evidence that early androgens do not play a role in moderating developmental plasticity, research should seek to characterize which if any of the known mechanisms most strongly influences individual differences in developmental plasticity. Cumulative genetic factors have been found to predict children's response to developmental influences, where

having more “plasticity genes” is associated with greater susceptibility to the environment (Beaver & Belsky, 2012), likely due to their expression of endophenotypes related to neurosensitivity (Belsky & Pluess, 2016). A separate, noncompeting hypothesis of stochastic sampling posits that individual differences in developmental plasticity can be an illusory conclusion, perhaps resulting from equally plastic individuals differentially sampling the stressors and boons of the same environment (Frankenhuis & Panchanathan, 2011). Similar studies to this one that employ multiple comprehensive scales of relevant childhood experiences are capable of also testing the importance of stochastic sampling by examining the effect that controlling for early experience homogeneity has on the conditional variance of adult traits. The requisite level of detail needed to characterize childhood experience was beyond the capabilities of the CAQ used here.

Further investigation is warranted into developmental plasticity and those factors that may influence it. While evolutionary mechanisms such as sexual selection can account for sex differences in plasticity (Geary, 2016, 2017), accounting for individual differences in degree of plasticity has been a more challenging. Several hormones have been implicated in studies of individual differences in developmental plasticity (e.g. cortisol, Pluess & Belsky, 2011), but none so far have been able to account for the male bias in plasticity observed in humans and other animals.

The inquiry into the mechanisms associated with human developmental plasticity is still in its early stages. Multiple evolutionary models and the results of scores of empirical studies are consistent with the hypothesis that individuals vary in their inherent degrees of developmental plasticity (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van IJzendoorn, 2011). Identifying those individuals most susceptible to environmental

influences can inform interventions by directing attention and resources to those most vulnerable to developmental disruptions or those most susceptible to positive intervention. A more robust understanding of human development and its influences will help refine decisions in both science and policy.

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Table 1

Means, standard deviations, and correlations with confidence intervals

Variable	*M*	*SD*	*d*	1	2	3	4	5
1. MRT	7.47(5.12)	3.95(3.00)	0.67		.11 [-.04, .25]	-.01 [-.15, .14]	.16* [.02, .30]	.04 [-.11, .18]
2. CAQ	0.37(-0.23)	0.40(0.44)	1.43	-.08 [-.25, .09]		-.17* [-.31, -.03]	-.10 [-.25, .05]	-.04 [-.19, .11]
3. Digit ratio	0.95(0.96)	0.03(0.03)	0.33	.01 [-.16, .18]	.21* [.05, .37]		-.03 [-.18, .12]	.14 [-.01, .28]
4. Vocabulary	9.42(8.63)	4.76(4.96)	0.16	.07 [-.10, .23]	-.11 [-.27, .06]	.05 [-.11, .22]		-.02 [-.17, .13]
5. HSC	3.07(6.64)	9.32(9.27)	0.38	-.01 [-.18, .16]	.03 [-.14, .20]	.03 [-.14, .20]	-.04 [-.20, .13]	

Note. Raw scores on the MRT are reported here. *M* and *SD* are used to represent mean and standard deviation, respectively. Means and standard deviations for females are given in parentheses. Values in square brackets indicate the 95% confidence interval for each correlation with correlations for males listed below the diagonal and correlations for females listed above the diagonal. The confidence interval is a plausible range of population correlations that could have caused the sample correlation (Cumming, 2014). * indicates $p < .05$. ** indicates $p < .01$.

Table 2

Regression results using MRT as the criterion for all participants

Predictor	*b*	*b* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	Fit
(Intercept)	3.56	[-0.83, 7.95]			
CAQ	-2.01	[-10.54, 6.51]	.00	[-.00, .01]	
Digit ratio	-0.93	[-5.50, 3.64]	.00	[-.00, .01]	
Vocabulary	0.03*	[0.01, 0.06]	.02	[-.01, .05]	
CAQ*Digit ratio	2.52	[-6.35, 11.38]	.00	[-.01, .01]	
					R^2 = .050** 95% CI[.01,.09]

Note. Scores on the mental rotation task were subjected to a Box-Cox transformation (λ = 0.63). A significant *b*-weight indicates the semi-partial correlation is also significant. *b* represents unstandardized regression weights. sr^2 represents the semi-partial correlation squared. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively.
* indicates p < .05. ** indicates p < .01.

Table 3

Regression results using MRT as the criterion for all participants

Predictor	*b*	*b* 95% CI [LL, UL]	sr^2	sr^2 95% CI [LL, UL]	Fit
(Intercept)	5.24**	[4.65, 5.83]			
CAQ	0.31	[-0.84, 1.45]	.00	[-.01, .01]	
Sex	2.60**	[1.60, 3.60]	.07	[.02, .13]	
CAQ*Sex	-1.04	[-2.89, 0.80]	.00	[-.01, .02]	
					R^2 = .107** 95% CI[.05,.17]

Note. Scores on the mental rotation task were subjected to a Box-Cox transformation (λ = 0.63). A significant *b*-weight indicates the semi-partial correlation is also significant. *b* represents unstandardized regression weights. sr^2 represents the semi-partial correlation squared. *LL* and *UL* indicate the lower and upper limits of a confidence interval, respectively.
* indicates p < .05. ** indicates p < .01.

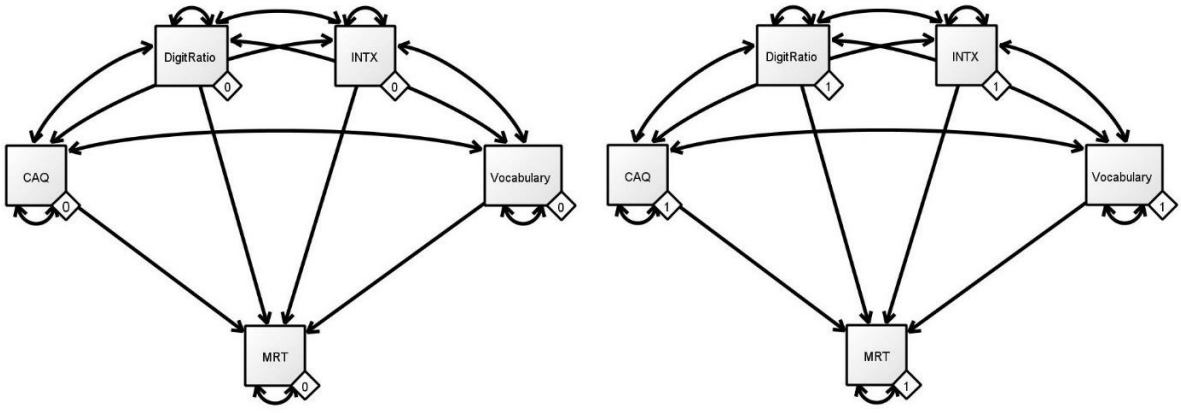

Figure 1. Shown is the structural equation model used in the multigroup regression. Group 0 corresponds to males and group 1 corresponds to females. CAQ: Childhood Activities Questionnaire, DigitRatio: right-hand digit ratio (2D:4D), INTX: the product indicator of the interaction between CAQ and digit ratio, MRT: Mental Rotation Task (Box-Cox transformed to meet the assumptions of the linear model, λ=0.67).

Appendix A: Demographic questionnaire

Please enter your participant number for this experiment. _____

Please indicate your age._____

What was your biological sex at birth?

Male

Female

Intersex/Other

What is your sexual orientation?

Heterosexual (straight)

Bisexual

Homosexual

None/Other

What is your ethnicity?

White/European

Hispanic/Latinx

Black/African/African American

Native American

Asian/Pacific Islander

Other

Estimate your household's yearly income when you were a child (3-12 years old):

$0 - $25,000

$25,000 - $75,000

$75,000 - $ 125,000

$125,000 +

Appendix B: Childhood Activities Questionnaire (CAQ)

This questionnaire aims to determine the activities that you enjoyed as a child. Accordingly, you should consider each of the activities listed below and indicate how frequently you practiced each of them as a child. To do this, you should put an X on the line at the approximate point that corresponds to your involvement. For example, if you never played air hockey, you would put your X as close as possible to "NEVER" on the line. However, if you sometimes practiced archery, you would place the X at a location somewhere between "NEVER" and "ALWAYS" to reflect this fact. For each activity, you can place the X at any point along the line as long as you feel that it reflects how often you practiced a given activity as a child. For the purpose of this study, childhood is understood to last from preschool to early adolescence (3–12 years). Do not hesitate to ask the experimenter if you have any questions.

1 Air hockey……...NEVER ---------- ALWAYS

2 Baby dolls…….…….. NEVER ---------- ALWAYS

3 Barbie dolls and similar…….……... NEVER ---------- ALWAYS

4 Baseball…….…… .NEVER ---------- ALWAYS

5 Basketball…….….. NEVER ---------- ALWAYS

6 Blocks……..… .NEVER ---------- ALWAYS

7 Cars and trucks……..… .NEVER ---------- ALWAYS

8 Coloring……... NEVER ---------- ALWAYS

9 Construction blocks…….. NEVER ---------- ALWAYS

10 Crafts……..……... NEVER ---------- ALWAYS

11 Dancing……..NEVER ---------- ALWAYS

12 Dodge ball……..NEVER ---------- ALWAYS

13 Doll house……..NEVER ---------- ALWAYS

14 Drawing 2D……NEVER ---------- ALWAYS

15 Football…….. NEVER ---------- ALWAYS

16 Hopscotch……..NEVER ---------- ALWAYS

17 Lego blocks……NEVER ---------- ALWAYS

18 Painting 2D…….NEVER ---------- ALWAYS

19 Ping pong……... NEVER ---------- ALWAYS

20 Play Doh or molding clay……. NEVER ---------- ALWAYS

21 Play kitchen objects…….. NEVER ---------- ALWAYS

22 Play musical instruments…….. NEVER ---------- ALWAYS

23 Puzzles……... NEVER ---------- ALWAYS

24 Shooting pool…….NEVER ---------- ALWAYS

25 Stuffed animal……....NEVER ---------- ALWAYS

26 Video games 2D……... NEVER ---------- ALWAYS

27 Watching television……... NEVER ---------- ALWAYS

Appendix C: Correlations of the spatial items on the CAQ with MRT

Spatial Item	All	Males	Females
1	0.059705	0.031788	0.07072
4	0.089764	0.02699	0.064061
5	0.042373	-0.09072	0.091195
6	0.111087	0.194927	0.001731
7	0.182906	0.04823	0.187689
9	0.112025	0.120592	-0.03901
12	-0.0022	-0.14521	-0.02491
15	0.044708	-0.0243	-0.02419
17	0.086896	0.03254	0.096029
19	-0.02201	-0.14686	0.042669
22	0.033214	0.087574	0.05596
23	-0.08366	-0.02231	-0.09686
24	0.041137	-0.04121	0.036675

Appendix D: Proof of the correction-for-guessing factor

Both the mental rotation task (MRT) and the vocabulary test informed participants that their final score would be their total number of problems correct minus "some fraction" of their problems incorrect so as to dissuade participants from guessing more often than necessary. A correction for guessing was not ultimately applied to MRT scores to permit Box-Cox transformation, but it was for the vocabulary test. By what fraction of incorrect scores the participants were to be penalized was not readily available. Below is the rationale and derivation of the penalty fraction assigned in this study.

The total number of responses provided by each participant having completed a test is the sum of their correct and incorrect responses:

$$C + W = T$$

where: C = number of correct responses

where: W = number of incorrect responses

where: T = total number of responses

We know that for a multiple choice test, all incorrect responses were necessarily the result of (best) guessing. However, some portion of guessed responses are expected to be correct by chance alone. Distinguishing between guessed and non-guessed responses, the equation above can be rewritten:

$$\left(C + \frac{1}{k}G\right) + \left(\frac{k-1}{k}G\right) = T$$

where: G = number of guessed responses

where: k = number of response options per question

Here, we can see that the number of correct responses provided by the participant is the sum of the number of correct responses non-guessed and the number of correct responses guessed. The number of guessed responses, however, is not known. To correct for guessing, the expected number of guessed correct responses will be subtracted from their total number of all correct responses. To determine this value from our known information, note that some proportion of guessed responses is expected to be equal to the number of incorrect responses; all incorrect responses are necessarily guessed on a forced-choice, multiple choice test:

$$W = \frac{k-1}{k} G$$

$$\frac{1}{k-1} W = \frac{1}{k-1} * \frac{k-1}{k} G$$

$$\frac{1}{k-1} W = \frac{1}{k} G$$

Thus, the number of guessed correct responses to be subtracted from the total number of correct responses is the number of incorrect responses divided by one less than the number of response options per question. The derivation above allows for the expression of a score corrected for guessing:

$$C - PW = S$$

where: C = number of correct responses

where: P = the penalty fraction

where: W = number of incorrect responses

where: S = the score, corrected for guessing

Using the penalty fraction results in the desired property of assigning a score of zero to an entirely guessed set of responses:

$$C - PW = S$$

$$\left(\frac{1}{k}T\right) - \left(\frac{1}{k-1}\right)\left(\frac{k-1}{k}T\right) = 0$$

$$\left(\frac{1}{k}T\right) - \left(\frac{1}{k}T\right) = 0$$

$$0 = 0$$

QED

Each question on the V-5 offered four response options, so a penalty fraction of $\frac{1}{(4)-1} = \frac{1}{3}$ was used. On the MRT, participants were required to find the two correct responses out of a set of four, so a penalty fraction of $\frac{1}{C(4,2)-1} = \frac{1}{5}$ was used.

Appendix E: Consent form

Consent Form to Participate in a Research Study

Name(s) Of Researcher(s): Joseph LaMendola V

Project IRB #: 2016271

Study Title: Hormones and developmental plasticity

This research study will investigate how hormones affect how people develop based on their experiences. This consent form tells you why we are doing the study and what will happen if you join the study. Please take as much time as you need to read this consent form. You can discuss it with your family, friends, or anyone you choose. If there is anything you do not understand, please ask us to explain. Then you can decide if you want to take part in the study or not. Dr. David Geary, professor of psychological sciences, is providing the funding for this study. Research studies help us to answer questions that may improve our understanding of human behavior, attitudes, beliefs, and interactions. Taking part in a research study is voluntary. You are free to say yes or no. We will only include you in this study if you give us your permission first by signing this consent form.

Why Is This Study Being Done?

The purpose of this research is to investigate how people may develop in different ways depending on the hormones they're exposed to in childhood. Some people are more sensitive to stressors and the environment than others. This study aims to explain how early hormones might play a role in determining that sensitivity.

How Many People Will Be In This Study?

About 370 people will take part in this study.

What Will Happen If I Take Part In This Study?

If you agree, you will do the following: A photograph of just your hands (palms to fingertips) will be scanned into a computer so that we can measure the lengths of your fingers. You'll then take a test of your spatial skills that will ask you to rotate an object in your mind. You will then complete a survey about your childhood play experiences and adversities and your personality. Lastly, you will take a short vocabulary test.

How Long Will I Be In The Study?

You will be in the study for about one hour, today only.

Can I Stop Being In The Study?

Yes, you can stop being in the study at any time without giving a reason. Just tell the researcher or study staff right away if you wish to stop participating. If you do choose to discontinue your participation after beginning, you will still be compensated fully for your participation.

Also, the researcher may decide to take you off this study at any time, even if you want to stay in the study. The researcher will tell you the reason why you need to stop being in the study. These reasons may be (1) a developmental disability or injury that affects the lengths of your fingers, (2) a developmental condition or life-event in which your childhood hormone levels were not sex-typical, such as being born intersex or undergoing hormone replacement therapy, or (3) other developmental or cognitive challenges that prevent you from completing the experiment. In the event that you do not

meet the inclusionary criteria, you will not be allowed to participate and will not be compensated for your time.

Are There Any Benefits To Taking Part In This Study?

There's no direct benefit to you from taking part in this study. However, the information we learn from you during this study may the scientific community learn more about the role hormones play in our development.

Are There Any Risks From Being In This Study?

Some of the questions in the survey may be uncomfortable to answer. Due to the sensitive nature of these items (such as asking about any childhood adversity that you have experienced), a breach in confidentiality could be embarrassing for you as a participant. You do not have to answer all the questions involved in this study and may withdraw your consent to participate at any time. If at any time during the experiment you feel distressed, please let the researcher know as soon as possible. We can omit your data from the study and direct you toward a free, confidential mental health resource, the University of Missouri Counseling Center, available 24/7 at (573) 882-6601. Participation in this experiment also includes the risk that the confidentiality of your data may be breached.

What Other Choices Do I Have If I Don't Take Part?

Instead of being in this study, your choices may include taking part in other research projects within the department or completing an alternate assignment such as a research paper in lieu of participating in an experiment for classes requiring it.

Will Information About Me Be Kept Private?

The information we collect about you will be stored in the researcher's electronic/computer or paper files. Computer files are protected with a password and the computer is in a locked office that only study team members can open. Paper files are kept in a locked drawer in a locked office that only study team members can open. We will give your records a code number and they will not contain your name or other information that could identify you. The code number that connects your name to your information will be kept in a separate, secure location. Information that may identify you may not be given to anyone who is not working on this study without your written consent, or if

required by law.

We will do our best to make sure that your personal information from this study is kept private, but we cannot guarantee total privacy. We may give out your personal information if the law requires it. If we publish the results of this study or present them at scientific meetings, we will not use your name or other personal information. We will keep the information we collect from you for this study to use in future research/to share with other investigators to use in future studies without asking for your consent again. Information that could identify you will be removed from your research information so no one will know that it belongs to you. We can only use the photographs taken of your hands during the study if you give us permission to use them. You will be able to look at them before you give your permission for us to use them.

Will I Be Paid For Taking Part In This Study?

You will not be paid for taking part in this study, but in return for your time and effort, you will be compensated with two credits to be dispersed same-day through

SONA for any course which requires research participation that you are currently taking. If you choose not to participate in this or any other research project, you may complete an alternate assignment such as a research paper for required class credits.

What Are My Rights as a Study Participant?

Taking part in this study is voluntary. If you do decide to take part, you have the right to change your mind and drop out of the study at any time. Whatever your decision, there will be no penalty to you in any way. We will tell you about any new information discovered during this study that might affect your health, welfare, or change your mind about taking part.

Who Can I Call If I Have Questions, Concerns, Or Complaints?

If you have more questions about this study at any time, you can call Joe LaMendola at

(505) 410-7131 or email him at Joseph.LaMendola@mail.missouri.edu. You may also contact Dr. David Geary at GearyD@Missouri.edu. You may contact the University of Missouri Institutional Review Board (IRB) if you:

Have any questions about your rights as a study participant;

Want to report any problems or complaints; or

Feel under any pressure to take part or stay in this study.

The IRB is a group of people who review research studies to make sure the rights of participants are protected. Their phone number is 573- 882-3181.

If you want to talk privately about your rights or any issues related to your participation in this study, you can contact University of Missouri Research Participant Advocacy by calling (888) 280-5002 (a free call) or emailing MUResearchRPA@missouri.edu.

We will give you a copy of this consent form. Please keep it where you can find it easily. It will help you to remember what we discussed today.

Signature of Participant

Consent to Participate in Research

By signing my name below, I confirm the following:

I have read/had read to me this entire consent form.

All of my questions were answered to my satisfaction.

The study's purpose, procedures/activities, potential risks and possible benefits were explained to me.

I voluntarily agree to take part in this research study. I have been told that I can stop at any time.

Subject's Signature	**Date**

Signature of Witness (if applicable)*	**Date**

Appendix F: Debriefing form

Hormones and developmental plasticity

Thank you very much for participating in our study! In this experiment, you were asked to scan your hands, perform a mental rotation task, complete a questionnaire, and test your vocabulary.

The purpose of this study was to investigate the factors that influence developmental plasticity, the ability to express conditional adaptations (a range of permanent or semi-permanent traits) depending on the pressures of our early environment. In a limited way, our bodies can tailor our development to meet the demands of our environment, and some of our early experiences can influence which adult traits we develop or how exaggerated they grow to become. Some people are more sensitive to these environmental pressures than others, and that sensitivity allows them to develop more flexibly than others. The factors that determine this sensitivity are not yet known, but testosterone has been hypothesized to play a role in determining the plasticity (i.e. flexibility) of our development.

Previous research has shown that spatial experiences in childhood can enhance the development of our adult spatial skills. It is also known that early childhood adversities can influence some of our adult personality traits. This experiment used measurements of your fingers to estimate your childhood androgen (e.g. testosterone) exposure. Together, these measures will allow us to test whether early androgen exposure predicts how much our early experiences influence our adult traits. We hope that the results will help define another complex role that hormones play in our development.

We would be happy to further discuss the experiment or our hypothesis with you or to answer any questions you may have now or in the future. You may contact the Principal Investigator, Joe LaMendola, at (505) 410-7131. If you feel any distress as a result of your participation today or for any reason, you should contact the University of Missouri Counseling Center at (573) 882-6601 or at 119 Parker Hall for free, confidential help. You may contact the Campus IRB Office at (573) 882-9585 to ask about your rights as a research subject or to report research related problems.

Thanks again for your participation!