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# Sexual Dimorphism in 2D:4D Digit Ratio is Linked to Anxiety in Rhesus Macaques (*Macaca mulatta*)

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## Abstract

In humans, administering androgens exogenously reduces anxiety. Because prenatal androgen exposure (PAE) has organizational effects on the brain, and because it is higher in males, this may explain why, on average, females are more likely than males to develop anxiety. To assess PAE, the pointer-to-ring-finger digit ratio (2D:4D ratio) is frequently used. Though this phenotype is sexually dimorphic across primate species, preliminary research in a small number of species indicates that PAE's effect on digit ratio may be in the opposite direction when comparing nonhuman primates and humans. In humans, males typically show lower 2D:4D ratios than do females, whereas in nonhuman primates, males exhibit a high 2D:4D ratio. We investigated whether this nonhuman primate digit ratio pattern is present in rhesus macaques (*Macaca mulatta*), and whether individual differences in 2D:4D ratio predicts infant anxiety. At 3-4 months of life, infant monkeys ( $n = 156$ ) were separated from their mothers to assess temperament using a standardized test, the Human Intruder Paradigm. Subjects' 2D:4D ratios were measured between 3-17 years of age ( $M = 7.91$ ). A t-test confirmed that the 2D:4D ratio in rhesus monkeys is consistent with the nonhuman primate pattern, with males exhibiting a higher left-hand 2D:4D ratio than females ( $t_{(74)} = -2.01, p = .049$ ). Controlling for weight and sex, regressions revealed that lower right-hand 2D:4D ratio predicted infant anxiety (as measured by *teeth grinding* and *yawns*) ( $R = .39, p = .022$ ), suggesting that higher PAE may mitigate threat-induced anxiety.

## Introduction

- During prenatal development, androgens have an organizational effect on the brain. Because the ring finger has a high number of androgen receptors, prenatal androgen exposure (PAE) increases the length of the ring finger, but not the length of the pointer finger.<sup>1</sup> As such, the pointer-to-ring-finger digit ratio (2D:4D ratio) tends to be sexually dimorphic, and is commonly used as a proxy measure for PAE.<sup>1</sup>
- Human males typically have a long ring finger and short pointer finger, resulting in low 2D:4D ratio (shown right). Human females typically show the opposite pattern, resulting in high 2D:4D ratio.<sup>1</sup>
- There are sex differences in rates of anxiety, a trait influenced by genetics and experience, with females more likely to suffer from anxiety than males.<sup>2</sup>
- In humans, exogenously administering testosterone mitigates anxiety,<sup>3</sup> and is a common treatment in some parts of the world.
- Through its effect on the developing brain, PAE may contribute to this sex difference by modifying the amygdala,<sup>4</sup> mitigating anxiety in males,<sup>5</sup> and potentially explaining why females are at greater risk to develop an anxiety disorder.<sup>4</sup>
- Because of their genetic and temperamental similarities to humans,<sup>6</sup> rhesus monkeys are often used to model human anxiety, allowing experimenters to better control environmental variables that contribute to anxiety.
- Across primate species, 2D:4D ratio is a validated measure of PAE.<sup>4,7</sup> However, preliminary research suggests the direction of PAE's effect on digit ratio is reversed in nonhuman primate species: males typically have a high 2D:4D ratio, and females typically have a low 2D:4D ratio.<sup>7,8</sup>



## Hypotheses

1. Because PAE appears to increase 2D:4D ratio in other nonhuman-primate species,<sup>8</sup> **we hypothesize that male rhesus monkeys will have higher 2D:4D ratio than females.**
2. Because androgens appear to mediate anxiety,<sup>4,5</sup> **we further hypothesize that 2D:4D ratio will predict infant anxiety.**

## Subjects

- $n = 156$  rhesus macaques
  - Females:  $n = 115$
  - Males:  $n = 36$
- Housed indoors and outdoors at California National Primate Research Center

## Methods

### Independent Variables: Sex and Digit Ratios

- Fingers measured between 3-17 years of age ( $M = 7.91$ ) using a digital caliper.
- Second and fourth digits measured at least twice, until two measurements within  $\pm 1.5$  mm were obtained.
- Subjects' 2D:4D ratio determined by dividing the length of the pointer (2D) by the length of the ring finger (4D).

### Dependent Variable: Anxiety

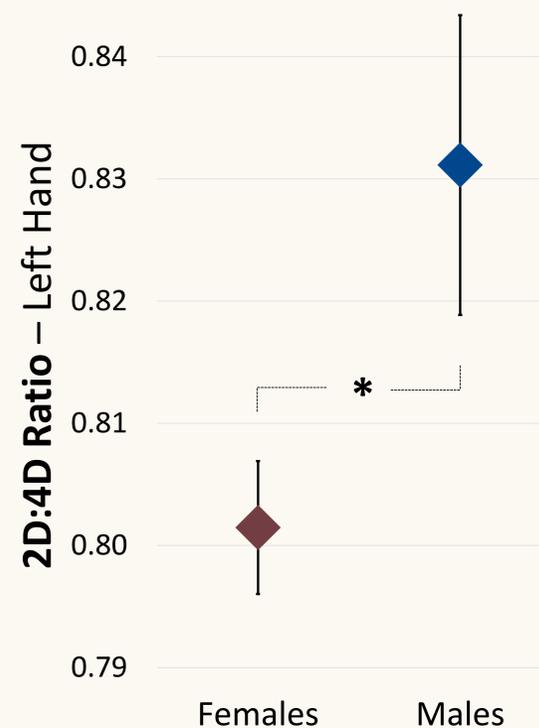
- Anxiety factors assessed at 3-4 months of age in a Biobehavioral Assessment.
- Threat-induced anxiety assessed using the Human Intruder Paradigm.
  - *Yawning* and *teeth grinding*

### Analyses:

- Performed using independent t-test and regression.

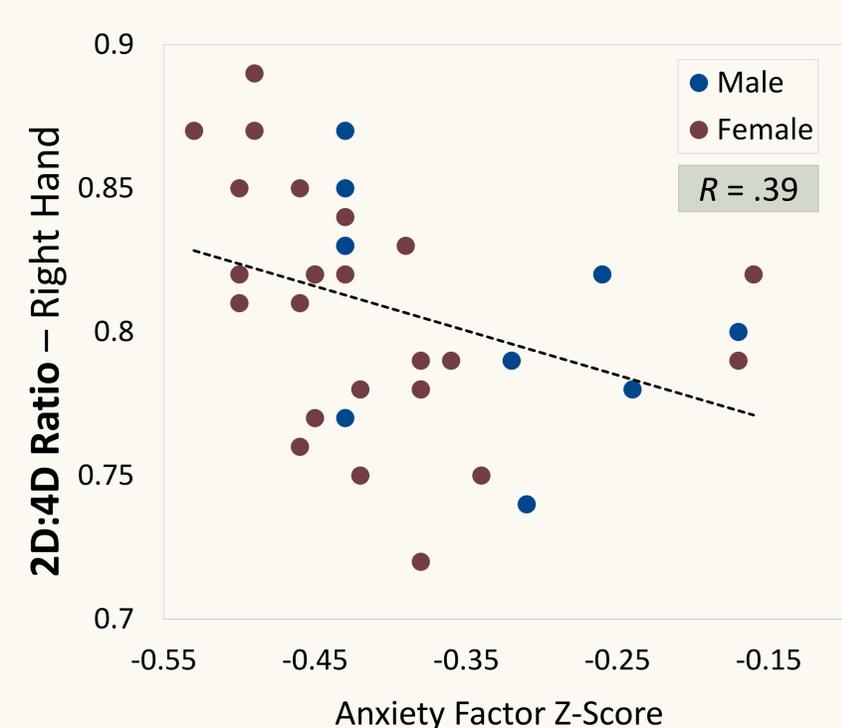
## Results

### Sex Difference in Left-hand 2D:4D



Independent t-test showed that males had higher left-hand 2D:4D ratio ( $M = 0.826, SD = 0.039$ ) than did females ( $M = 0.797, SD = 0.044, t_{(74)} = -2.01, p = .049$ ).

### Low Right-hand 2D:4D Predicts High Anxiety



Regression showed that lower right-hand 2D:4D ratio predicted threat-induced anxiety ( $F_{(1, 34)} = 5.74, R = .39, p = .022$ ). Neither sex, weight, nor age were retained in the model.

## Discussion

- As hypothesized, there was a sex difference in rhesus monkeys' digit ratios, and in the expected direction for nonhuman primates:<sup>8</sup> males had higher 2D:4D ratio than females. Though several studies have previously investigated 2D:4D ratio in rhesus monkeys, this is the first report of a significant sex difference in this particular species.
- Consistent with previous research and our hypothesis, 2D:4D ratio predicted temperamental anxiety. Infants with lower digit ratios (lower PAE) displayed greater anxiety when confronted by a simulated predator. This suggests PAE has an organizational effect on the brain that buffers against threat-induced anxiety.
- It is possible that higher prenatal androgen exposure explains, in part, why human males are at decreased risk for developing an anxiety disorder.<sup>4</sup>

## Conclusions

1. **Like other nonhuman primates, rhesus monkeys show sexually dimorphic 2D:4D, with males having higher ratios than females.**
2. **Androgens may prenatally program parts of the brain responsible for anxiety, which may explain why females are at greater risk for anxiety disorders.<sup>2,4</sup>**

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