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

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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 the developing brain 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 predict 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(120) = 2.01, p = .049). Controlling for weight and sex, regressions revealed that higher right-hand 2D:4D ratio predicted infant anxiety (as measured by teeth grinding and yawning) (R = .39, p = .022), suggesting that higher PAE may mitigate threat-induced anxiety.

### Hypotheses

1. Because PAE appears to increase in other nonhuman-primate species, we hypothesize that male rhesus monkeys will have higher 2D:4D ratio than females.
2. Because androgens appear to mediate anxiety, we further hypothesize that 2D:4D ratio will predict threat-induced 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 ± 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

<table>
<thead>
<tr>
<th>Gender</th>
<th>2D:4D Ratio – Left Hand</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>0.81</td>
</tr>
<tr>
<td>Females</td>
<td>0.79</td>
</tr>
</tbody>
</table>

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(120) = 2.01, p = .049).

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

<table>
<thead>
<tr>
<th>Anxiety Factor Z-Score</th>
<th>Low Right-hand 2D:4D Predicted Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.75</td>
<td>0.88</td>
</tr>
<tr>
<td>0.8</td>
<td>0.9</td>
</tr>
</tbody>
</table>

Regression showed that lower right-hand 2D:4D ratio predicted threat-induced anxiety (F (1,74) = 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: 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 temperament 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.

### 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.

### References


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