

# PHYSIOLOGICAL RISKS AND NEURAL UNDERPINNING OF ANXIETY-LIKE BEHAVIORS IN INFANT RHESUS MACAQUES

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## Introduction

- **Anxiety disorders** exhibit a **treatment-prevalence paradox**, characterized by increased treatment rates without a corresponding reduction in prevalence <sup>1, 2</sup>
  - **Early prevention and interventions** are promising approaches to address this paradox in anxiety disorders, necessitating the **early identification of anxiety symptoms**
  - **MRI studies** have provided insights into early neuroanatomical changes associated with anxiety disorders <sup>3, 4</sup>
  - There remains a gap in understanding how **early physiological factors** contribute to the developmental trajectories of **anxiety-related behaviors** and brain volume
- ⇒ This study aims to investigate the association between (1) **early anxiety-like behaviors** and **physiological precursors**, focusing on **gut microbiome imbalance** and **iron deficiency** and (2) their individual correlations with brain structural volumes in infant Rhesus macaques during their first year of life.

## Methods

**Sample (n = 41)**

- Females = 19 & Males = 22
- Iron Deficiency = 15 (only 12 got treatment)
- All subjects displayed no developmental abnormalities or preceding conditions affecting their responses to stimuli

### Physiological Precursors

- Proteobacteria Imbalance
- Iron Deficiency

### Structural Volume (12 months)

- Amygdala
- Cingulate Cortex
- Hippocampus
- White & Gray Matter
- Total Brain Volume

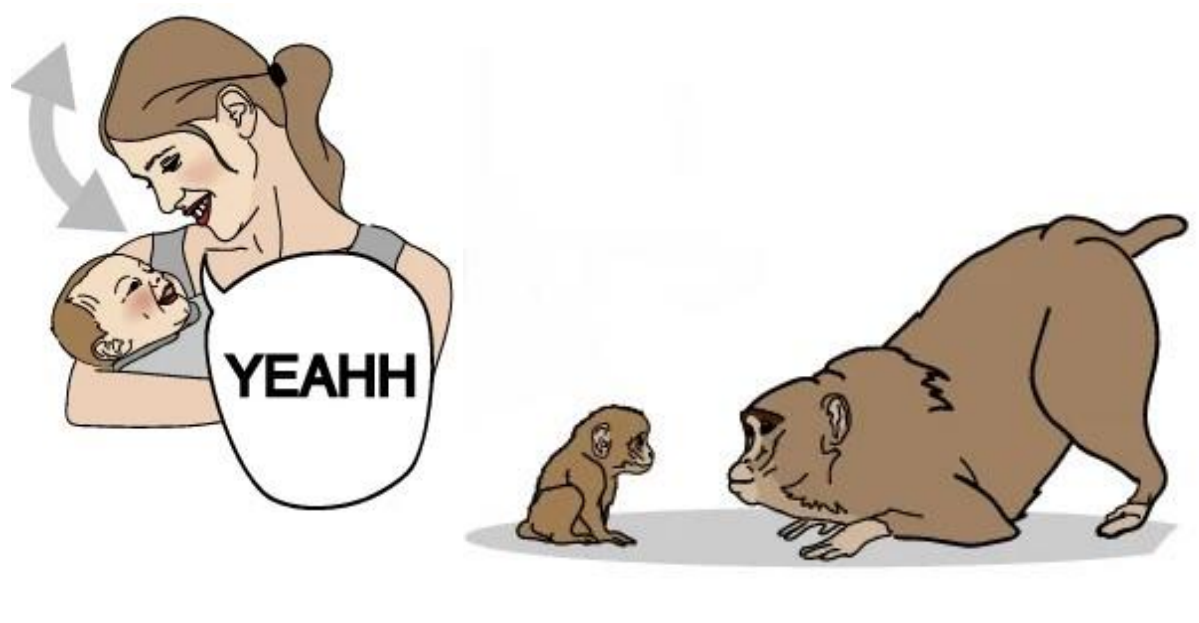
### Anxiety-Like Behaviors

#### Mother-Infant Scoring

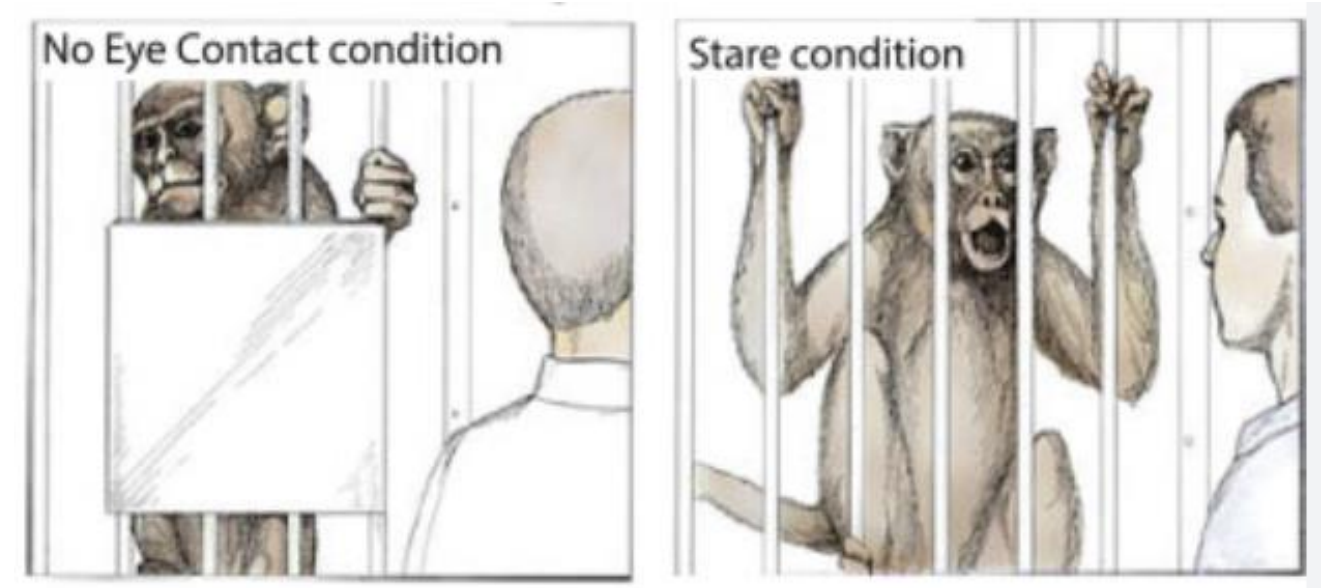
- Pre-Weaning (1-4 months)
- ↑ Mother-Infant Contact
  - ↓ Exploration

#### Human Intruder Test

- Post-Weaning (8 months)
- ↑ Freezing
  - ↑ Barking

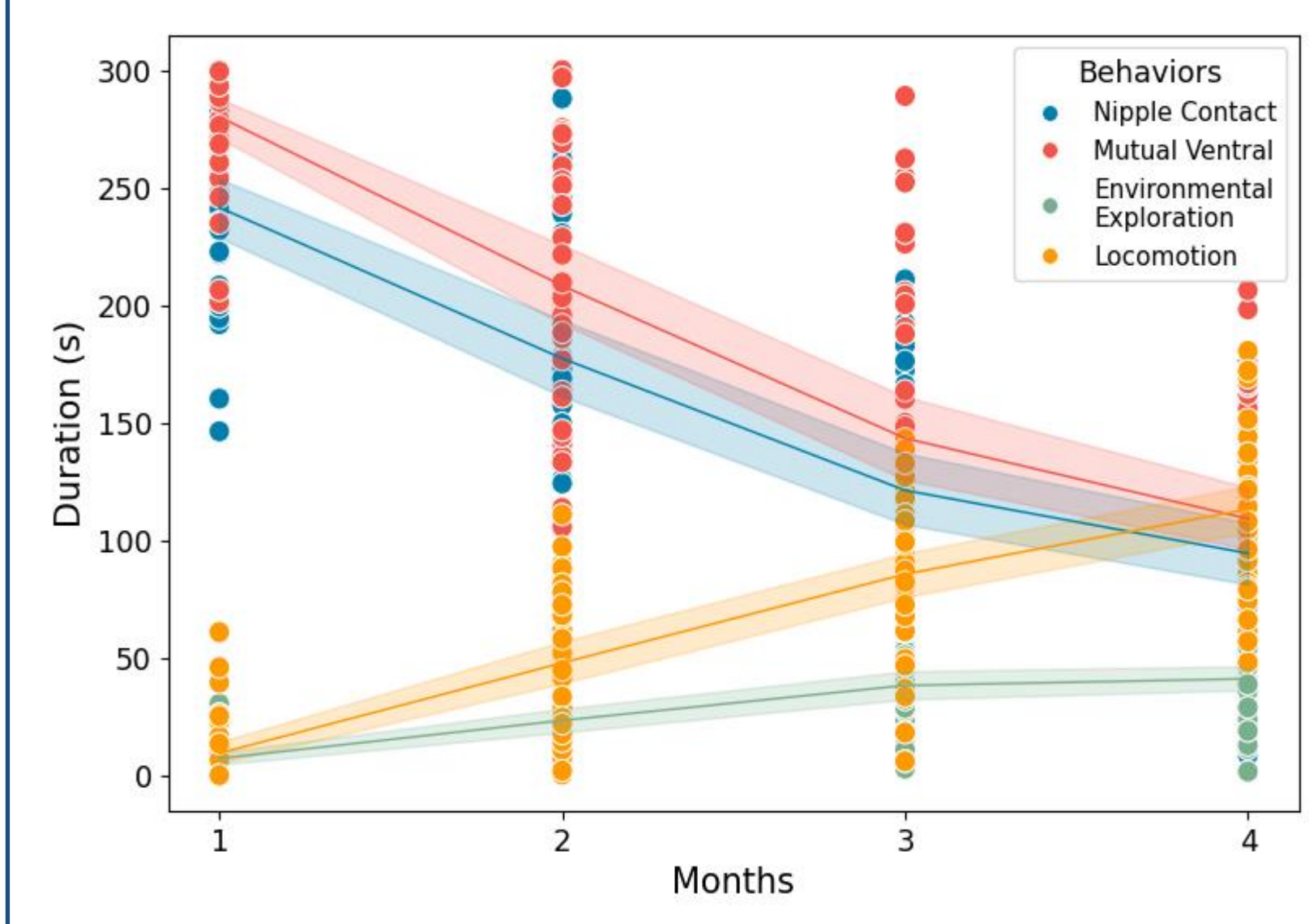


<https://doi.org/10.1038/ncomms11940>

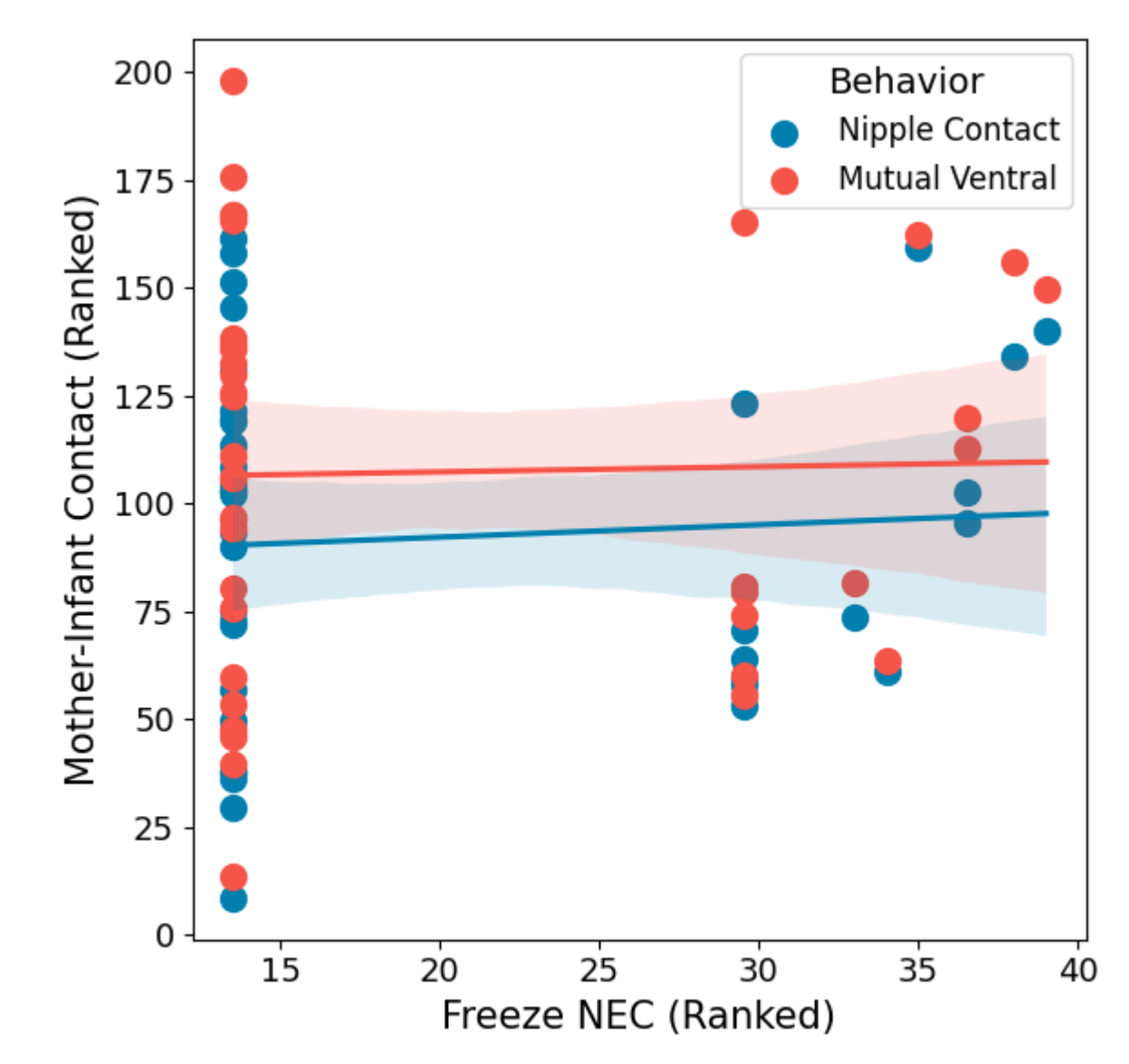


<https://doi.org/10.1016/j.neuro.2017.03.004>

## Anxiety-Like Behaviors

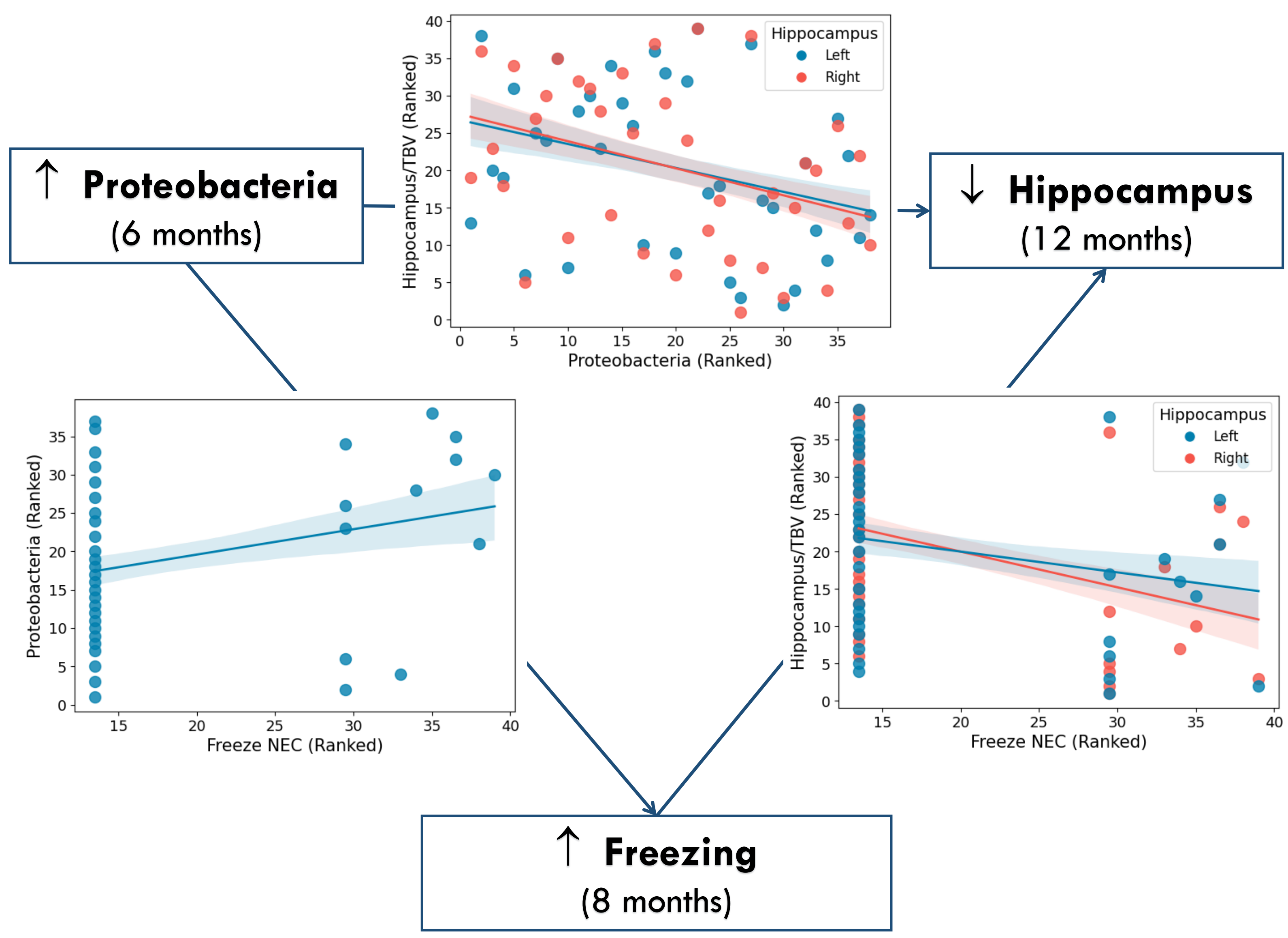


**Figure 1.** Line plots with scatter dots for the four behaviors in Mother-Infant Scoring at four different months after birth. Across the observed months, there is a decrease in nipple contact and mutual ventral and increase in environmental exploration and locomotion, representing decreased mother-infant contact and increased exploration, respectively.



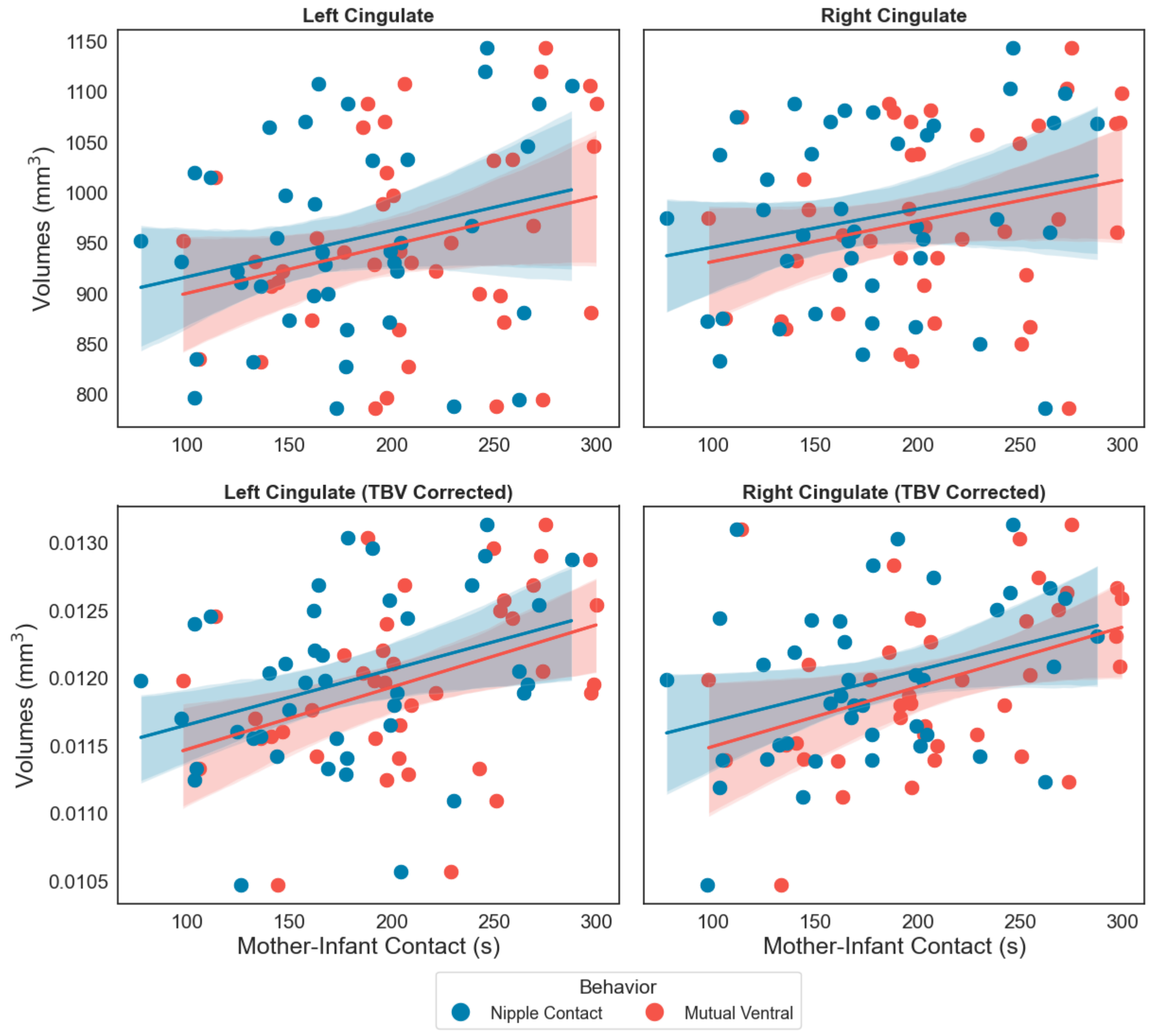
**Figure 2.** Scatter plot with best-fit line for the correlation between behaviors in Mother-Infant Scoring and Human Intruder Test. Mutual ventral and nipple contact behavior at 4 months is positively correlated with freezing behavior in no-eye contact condition at 8 months ( $p < 0.05$ ).

## Anxiety-Like Behaviors Proteobacteria & Hippocampus



**Figure 3.** Scatter plots with best-fit line for the correlations between behaviors in Human Intruder Test, Proteobacteria level, and hippocampal volume. There is a positive correlation between Proteobacteria level at 6 months and freezing behavior during no-eye contact condition in Human Intruder Test at 8 months. Both factors also negatively correlate with left and right hippocampal volume corrected for total brain volume (TBV) at 12 months. All correlations have  $p < 0.05$ , except the one between freezing behavior and left hippocampus.

## Anxiety-Like Behaviors Cingulate Cortex



↑ **Mother-Infant Contact** (4 months) → ↑ **Cingulate Cortex** (12 months)

**Figure 4.** Scatter plots with best-fit line for the correlation between behaviors in Mother-Infant Scoring and cingulate cortex volume. Mutual ventral and nipple contact behavior at 4 months are positively correlated with left and right cingulate cortex volume with and without total brain volume correction (TBV) at 12 months ( $p < 0.05$ ).

## Conclusion

- There is a **consistency of anxiety-like behaviors** during the first year of life
- Anxiety-like behaviors are associated with **higher Proteobacteria abundance**, **larger cingulate cortex**, and **smaller right hippocampus**

## References

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