

Prefrontal Connections to the Extended Amygdala and Their Role in Early-Life Inhibited Temperament in Adolescent Rhesus Monkeys

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The extended amygdala has been implicated in the expression of fear and anxiety¹. However, how these regions interact with newly expanded areas of the primate frontal cortex remains largely unknown. Using behavioral data collected from the BioBehavioral Assessment (BBA)² program at the CNPRC, we explore the contributions of prefrontal-connections in early-life inhibited temperament, a risk factor for the later development of anxiety disorders.

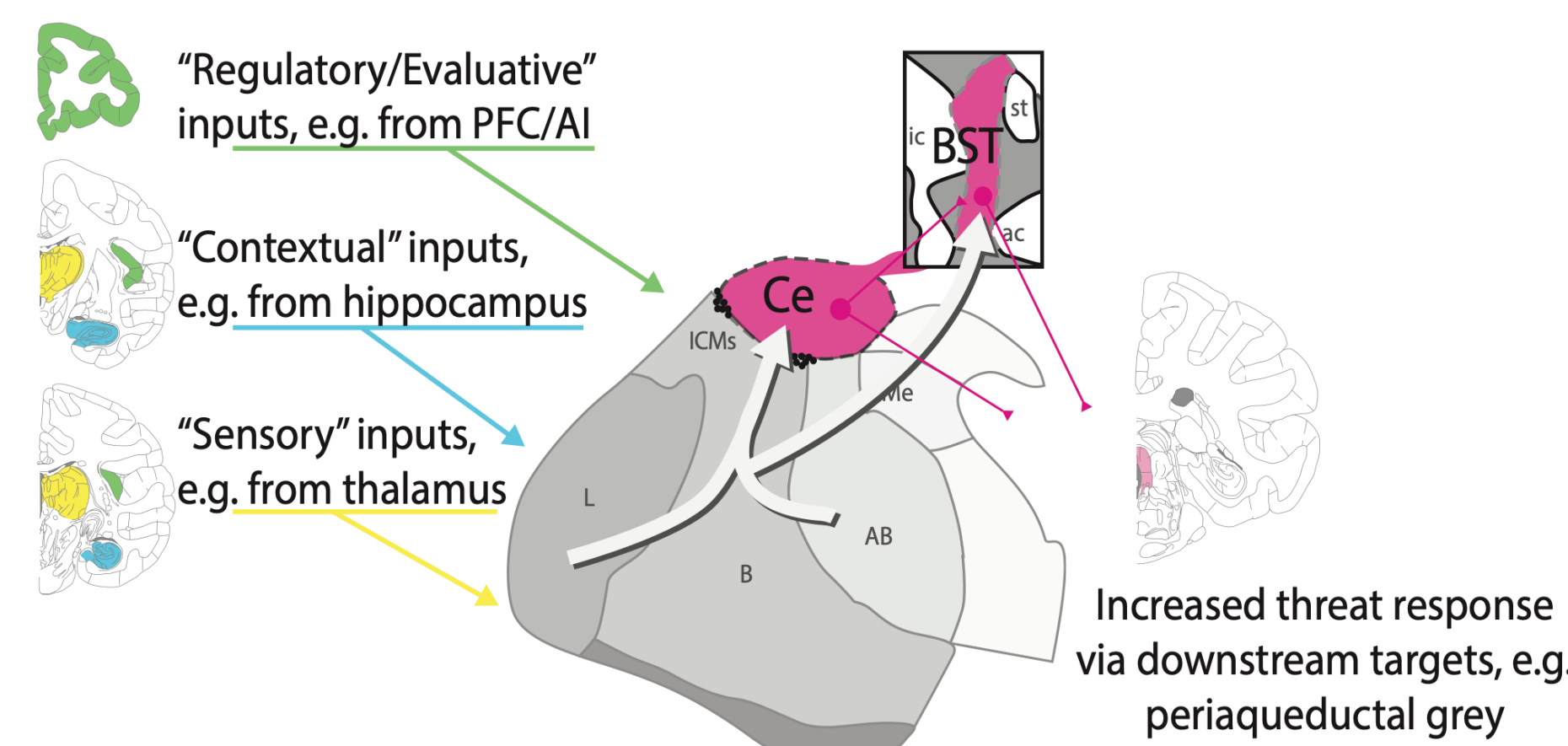


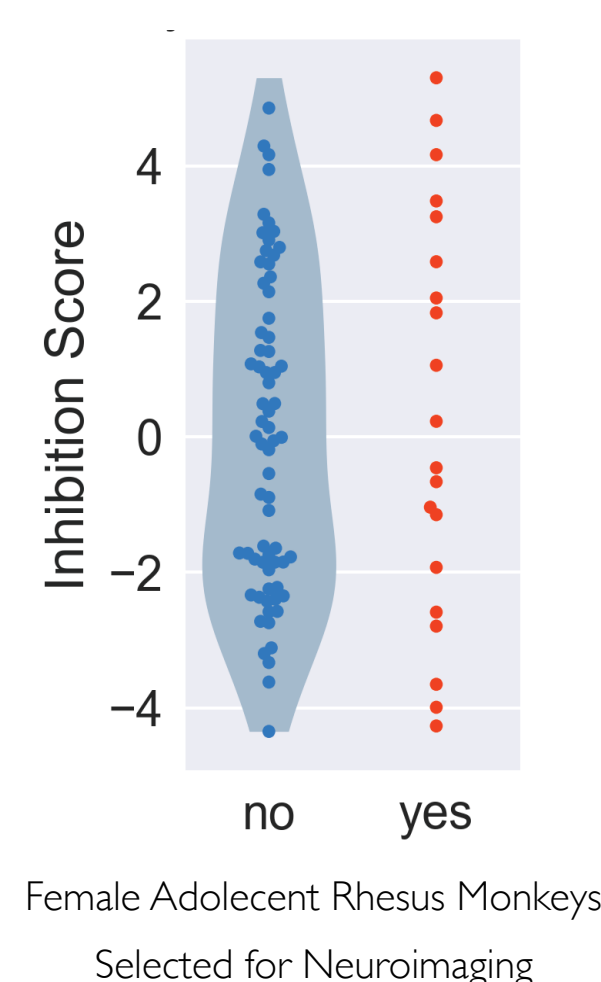
Image adapted from Fox et al. (2015)

Methods

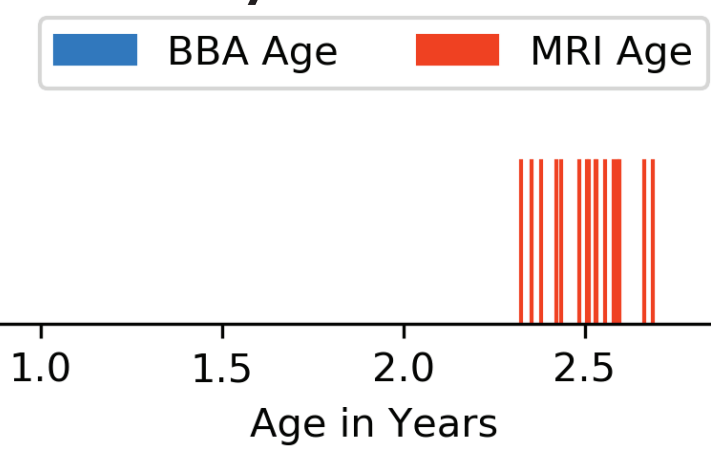
Defining Inhibited Temperament. Our measure of inhibited temperament (IT) is based on behavioral data collected during infancy².

- BBA (age: 3-4 months)
- Behavioral observations^{11,12}
- Novel objects reaction¹¹
- Blood samples^{11,12}
- Recognition memory¹¹
- Aggressive video reaction¹¹
- Brief human intruder¹¹
- DEX suppression test¹¹
- Temperament ratings¹¹

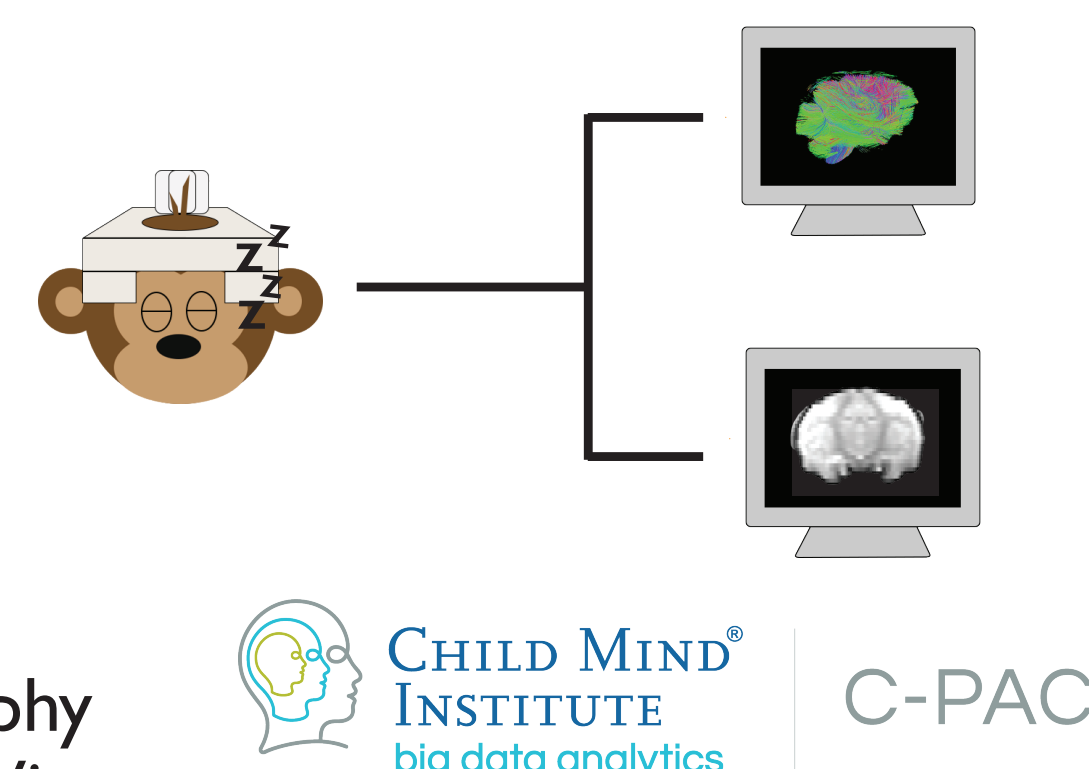
Animal Selection. Twenty 2-3 year old female rhesus macaques (*macaca mulatta*), previously assessed for IT at ~3-4 months of age were selected for this study.



Female Adolescent Rhesus Monkeys Selected for Neuroimaging



MRI. MRI was collected using a Siemens Skyra MRI scanner and a dedicated rhesus 8-channel surface coil. Scans were collected under light isoflurane anesthesia. For DTI, images were preprocessed, standardized, and normalized using neuroimaging software like FSL, Camino, and DTI-TK. Fiber tractography analyses were performed using TrackVis.



Resting-state fMRI were preprocessed using the Configurable Pipeline for the Analysis of Connectomes (C-PAC) by the Child Mind Institute³. C-PAC is a configurable, open-sourced, nipy-based automated processing pipeline. fMRI analyses were done using Nilearn.

Acquisition Parameters:
For DTI: TR = 6300 ms, TE = 90 ms, matrix = 200x200, FoV = 140 mm, 1.4 mm contiguous slices, echo spacing = 0.96 ms, b-value = 1200 s/mm², 60 non-collinear directions
For rs-fMRI: TR = 2000 ms, TE = 23.40 ms, flip angle = 80 degrees, matrix = 168x140, FoV = 152 mm, 35 slices

Acknowledgements

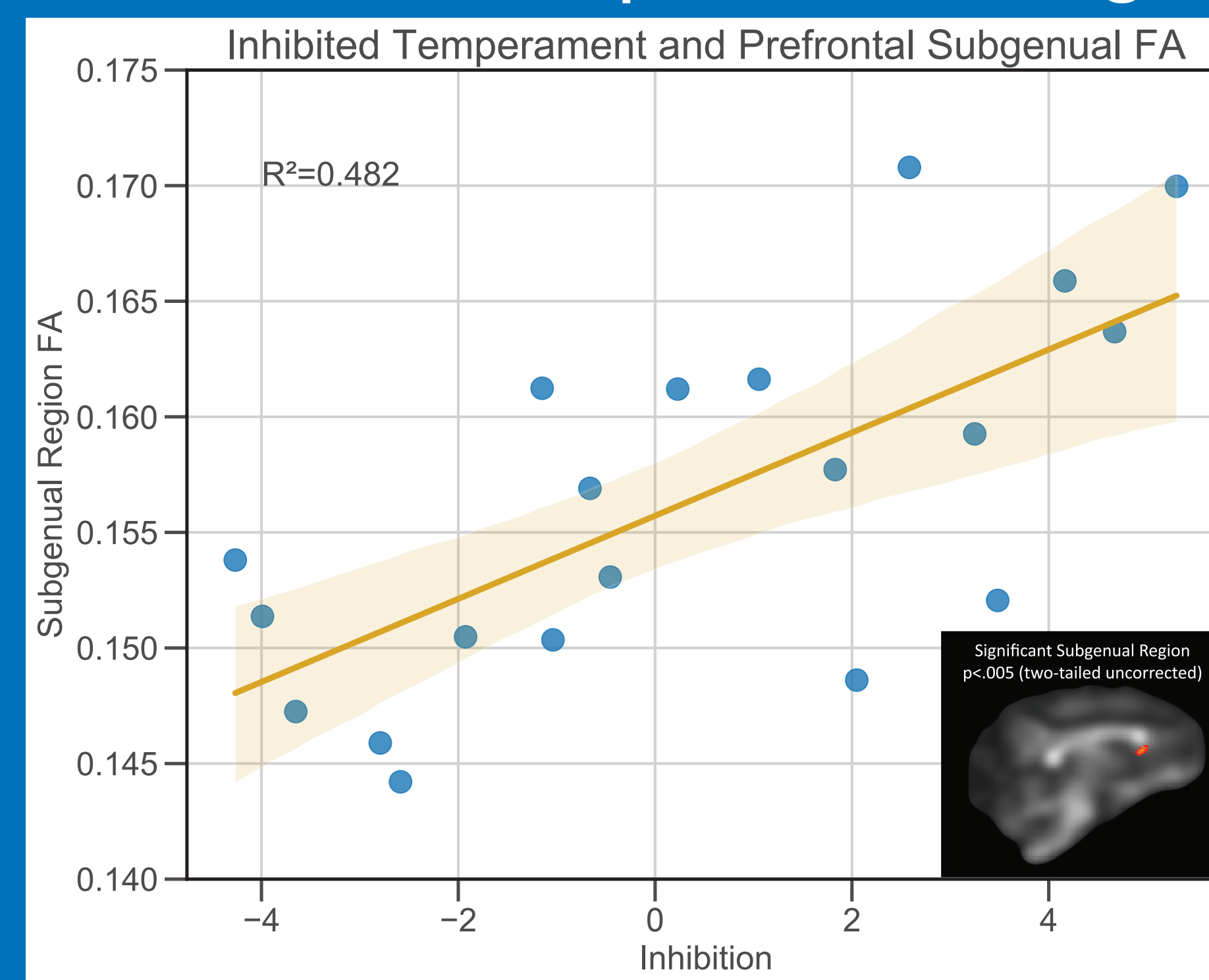
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DTI Results

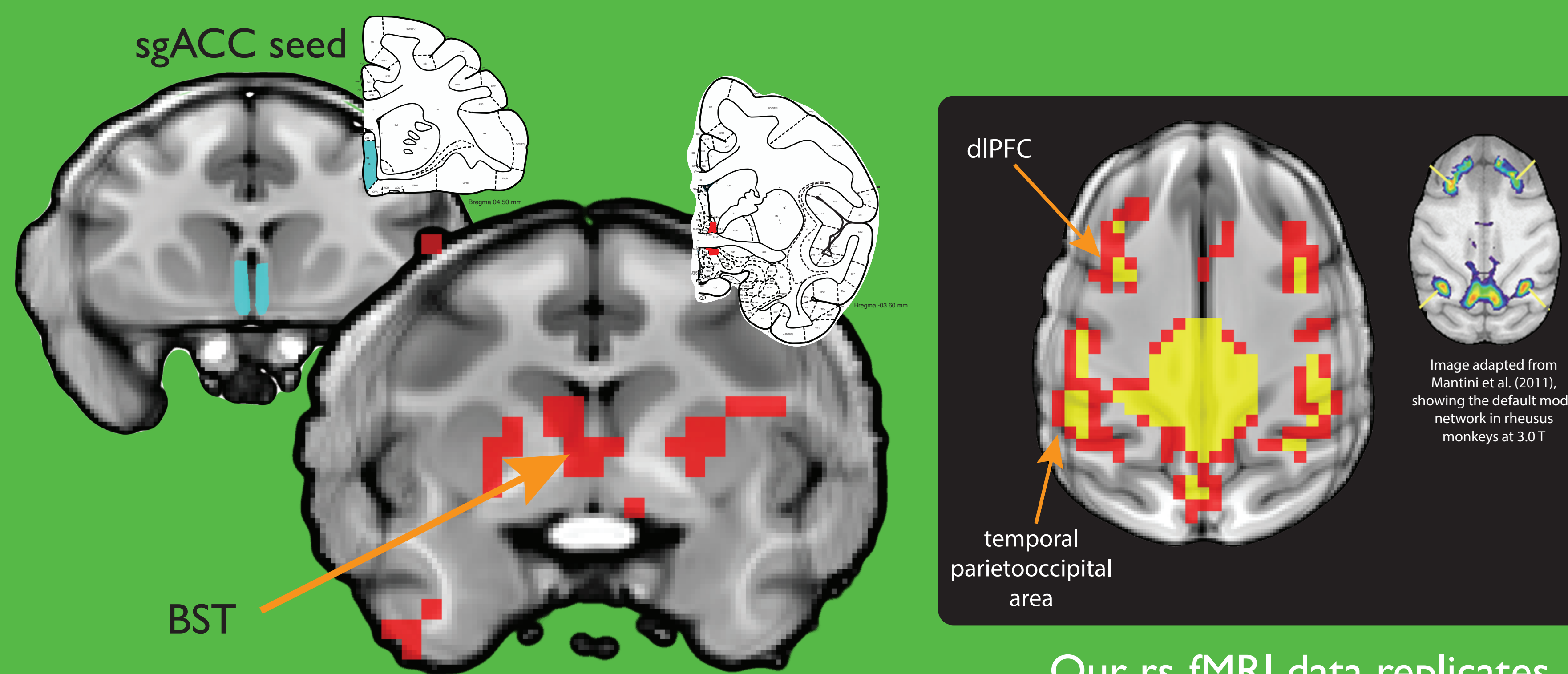
Inhibited Temperament is significantly correlated with FA in subgenual prefrontal cortical white matter.



Whole-brain voxelwise analyses demonstrated a significant positive correlation between IT and FA in the subgenual prefrontal cortical white matter ($p < .005$, two-tailed uncorrected).

rs-fMRI Results

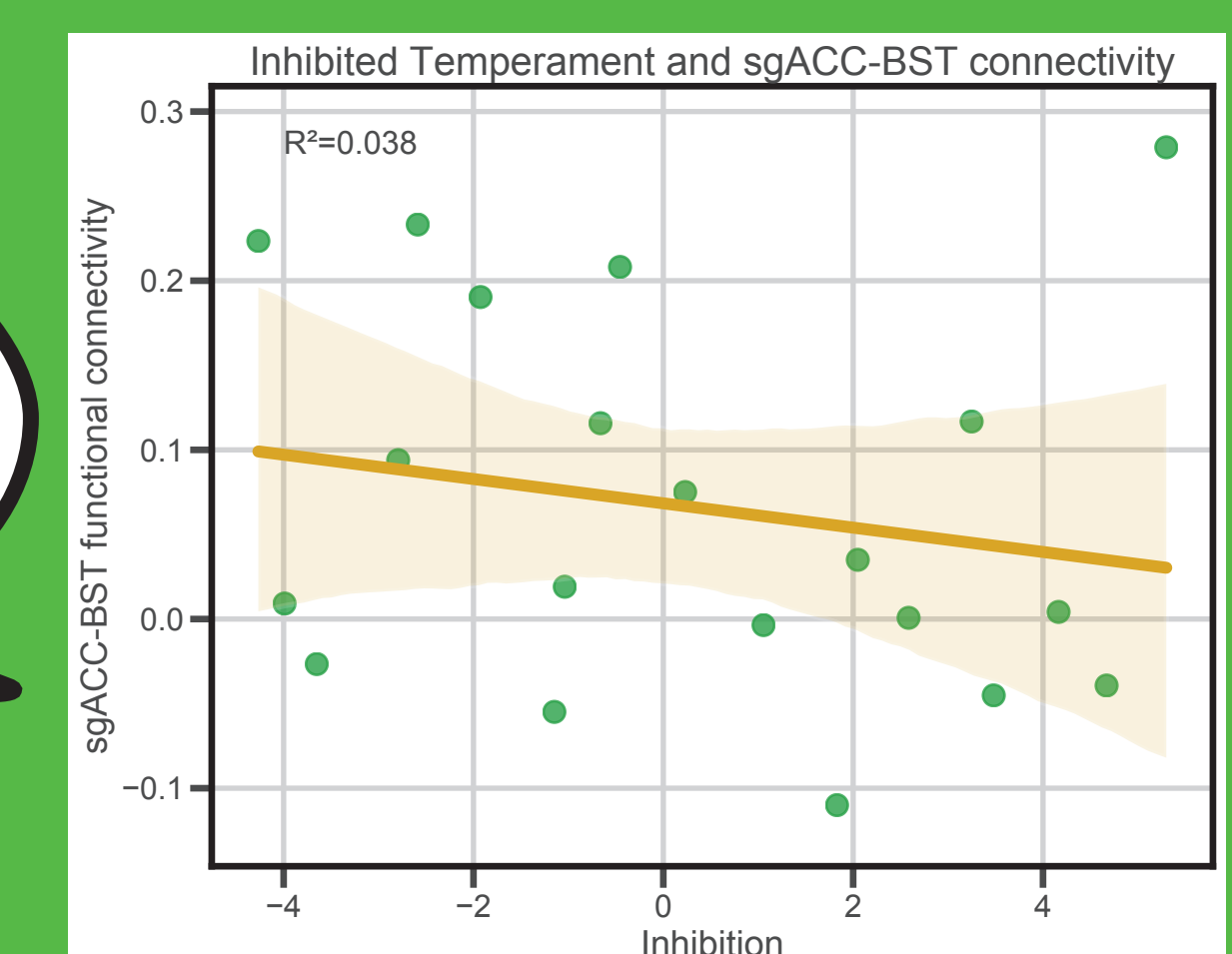
The Subgenual Anterior Cingulate Cortex is functionally connected to BST.



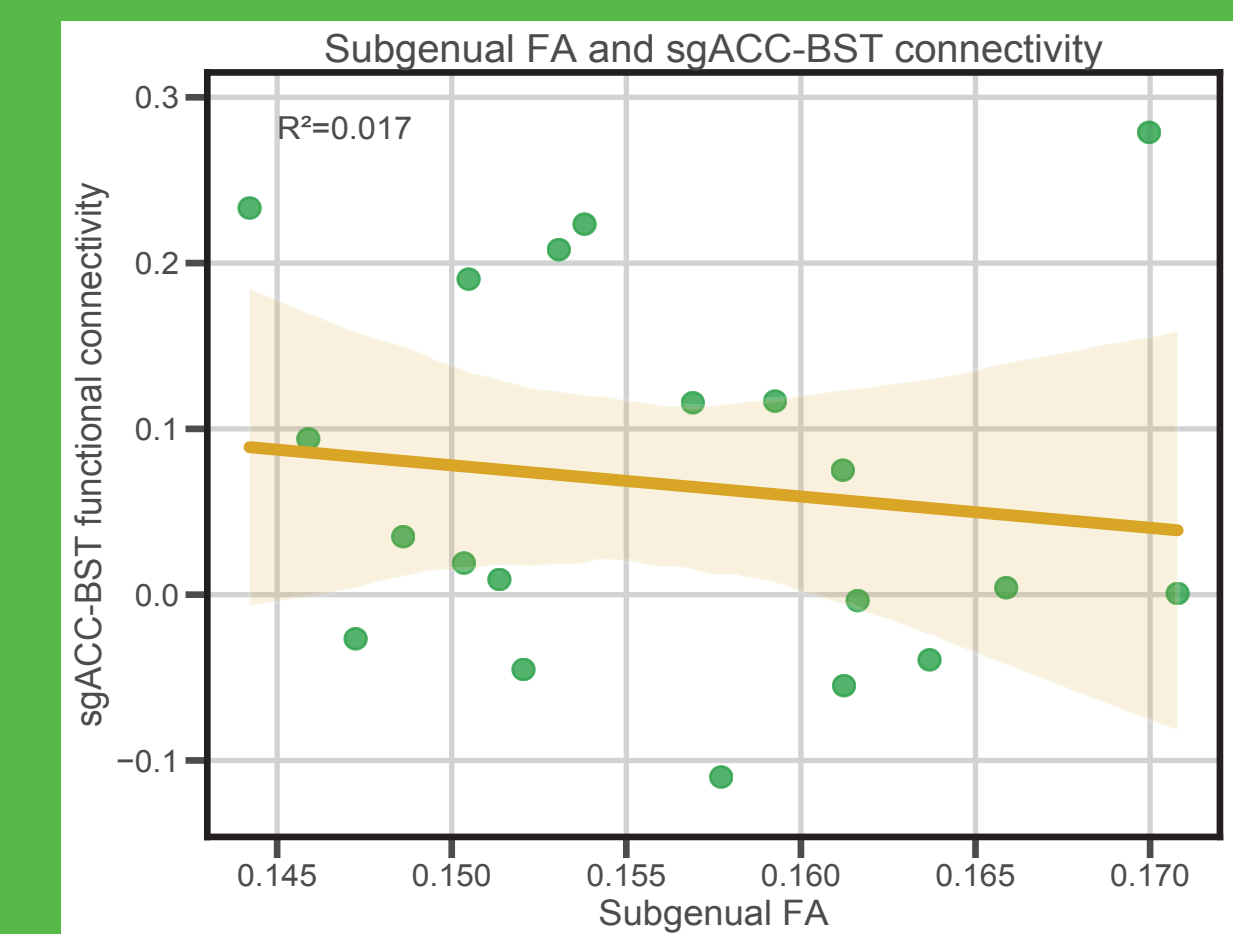
Seed-based Correlation Analysis revealed that sgACC and BST are functionally connected.

Our rs-fMRI data replicates default-mode network.

Is IT associated with sgACC-BST connectivity?



Is subgenual FA associated with sgACC-BST connectivity?



Discussion

Our previous work found metabolism in regions of the BST and sgACC to be heritable and co-inherited with individual differences in adolescent behavioral inhibition⁴. These new data suggest that infant behavioral inhibition is associated with changes in white-matter integrity within the accumbofrontal fasciculus during adolescence. We further demonstrated resting-state connectivity between the BST and sgACC in rhesus monkeys, suggesting a plausible mechanism by which these regions could work together to initiate inhibition. However, individual differences in BST-sgACC connectivity were not significantly associated with inhibition or accumbofrontal fasciculus FA. Our ongoing work will replicate and extend these findings to a larger sample of adolescent and young adult animals that underwent BBA testing ($n > 100$).

Heritable regional AT-related brain metabolism

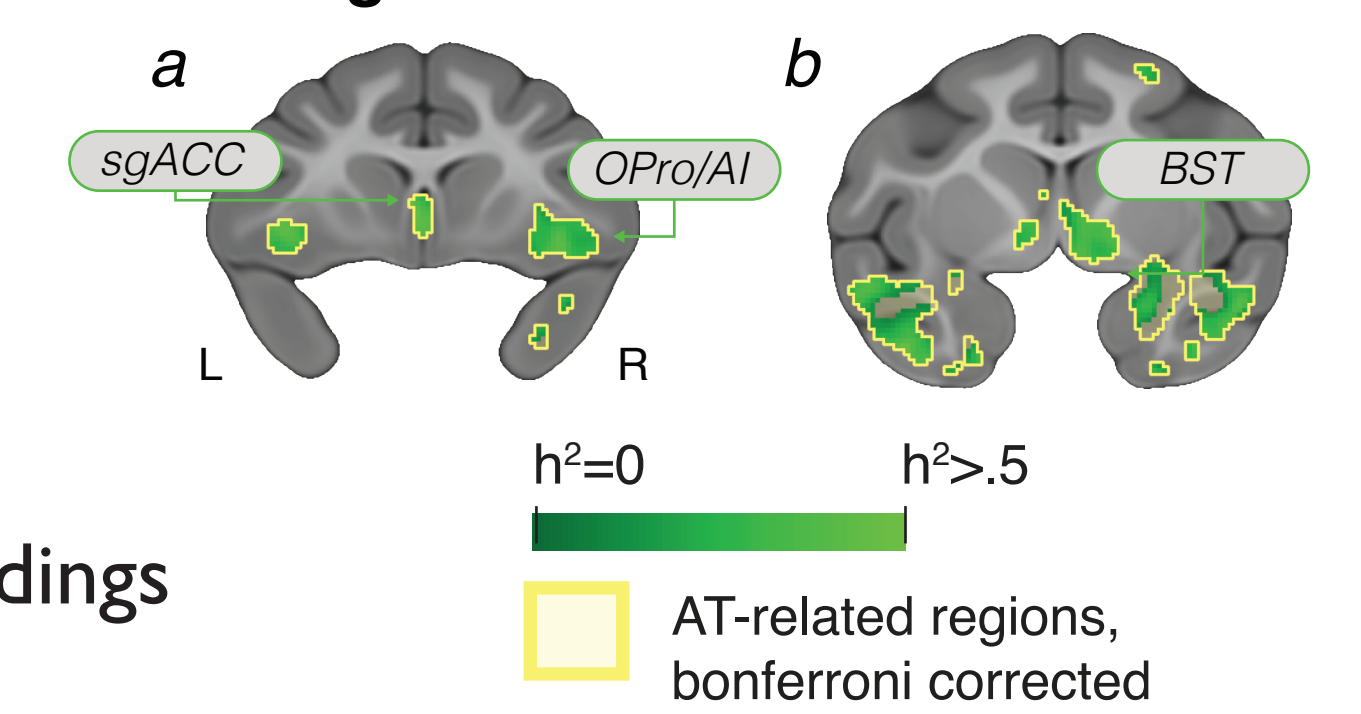


Image adapted from Fox et al. (2015)