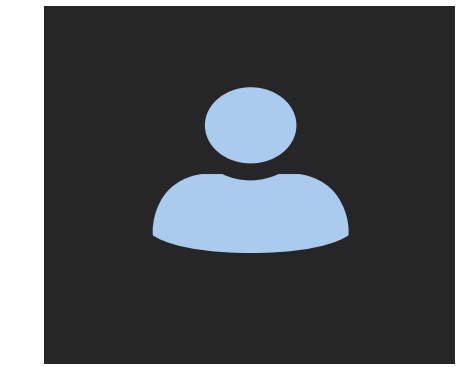


Characterizing the Neural Substrates of Irritability in Women: A 7T fMRI Study



Authors

Megan Hynd

Erin Walsh, PhD, Josh Bizzell, MS,
Kathryn Gibson, BS, Melissa Walsh, PhD, Danielle Swales, PhD, Gabriel Dichter, PhD, Crystal Schiller, PhD

BACKGROUND

- Irritability, a prominent feature of perinatal depression, detrimentally impacts maternal mental health and child development; yet it remains poorly understood and understudied.
- Hormone manipulation in euthymic non-pregnant women produces transient affective symptoms -- including irritability -- like that experienced in the perinatal period.

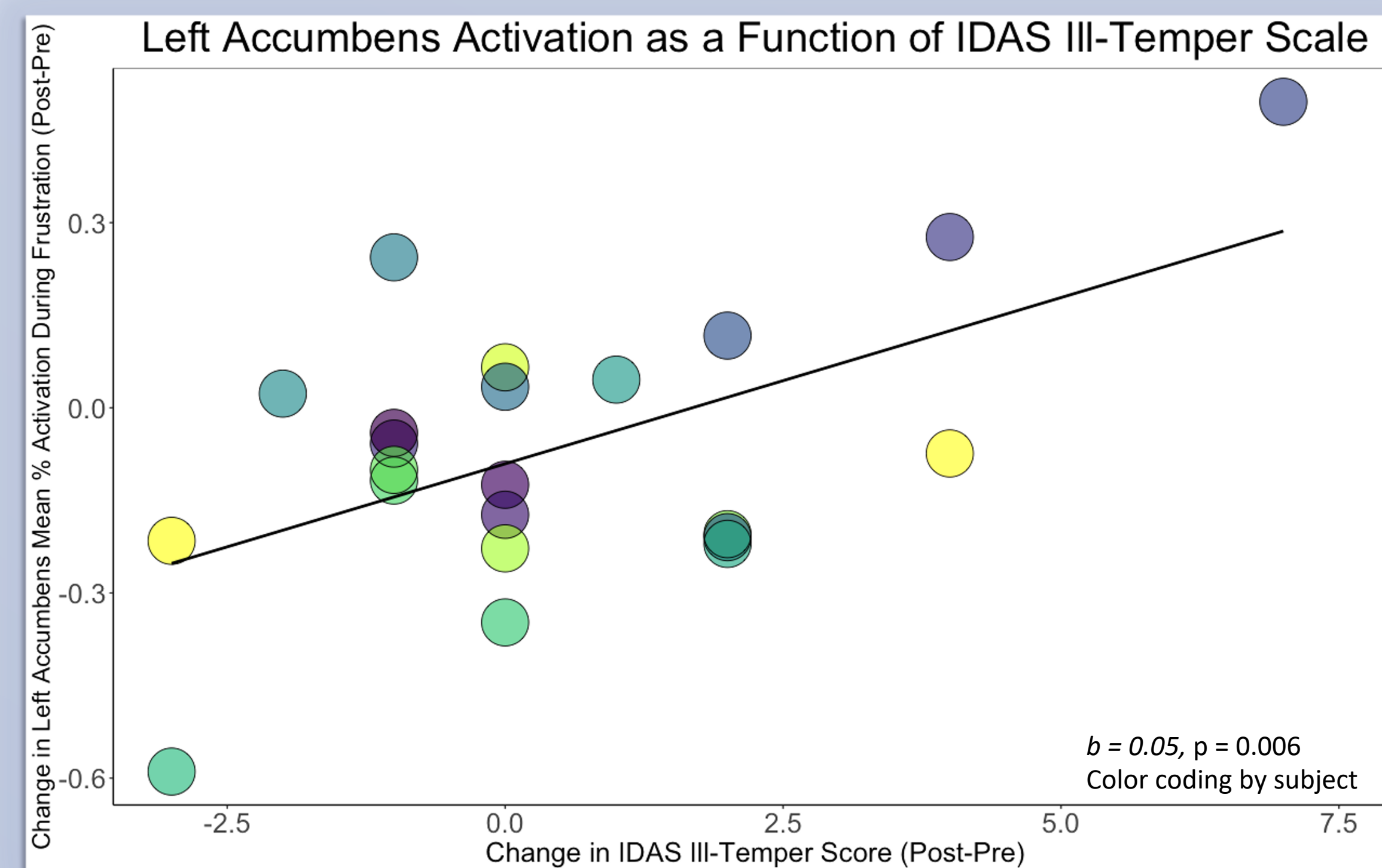
METHODS

- Participants (n=22) completed an 8-week hormone manipulation protocol using Lupron that included a pre- and post-manipulation 7T fMRI scan.

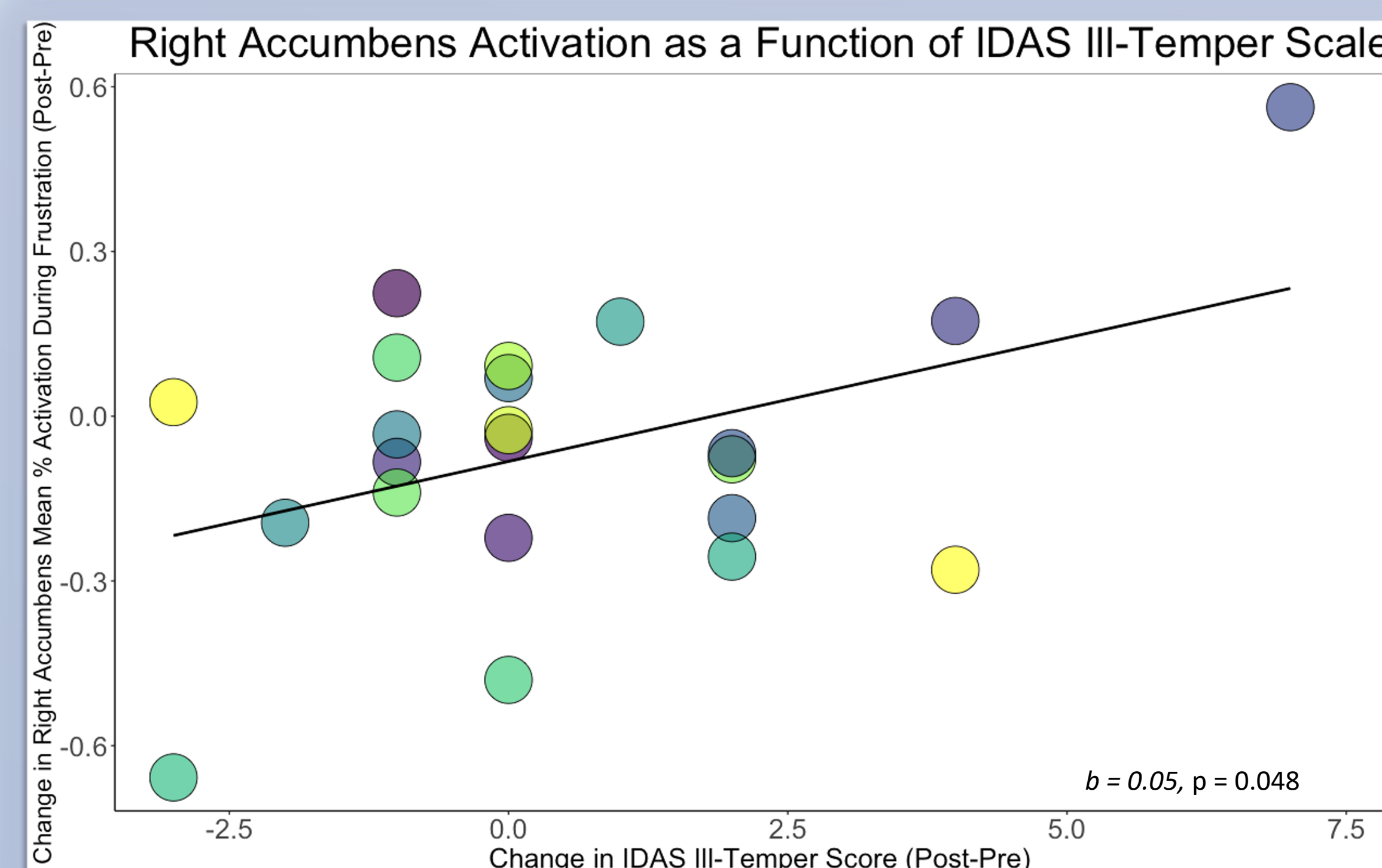
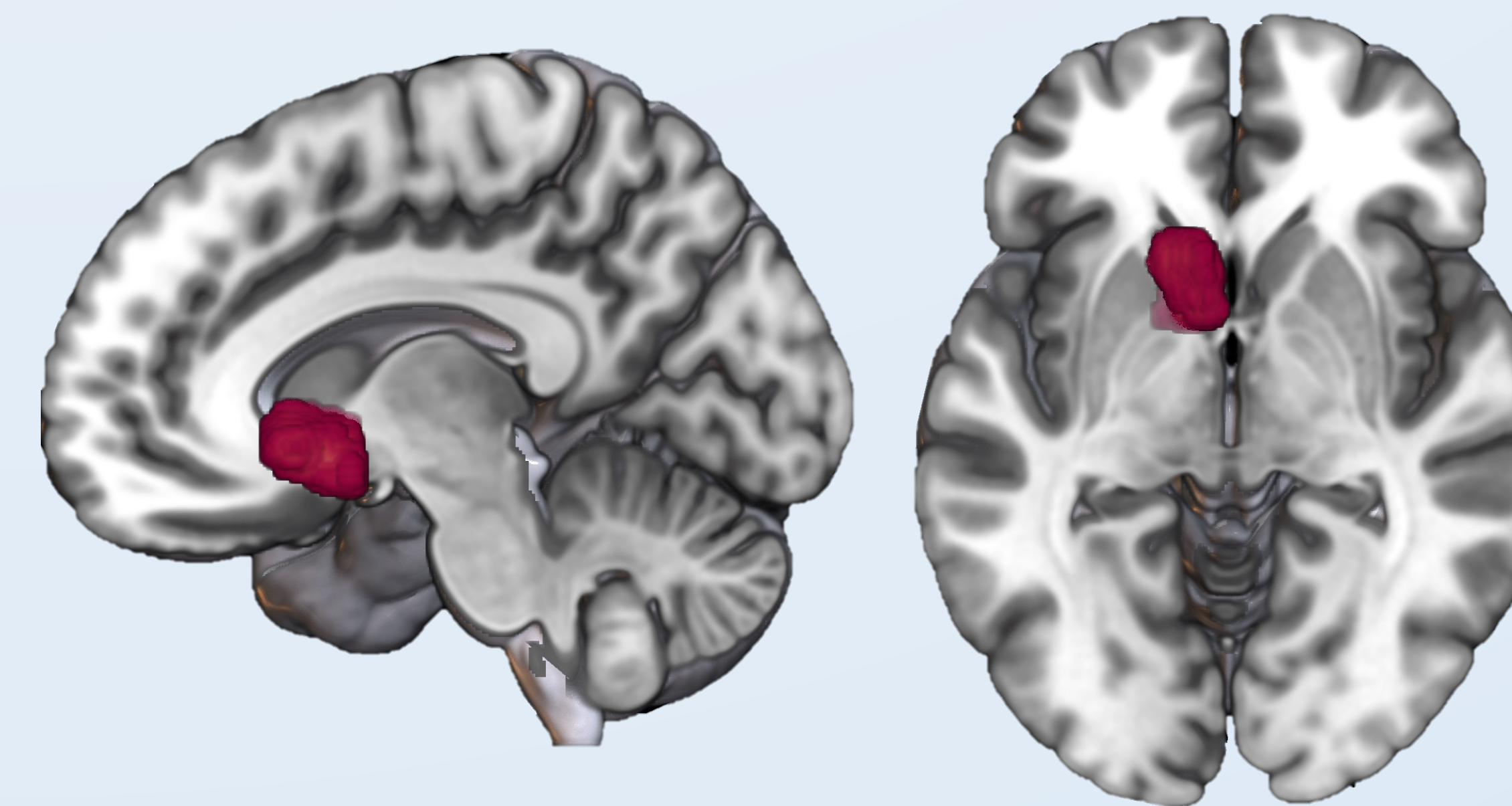
Participant Characteristics (n=22)		
Variable	Mean	SD
Age	35.8	3.9
Number of pregnancies	3.1	1.6
IDAS III-Temper Change (Post-Pre)	0.5	2.4
BOLD Activation Change (Post-Pre)		
Left Accumbens	-0.06	0.23
Right Accumbens	-0.06	0.25
Right Amygdala	-0.02	0.23

- Each fMRI visit included the Affective Posner Task, designed to induce frustration through rigged feedback (60% of correct responses rigged to provide "Too Slow" feedback with no reward).
- Because previous research implicated the nucleus accumbens, amygdala, caudate, and putamen in irritability, we extracted BOLD % signal change from these structurally derived ROIs during induced frustration in the Affective Posner Task.
- Univariate regressions compared the relationship between change in ROI BOLD activation during induced frustration (post-pre) and change in a self-reported measure of irritability (post-pre).

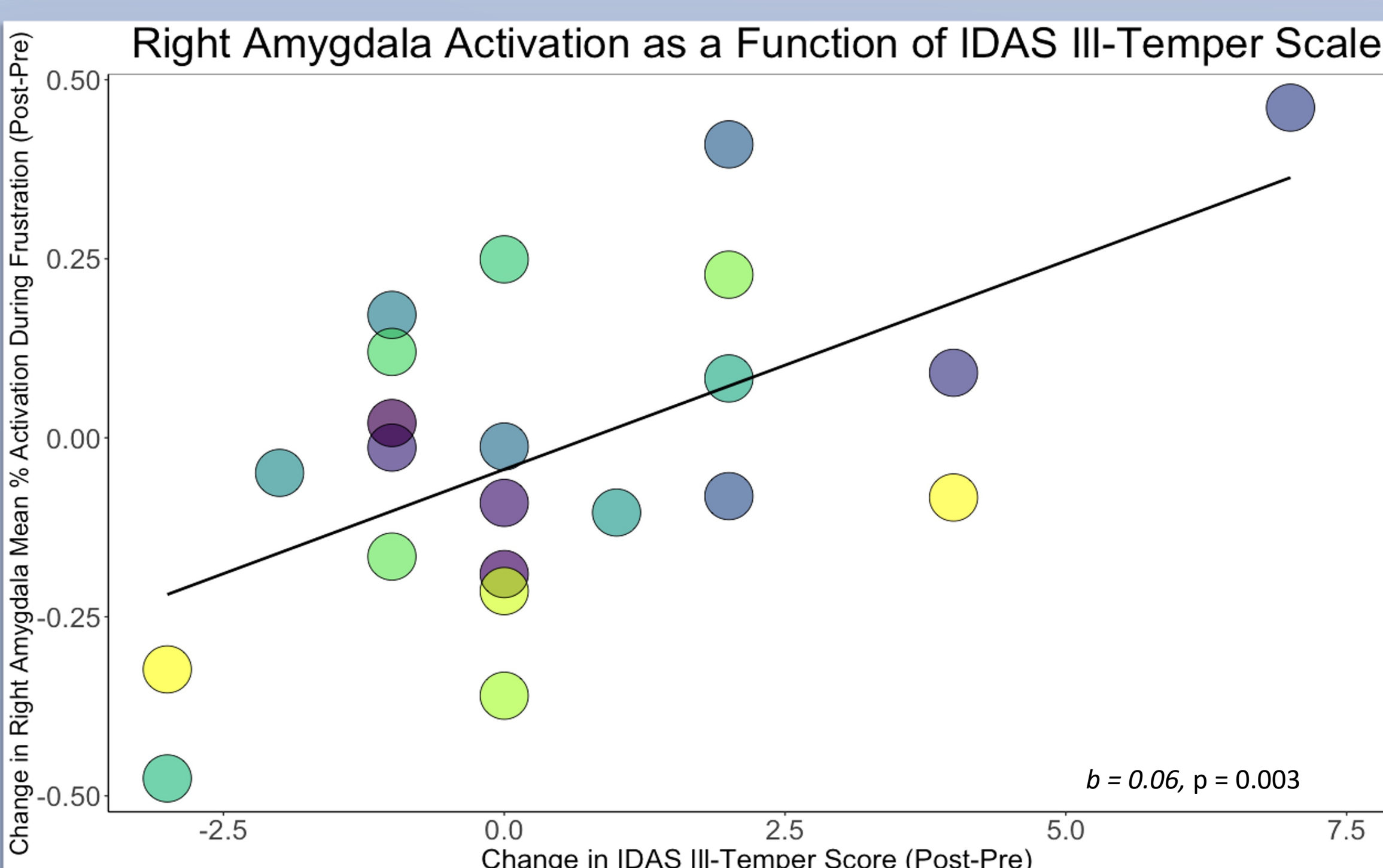
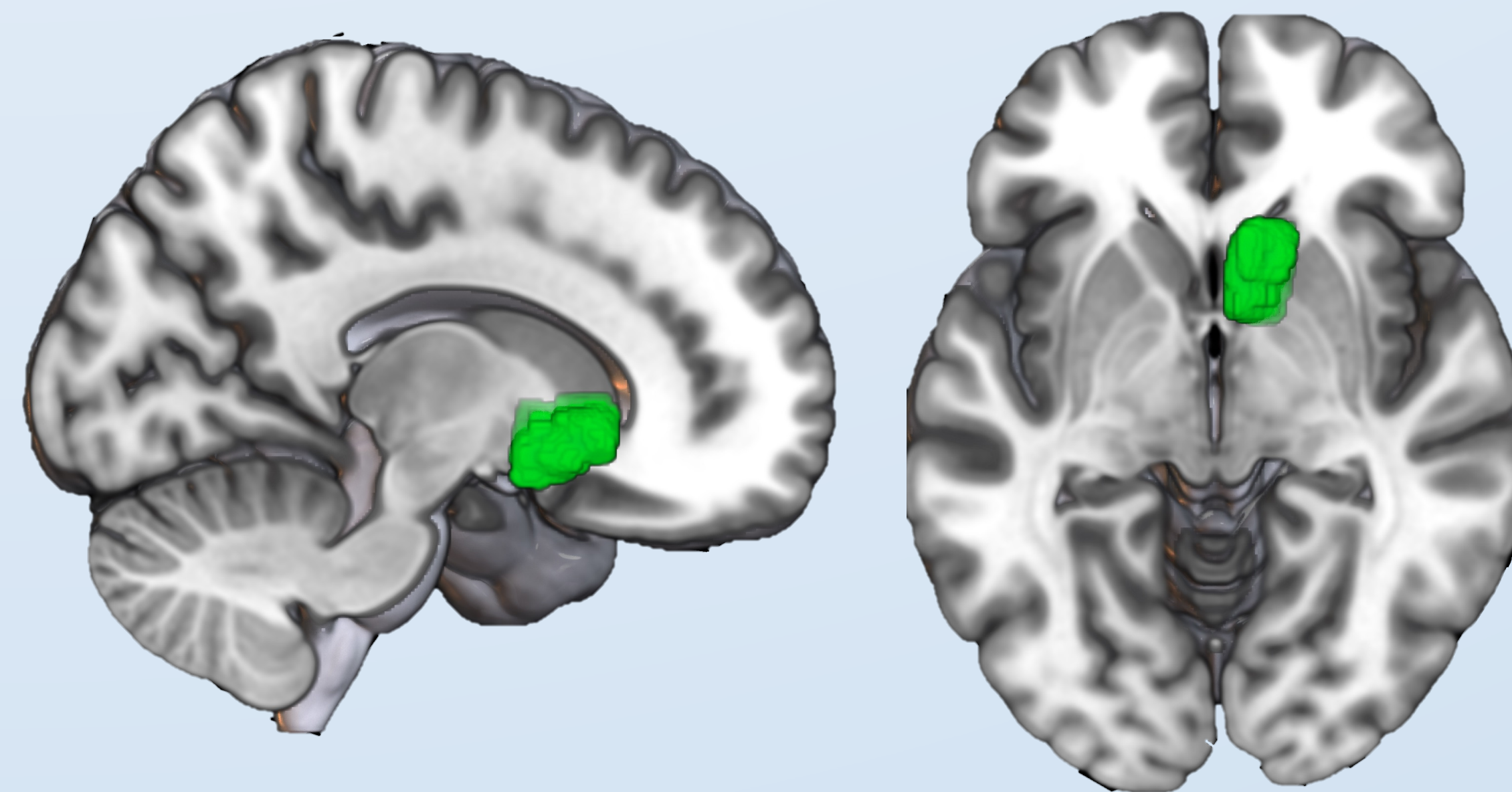
Increased self-reported irritability predicts increased striatal activation to frustration.



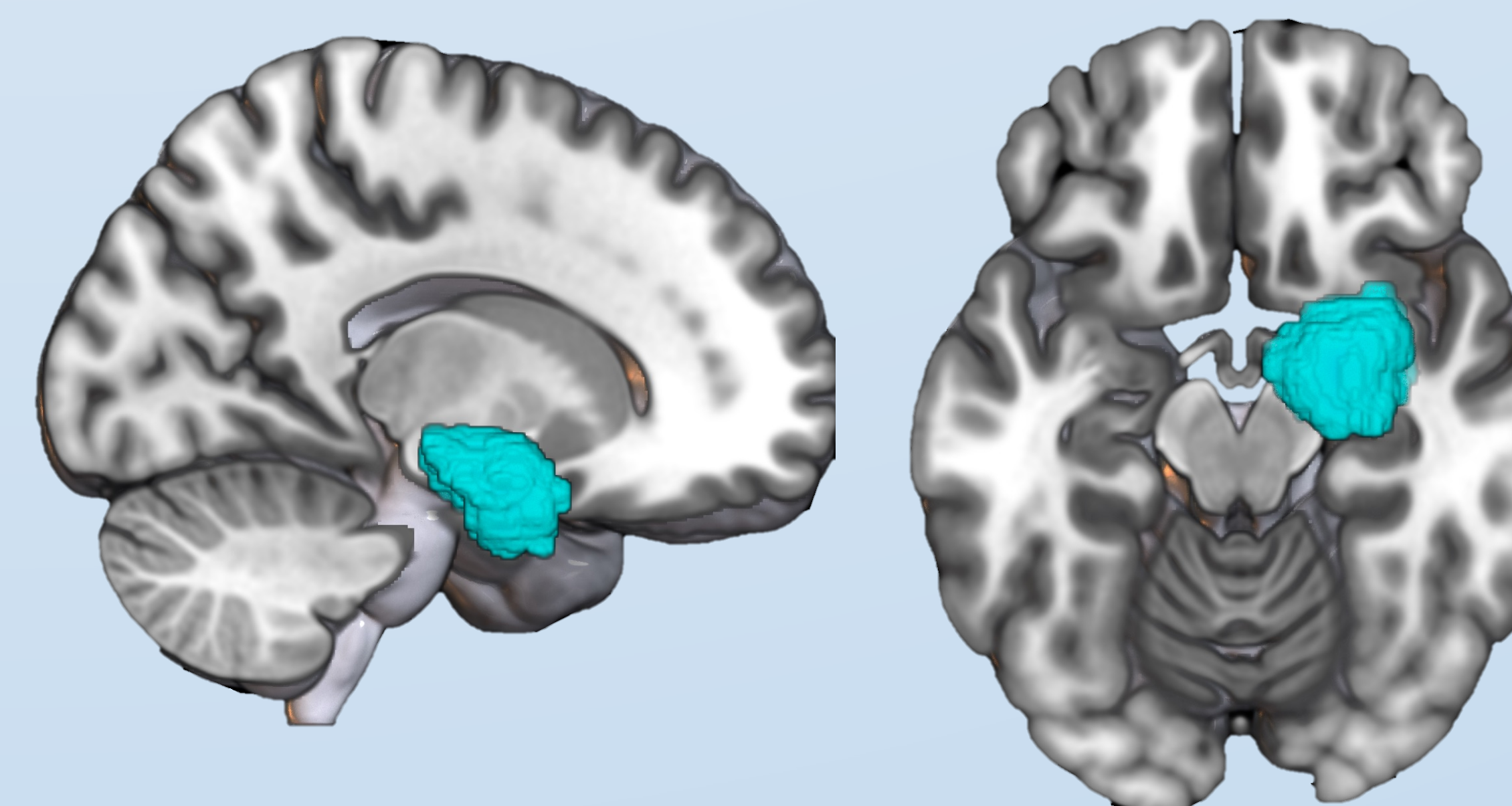
Left Accumbens



Right Accumbens



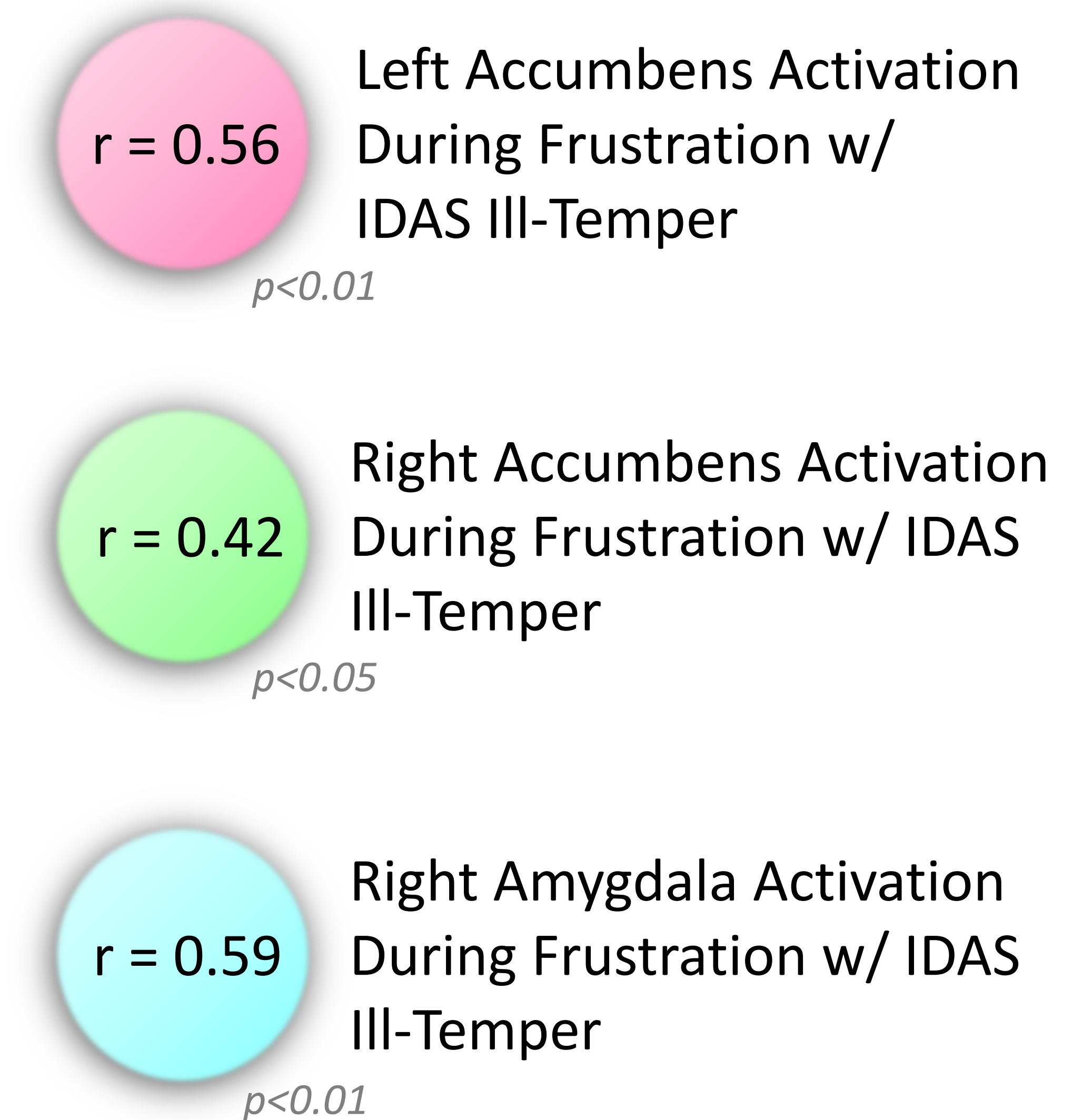
Right Amygdala



RESULTS

- Three key striatal/limbic region activation changes from pre- to post-hormone manipulation positively correlated with IDAS III-Temper change:
 - Left accumbens (t=3.04, p<0.01, adjR²=0.28)
 - Right accumbens (t=2.10, p<0.05, adjR²=0.14)
 - Right amygdala (t=3.29, p<0.01, adjR²=0.32)

Clinical Correlations:



DISCUSSION

- The nucleus accumbens and right amygdala are significantly implicated in hormonally-induced irritability and correlate with a well-established clinical outcome.
- This is the first study using 7T fMRI to elucidate the neurobiology of irritability with a homogenous onset; establishing a potential biological target for treatment of irritability and perinatal depression.

Disclosures & Funding

This research was supported by NIMH (R01 MH128238 to GSD and CES; R21 MH119615 to CES).

