



Altered Lateral Prefrontal Cortex Functioning During Emotional Interference Resistance is Associated with Affect Lability in Adults with Persisting Symptoms of ADHD from Childhood

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Background & Motivation

ADHD, Symptom Persistence, and Emotion Dysregulation

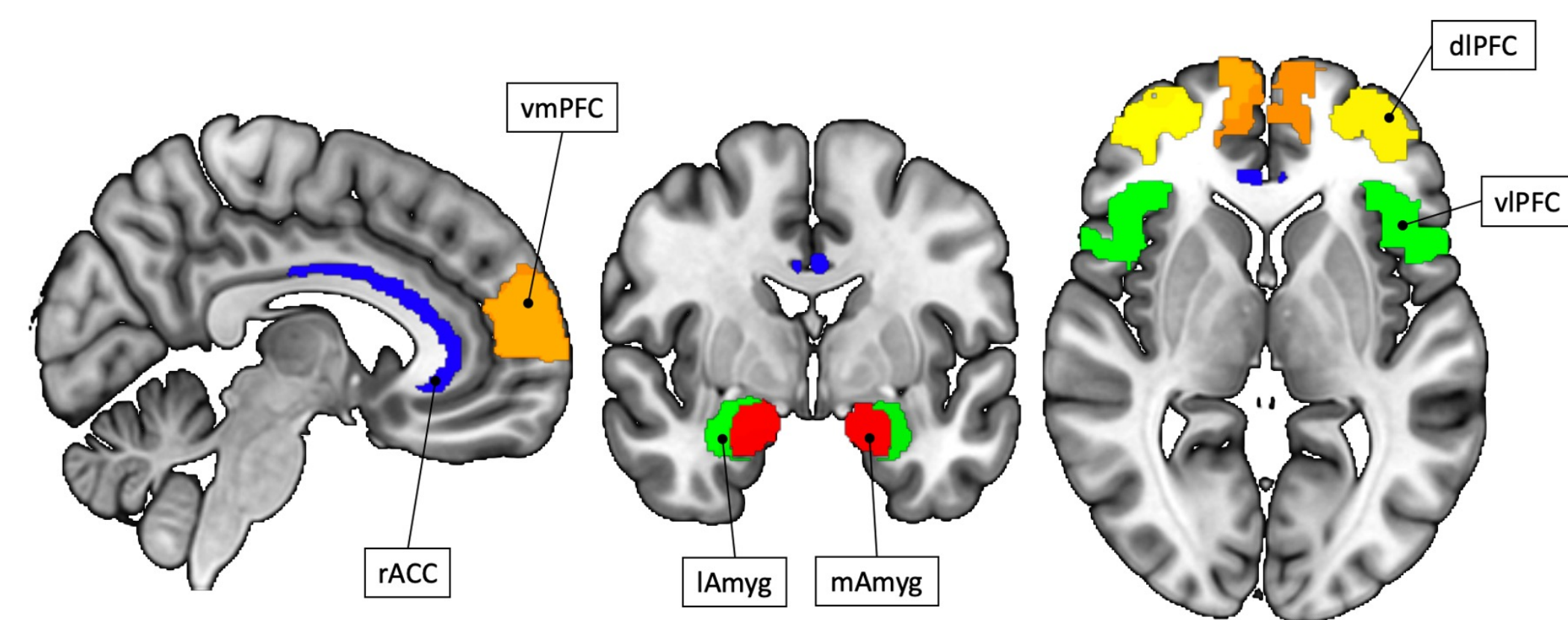
- Attention-Deficit/Hyperactivity Disorder (ADHD) is a common neurodevelopmental disorder characterized by inattention and/or impulsivity-hyperactivity.
- Emotional symptoms (e.g., affect lability, anger-irritability) are common features of the disorder in children (25-45%) and adults (30-70%)¹ and worsen clinical outcomes².
- However, our understanding of the neurobiological mechanisms underpinning the affective dimensions of ADHD remains poorly characterized.

Hypothesis

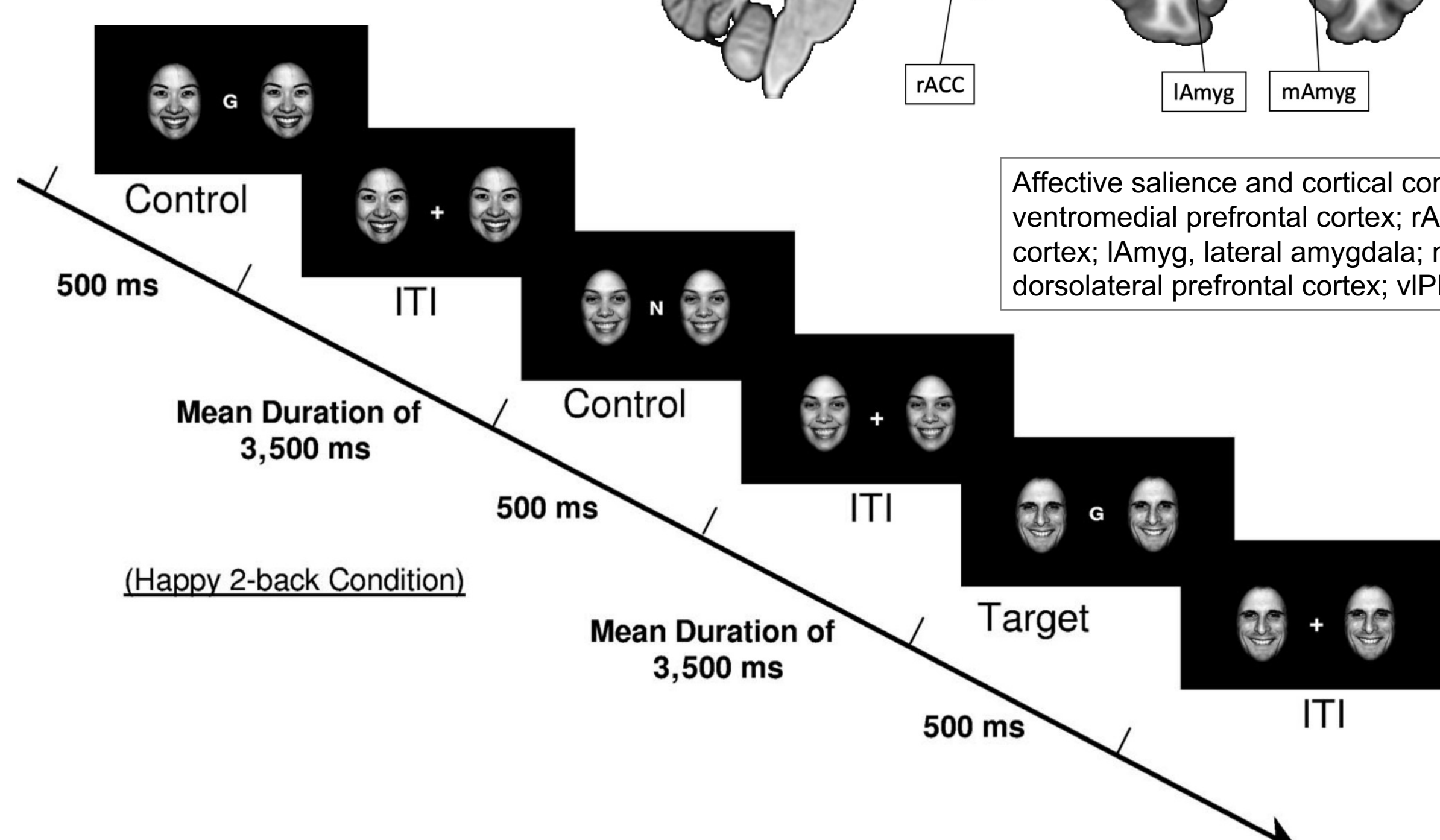
We expect greater recruitment of affective salience regions and reduced engagement of cortical control regions during emotional interference resistance to relate to emotional symptoms in adults with persisting ADHD.

Study Design & Analyses

- Participants with persisting ADHD (ADHD-P, $n = 47$), desisting ADHD (ADHD-D, $n = 93$), and no ADHD history (ADHD-NA, $n = 42$) were recruited into the study from the Pittsburgh ADHD Longitudinal Study (PALS), a sample diagnosed as children between 1987-1996 using multi-informant reports³.
- Neuroimaging data was acquired on two 3 Tesla MRI scanners, which were harmonized using NeuroComBat to account for between scanner differences⁴.
- The Emotional Face N-Back (EFNBACK) fMRI task is a modified visual sequential letter working-memory N-back task with emotional faces presented as distractors⁵ and has previously been used to probe differences in brain activation across affective psychopathologies⁵⁻⁷. The present study focuses on 2-back trials with distractor faces, to examine executive functioning and emotion regulation (EF+/ER+).
- Emotional symptoms were quantified using the Affect Lability Scale (ALS)⁸.
- After identifying task effects, we tested how neural activation in affective salience regions (i.e., vmPFC, rACC, mAmyg, lAmyg) and cortical control regions (i.e., dlPFC, vlPFC) was related to EFNBACK performance and emotional symptoms.
- We applied Bonferroni corrections to account for multiple comparisons.



Affective salience and cortical control ROIs. Abbreviations: vmPFC, ventromedial prefrontal cortex; rACC, rostral anterior cingulate cortex; lAmyg, lateral amygdala; mAmyg, medial amygdala; dlPFC, dorsolateral prefrontal cortex; vlPFC, ventrolateral prefrontal cortex

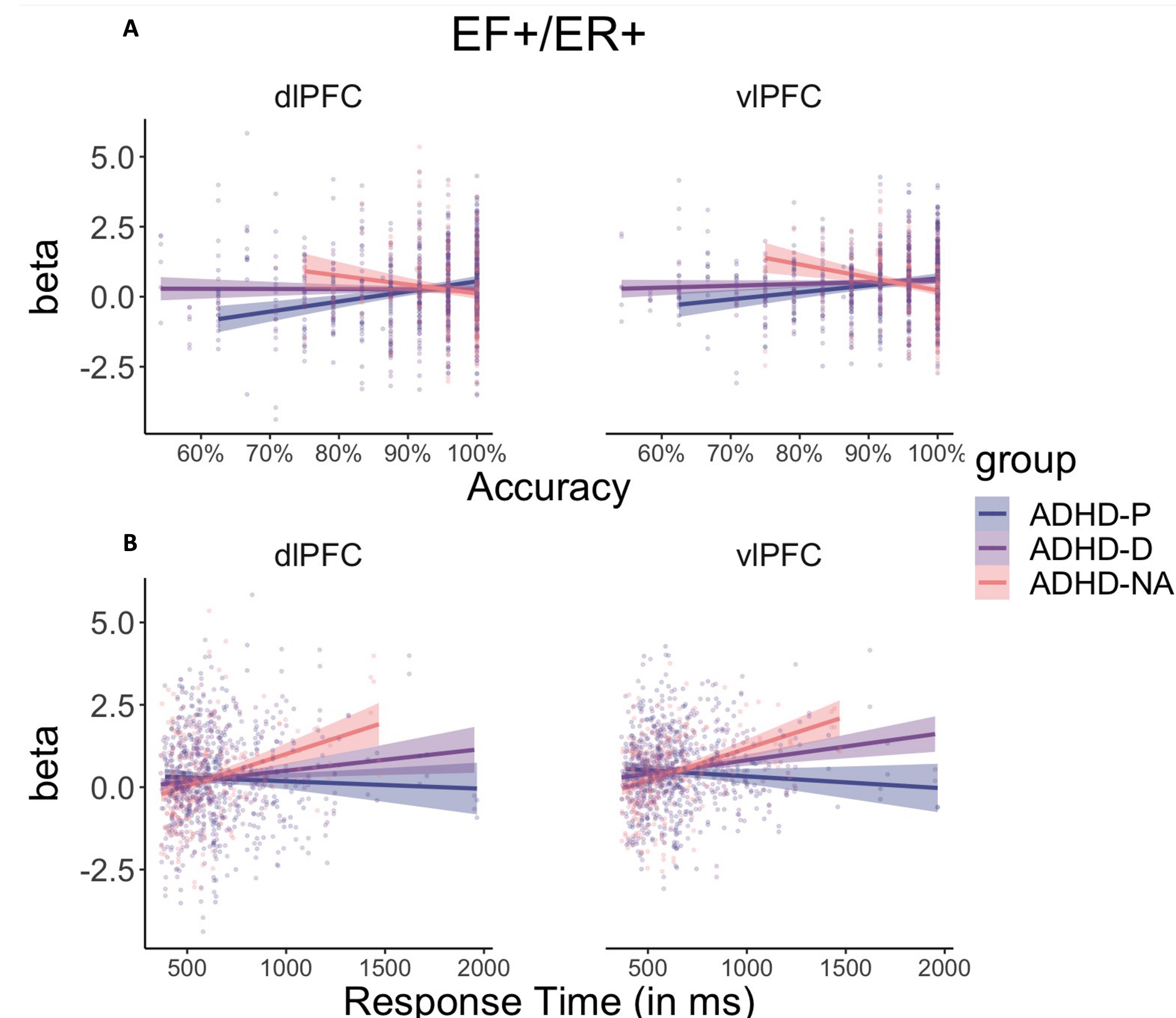


EFNBACK task schematic. Reproduced from Ladouceur et al., 2009.

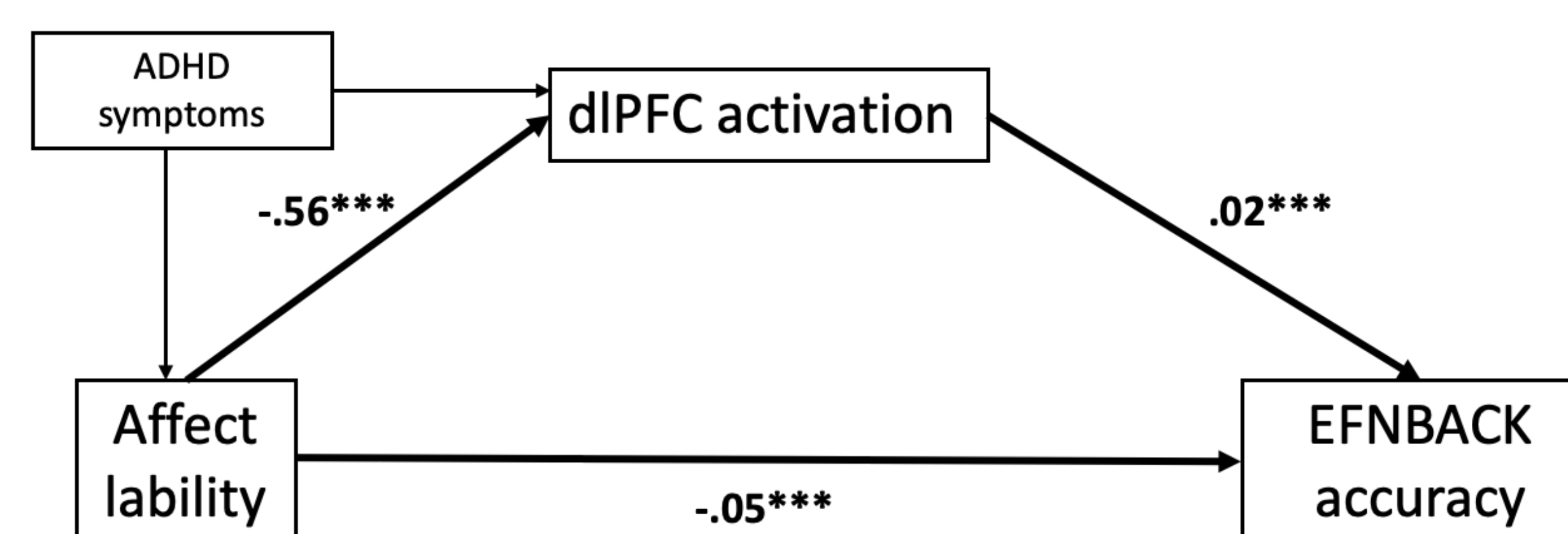
Results

EFNBACK EF+/ER+ Performance and Neural Activation

- EFNBACK accuracy was associated with stronger activation in the dlPFC ($F = 21.907$, $p < .001$), vlPFC ($F = 11.805$, $p < .001$), and CMA ($F = 6.336$, $p = .012$) in the ADHD-P group; in contrast, EFNBACK accuracy was associated with *weaker* activation in the ADHD-NA group: dlPFC ($F = 4.656$, $p = .032$), vlPFC ($F = 13.538$, $p < .001$), CMA ($F = 4.459$, $p = .036$), whereas accuracy was not associated with neural activation in the ADHD-D group ($ps \geq .122$).
- Stronger activation in cortical control ROIs was associated with longer response times in the ADHD-NA (dlPFC: $F = 27.628$, $p < .001$; vlPFC: $F = 37.788$, $p < .001$) and ADHD-D (dlPFC: $F = 6.154$, $p = .013$; vlPFC: $F = 16.125$, $p < .001$) groups, but not in the ADHD-P group ($ps \geq .202$).



- Greater affect lability was associated with reduced EF+/ER+ EFNBACK accuracy in ADHD-P participants ($F = 14.558$, $p < .001$), as well as with reduced activation in top-down cortical control ROIs (dlPFC: $F = 18.468$, $p < .001$; vlPFC: $F = 23.356$, $p < .001$) but not in affective salience ROIs ($ps \geq .442$).



- Exploratory mediation analyses revealed that dlPFC activation on EF+/ER+ trials mediated the relationship between affect lability and EFNBACK accuracy ($\beta = .16$, $p = .004$).

Discussion

- Our findings partially supported our hypothesis: although reduced lateral PFC activation was associated with more emotional symptoms in ADHD-P and greater recruitment of these structures was associated with better performance on EF+/ER+ trials, we did not observe a significant association with affective salience regions.
- Notably, these associations were unique to participants with persisting but not desisting ADHD symptoms, even after controlling for symptoms of inattention and impulsivity-hyperactivity, suggesting that lateral PFC dysregulation may confer emotional symptoms in ADHD symptom persistence.
- Taken together, our findings further our understanding of affective symptomatology in ADHD by identifying reduced dlPFC engagement during emotional interference control in cognitive performance and emotional dysregulation (i.e., affect lability).

Future Directions

- Previous work has found dlPFC stimulation using deep Transcranial Magnetic Stimulation (dTMS) to improve cognitive performance on a working memory task⁹.
- Others have suggested that dlPFC sensitivity to dopamine and norepinephrine, which underlie attentional and motivational processes¹⁰⁻¹⁴, may be one mechanism by which ADHD neural pathoetiology contributes to cognitive and emotional symptoms¹⁵⁻¹⁹.
- We suggest future researchers test targeted treatment of dlPFC recruitment during emotional interference control to potentially ameliorate emotional symptoms in adults with persisting ADHD.

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