Neural Responses to Error Processing Predict Treatment Outcomes in Youth with Anxiety

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Background

- Exposure-based Cognitive Behavioral Therapy (CBT) is a well-established and effective treatment for anxious youth[1]; however, many fail to fully respond.[2]
- Heterogeneity in outcomes highlights need to identify neurocognitive markers associated with treatment response.
- Cognitive control processes, thought to be disrupted in anxiety, are targeted directly during CBT.[3]
  - Exposure exercises rely on the inhibition of automatic avoidance behaviors.
  - Cognitive restructuring requires monitoring and updating of negative thoughts.
- Youth with anxiety disorders exhibit heightened sensitivity to errors reflected in atypical neural responses within medial prefrontal regions.[4,5]
- Dysfunction in these error processing systems may contribute to differences in treatment response.

Objective

Examine whether pre-treatment neural responses during error processing predicts CBT improvement in youth with anxiety disorders.

Hypotheses

1. Clinician-reported anxiety symptoms will decrease over course of CBT.
2. Greater error-related neural activity in error processing and cognitive control regions will associate with poorer treatment response.

Methods

N = 51 treatment-seeking youth with an anxiety disorder

Characteristic	Value
Age, mean (SD)	14.01 (2.55)
IQ, mean (SD)	111.60 (13.07)
Sex, No. (%)	
Female	33 (65%)
Male	18 (35%)
Primary Diagnosis, No. (%)	
Generalized Anxiety	32 (63%)
Separation Anxiety	4 (8%)
Social Anxiety	14 (28%)
Race, No. (%)	
American Indian or Alaskan Native	1 (2%)
Asian	2 (4%)
Black or African American	5 (10%)
Multiple Races	9 (17%)
White	31 (62%)
Not Reported	3 (6%)
Ethnicity, No. (%)	
Not Hispanic or Latino	39 (77%)
Hispanic or Latino	9 (18%)
Not Reported	3 (6%)

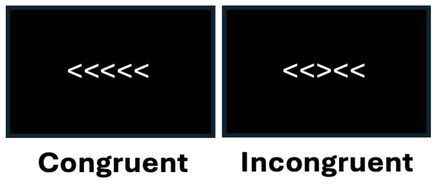
Anxiety Measure

- Clinician-administered Pediatric Anxiety Rating Scale (PARS), 50–item checklist across 7 dimensions[6]

Cognitive Behavioral Therapy

- Manualized CBT, delivered by a licensed clinical psychologist
- Early sessions: principles of CBT, psychoeducation and self-monitoring of emotions, thoughts and behaviors
- Later sessions: in-vivo exposures, cognitive restructuring exercises and at-home practice skills

fMRI Flanker Task



Computer-generated feedback at the end of each block
< 75% ”be more accurate”
> 90% ”respond faster”
75% - 90% “good job”

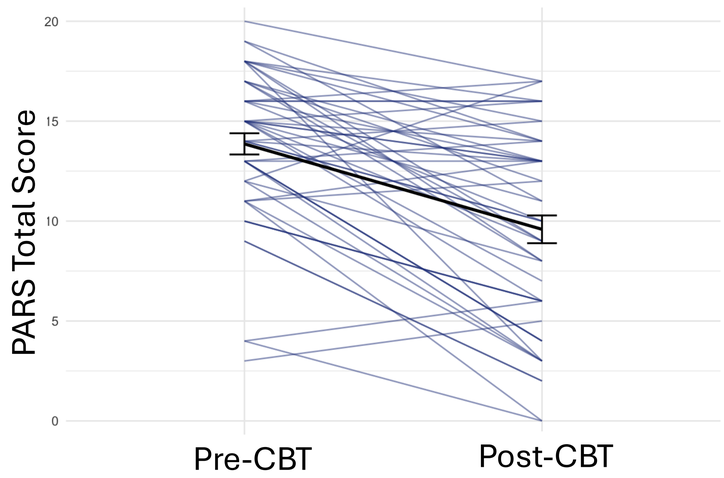
- Task contrast: Incongruent Error – Incongruent Correct

Statistical Analyses

- Whole-brain Linear Mixed Effects Model, $p < .005$ threshold, FWE-corrected, k> 55

Results

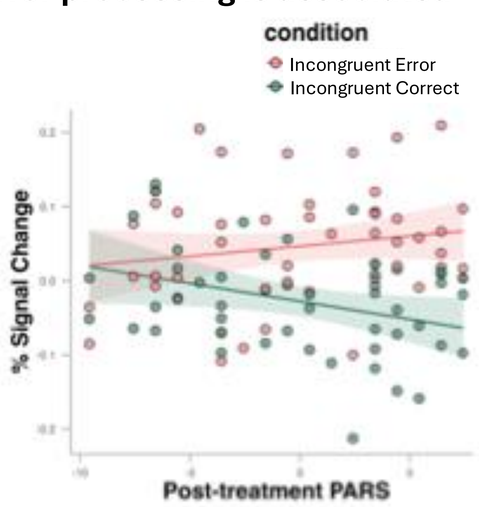
1. Anxiety symptoms improved with CBT in anxious youth



$PARS_{change}$: $t(50)=-7.19$, $p<.001$, $d=-1.01$

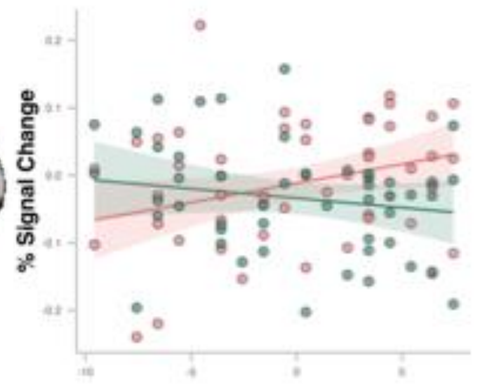
2. Neural activity during error processing is associated with improvement

Left Middle Cingulate Cortex



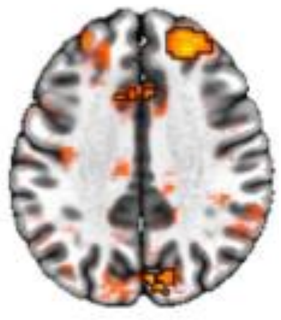
$\beta=0.32$, $t(93)=2.56$, $p=.012$

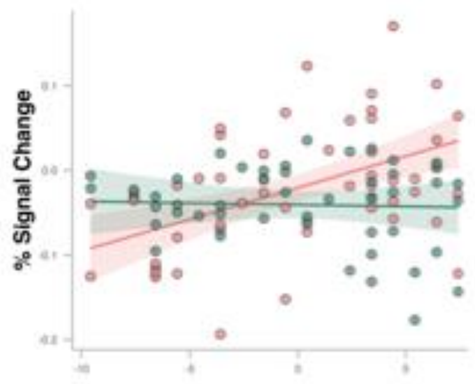
Right Cuneus



$\beta=0.34$, $t(93)=2.47$, $p=.015$

Right Superior Frontal Gyrus





$\beta=0.44$, $t(93)=3.38$, $p=.001$

Results Summary

- Anxiety symptoms improved with treatment; significant variability in treatment response.
- Error-related activity in several frontal and midline brain regions was related to treatment response.
- Post-hoc tests suggest that neural responses to error and correct trials differentially associates with treatment response across regions.

Conclusion

- Findings indicate that neural activity associated underpinning **error processing** associates with **psychosocial treatment response**.
  - Independent of behavioral performance.
- Provides support that neural responses to **errors versus correct** responses *differentially modulate* treatment-driven changes in anxiety.
  - Preliminary suggestion that error processing and monitoring may be important targets for future treatments.
- Future analyses will assess:
  - Replication in larger samples
  - Specificity to anxiety or internalizing disorders

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