

# Examining the relationship between externalizing and internalizing behaviour and the cortico-amygdalar network in children with neurodevelopmental disorders: a multi-modal imaging study

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## BACKGROUND

- Children with neurodevelopmental disorders (NDDs), including autism spectrum disorder (ASD), obsessive compulsive disorder (OCD) and attention-deficit/hyperactivity disorder (ADHD) exhibit high rates of externalizing and internalizing behaviours [1-3]
- These behaviours have been linked to variation in cortico-amygdalar connectivity in typically developing children (TDC) [4-6]
- There is limited understanding of whether this relationship extends to children with NDDs
- Research using transdiagnostic samples can provide insight into whether brain-behaviour relationships are shared or distinct across diagnoses

Objective: Investigate whether variation in cortico-amygdalar connectivity relates to internalizing and externalizing behaviours in a sample of children with different NDDs

## METHODS

- T1-weighted images from 304 children with ASD, ADHD, OCD and TDC from the Province of Ontario Neurodevelopmental Disorder (POND) network were analyzed
- Resting state functional MRI (rs-fMRI; n=139) and diffusion MRI (dMRI; n=188) data were analyzed for a subset of the sample
- Externalizing and internalizing behaviours were measured from the parent-report Child Behavioral Checklist (CBCL)
- Cortico-amygdalar connectivity was characterized using: 1. cortical thickness, 2. structural covariance, 3. seed based functional connectivity, 4. diffusion metrics of the uncinate fasciculus and cingulum bundle
- Separate linear models were used to investigate this relationship across the entire sample
- T1w and rs-fMRI data was analyzed using FSL's Permutation Analysis of Linear Models (PALM) with Threshold Free Cluster Enhancement (TFCE) used to determine clusters of vertex-wise significance
- White matter tracts were delineated using the Slicer dMRI software using a dataset-specific atlas

The Linear Model: Brain Index = Intercept +  $\beta_1$ (externalizing or internalizing behaviour CBCL score) +  $\beta_2$ (age) +  $\beta_3$ (gender) +  $\beta_4$ (medication status) +  $\beta_5$ (modality specific covariates) +  $e_j$

## RESULTS

No significant associations found between externalizing or internalizing behaviour and cortical thickness, cortico-amygdalar structural covariance, seed-based functional connectivity or diffusion metrics of the uncinate fasciculus and cingulum bundle

## DISCUSSION

Our results do not provide evidence of a relationship between externalizing or internalizing behaviours and indices of cortical thickness and cortico-amygdalar connectivity across a sample of children with different NDDs and TDC.

There are several reasons why we may not have found a relationship:

- Transdiagnostic samples are more heterogeneous than single diagnosis or TDC samples and thus a larger sample may be required to find shared relationships
- Using parent-report measures as the only measure of behaviour may not be sensitive enough to find these relationships in a heterogeneous sample
- The relationship between externalizing and internalizing behaviours and cortico-amygdalar connectivity may be more complex in a transdiagnostic sample compared to a typically developing or single diagnosis sample. Delineating this relationship may require multivariate statistics
- It is possible that finding brain-behaviour relationships in a sample with different NDDs may require clustering or biotyping approaches

## REFERENCES

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ANY QUESTIONS? Feel free to email me:  
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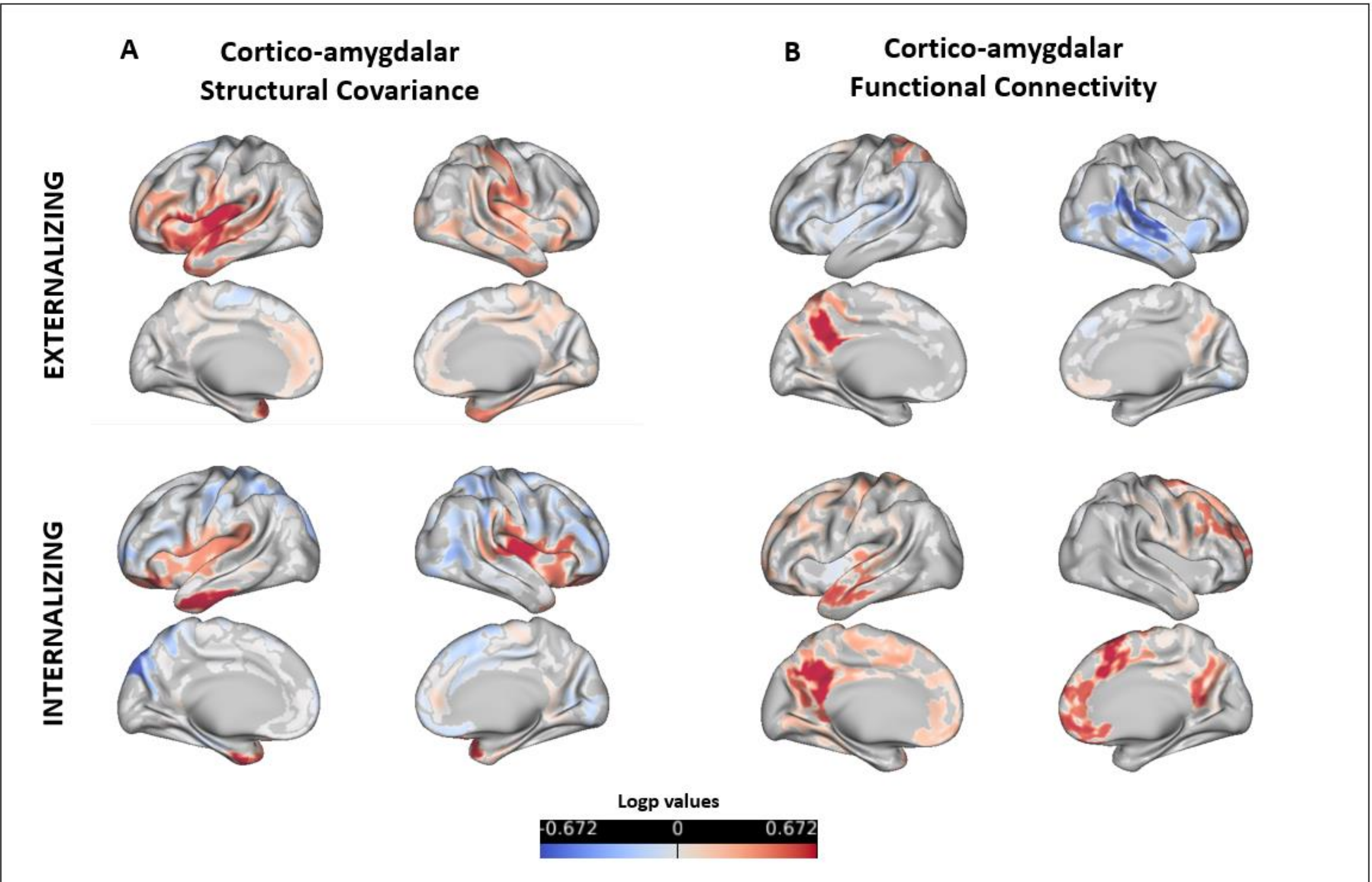


Figure 1. Unthresholded t-map illustrating relationship between externalizing and internalizing behaviour and cortico-amygdalar structural covariance (Panel A) and functional connectivity (Panel B). These results did not meet the significance threshold.

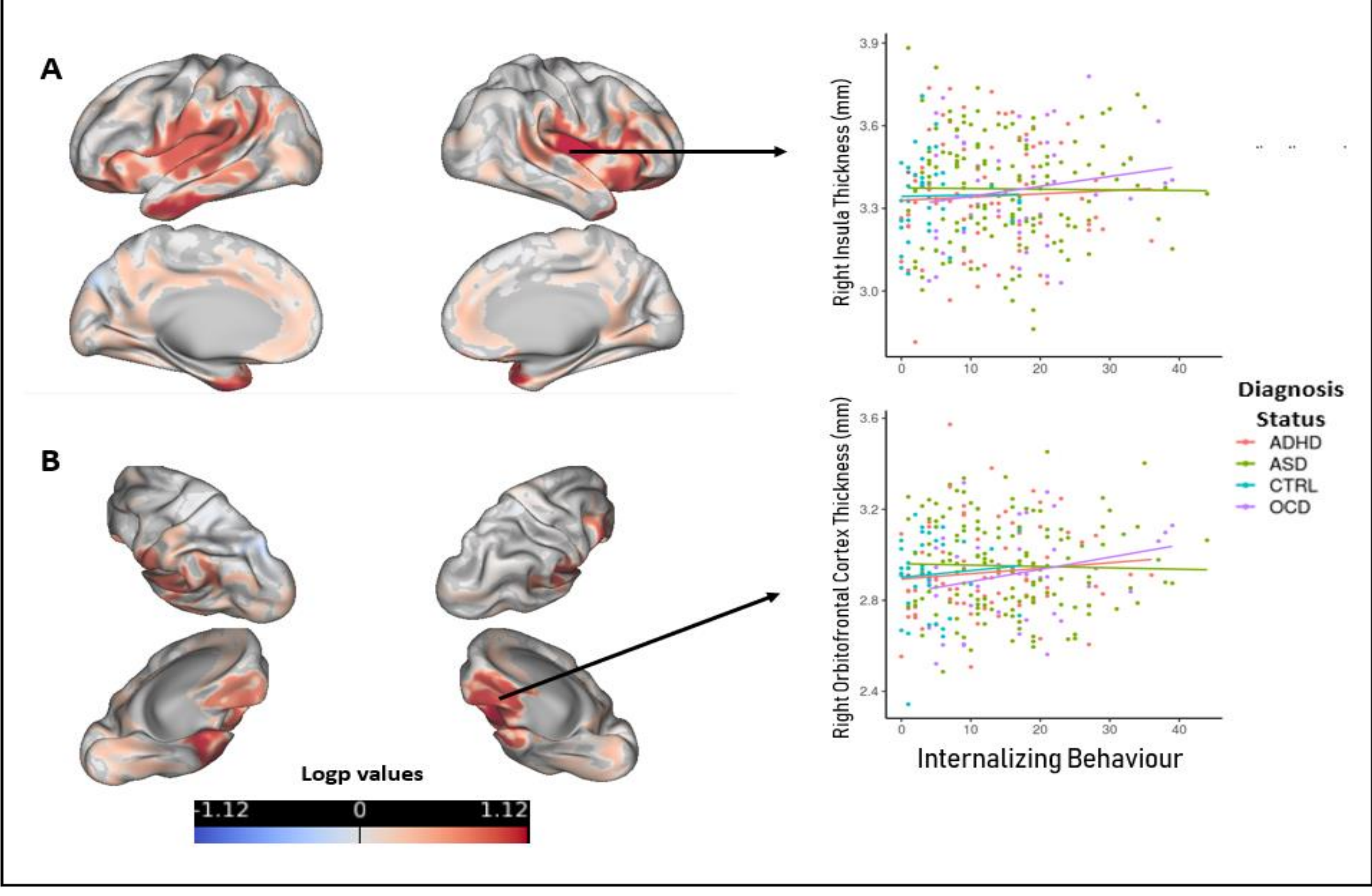


Figure 2. Internalizing behaviour regressed onto vertex-wise cortical thickness. The figure illustrates the brain-behaviour relationship by diagnosis. These results did not meet the significance threshold.

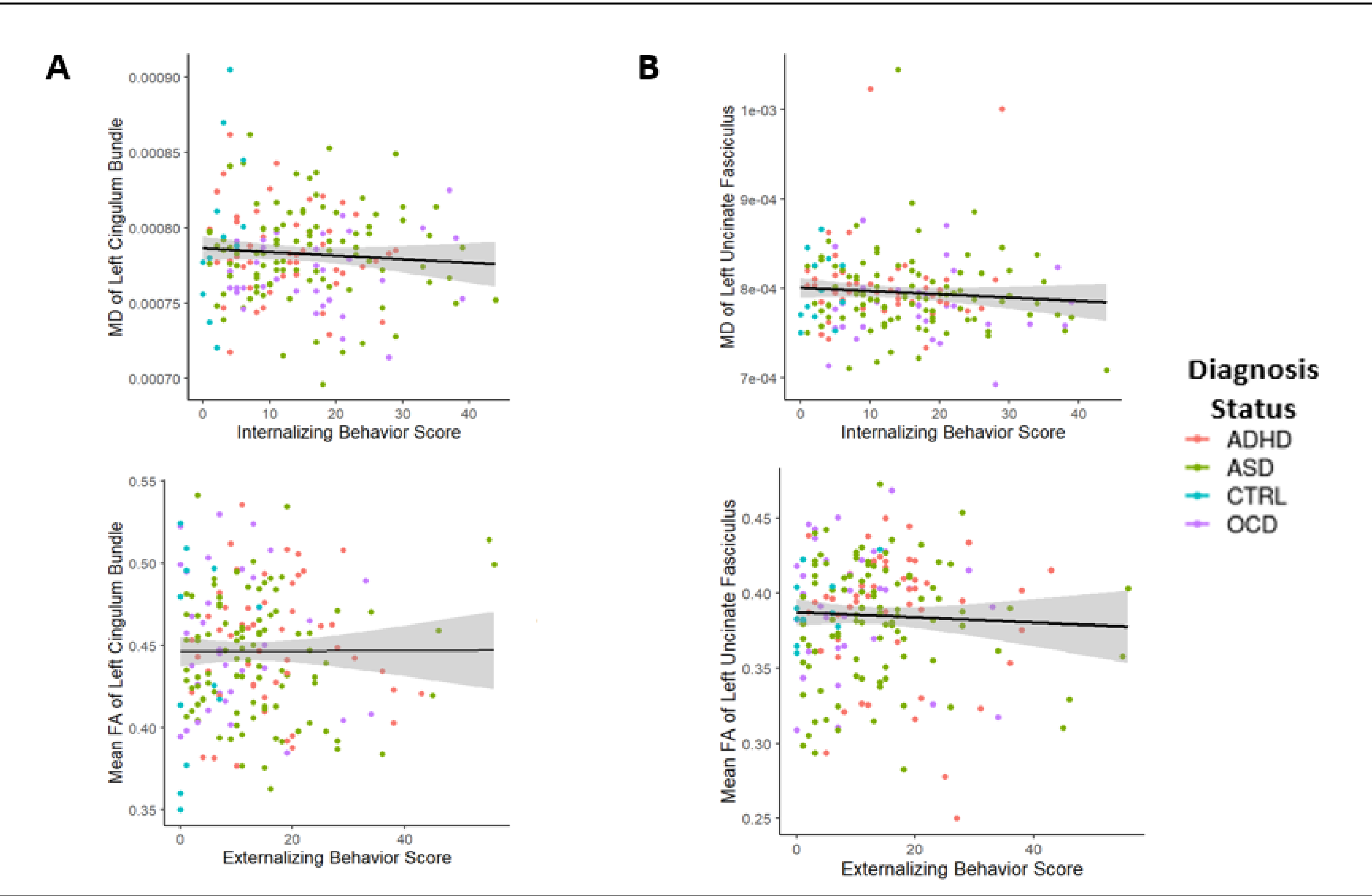


Figure 3. The relationship between externalizing and internalizing behaviour and white matter indices of the cingulum bundle (Panel A) and uncinate fasciculus (Panel B). These results are not significant.

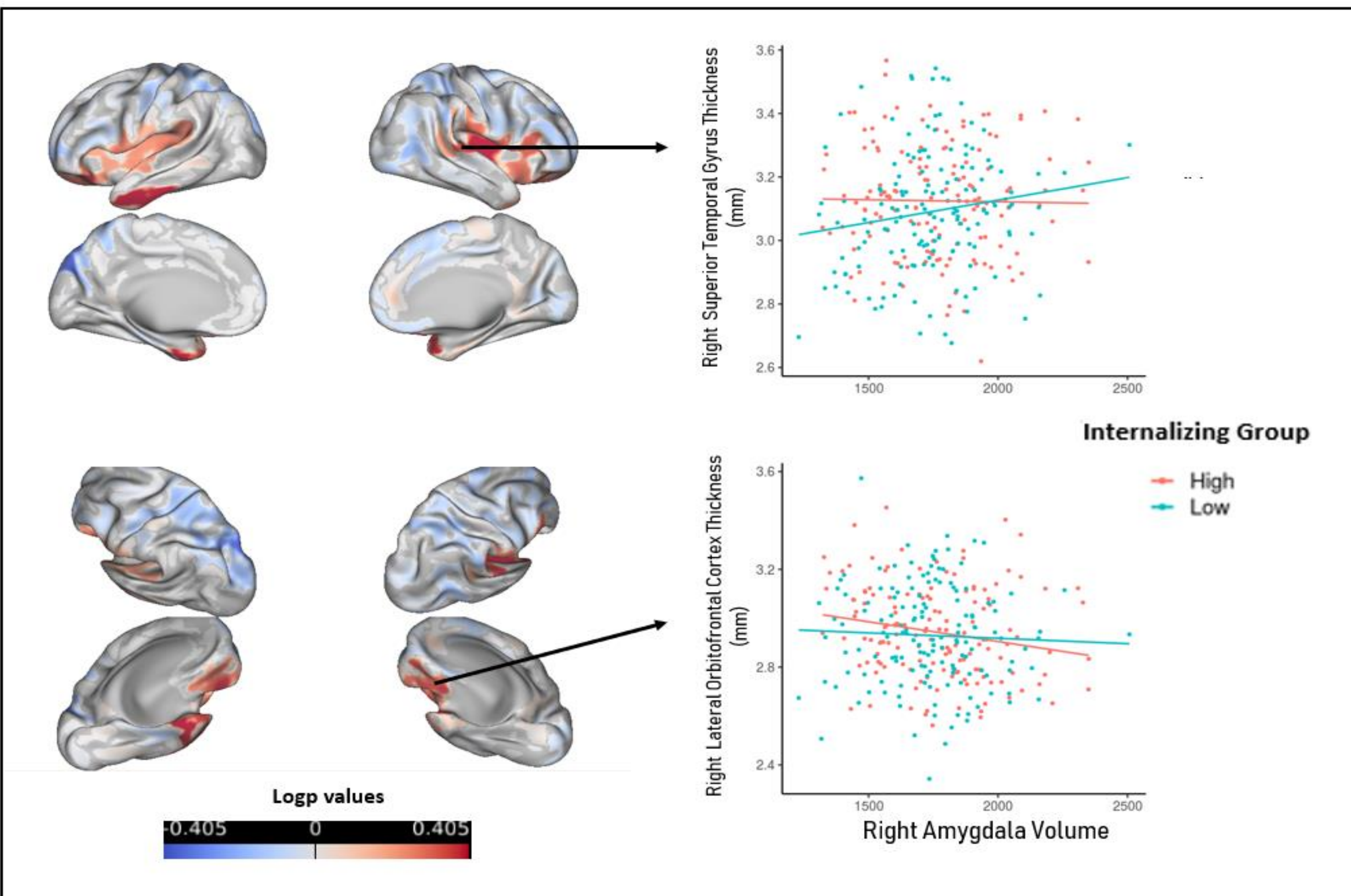


Figure 4. Relationship between cortico-amygdalar structural covariance and internalizing behaviour across the POND sample. This figure depicts internalizing groups as high or low based on a median split. These results did not meet the significance threshold.