

Background

- Child Behavior Checklist (CBCL) is a widely used clinical tool that assists in DSM diagnosis for psychiatric disorders in children ages 6 - 18 [1,2,3,4]. It has also been found to predict later development of mood disorders in children [2,3,5].
- CBCL AAA profile has been established as an effective screening measure to identify non-disordered children at greater risk for affective disorders, whereas CBCL DSM profile shows validity primarily in diagnosis on clinical populations [4]. Yet, the underlying neural mechanisms of these measures remain unknown.
- In this study, we aim to identify brain regions associated with risk factors for affective disorders and the neurocognitive processes underlying CBCL measurement.
- CBCL AAA profile, also known as the emotional dysregulation profile (ED), constitutes three CBCL syndrome scales: Attention, Aggression, and Anxiety/Depression [1,2,3,5].

Hypothesis

- Higher CBCL AAA profiles (more behavioral problems) should correlate with brain regions as risk factors that can contribute to affective disorder related pathological processes
- CBCL DSM Affective scale should be more related to brain regions commonly seen in affective disorders

Subjects

Recruited from MGH advertisement:

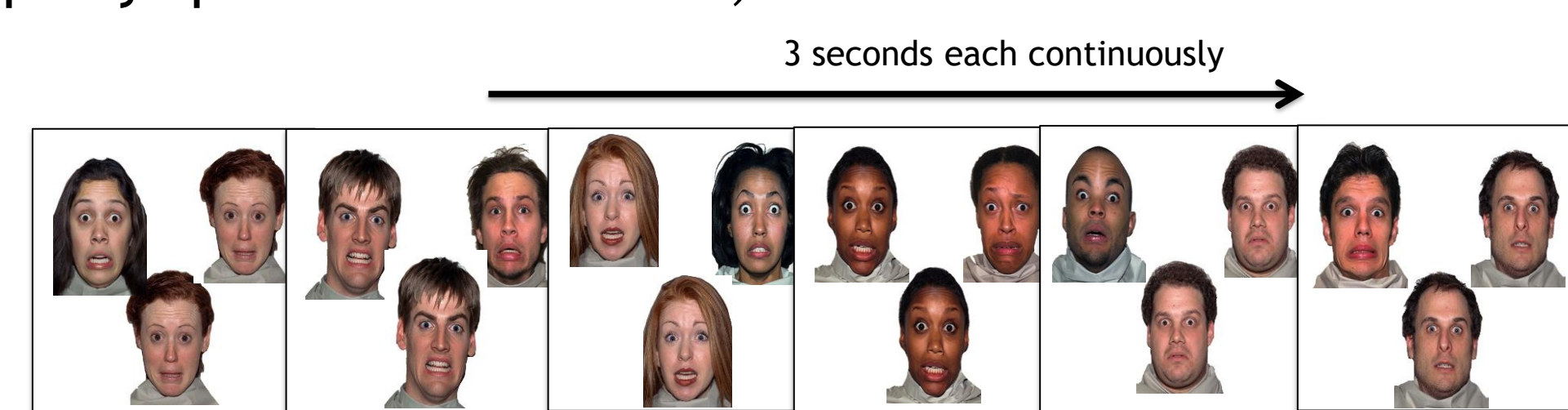
- English Speakers
- Behavioral assessment using CBCL, recruiting high risk (<180) and lower risk (<180) subjects
- Equal numbers of male and female, age 6-16 yrs

Exclusion Criteria:

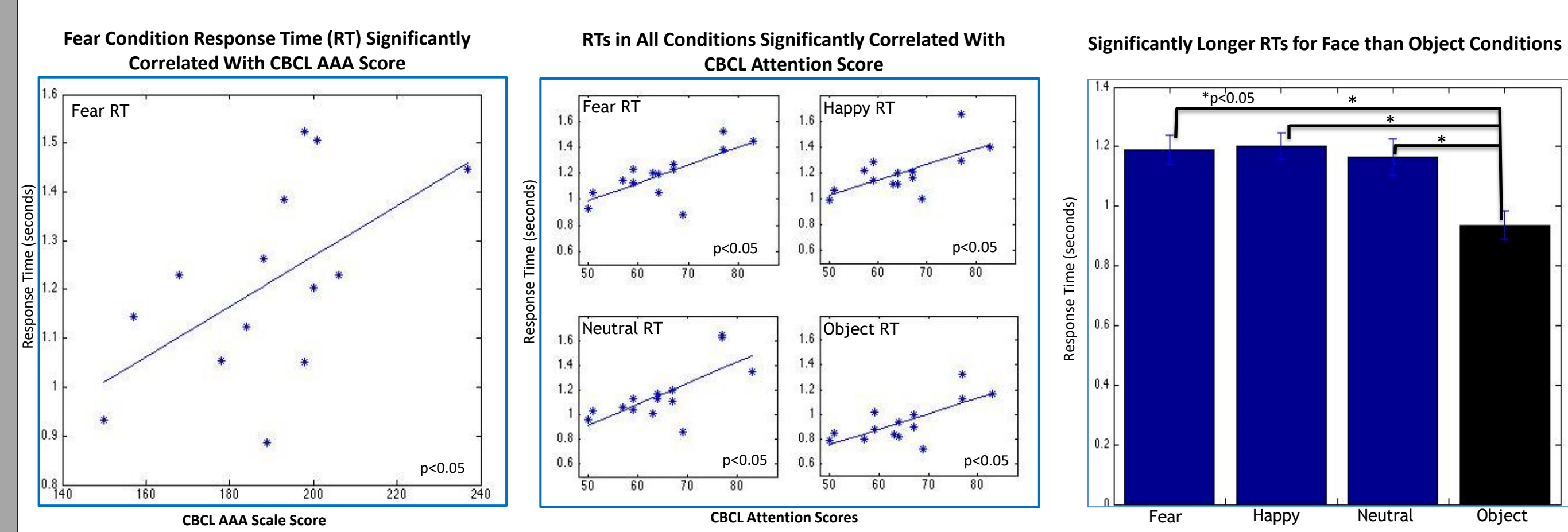
- Major medical illness
- History of neurological or psychiatric diseases or symptoms
- Impaired cognitive function (parental report or school report, or cognitive assessment completed within 3 months in other studies within the department)

Emotional Face Matching Task

- Conditions: Fearful, Happy, Neutral, Object, Fixation
- 36 total trials per condition (split in 6 blocks); 3 seconds per trial
- Each block = 6 trials (18 seconds)
- Pseudorandom order applied
- All conditions equally split into 2 fMRI runs; each run ~4.5 min



Behavioral Results



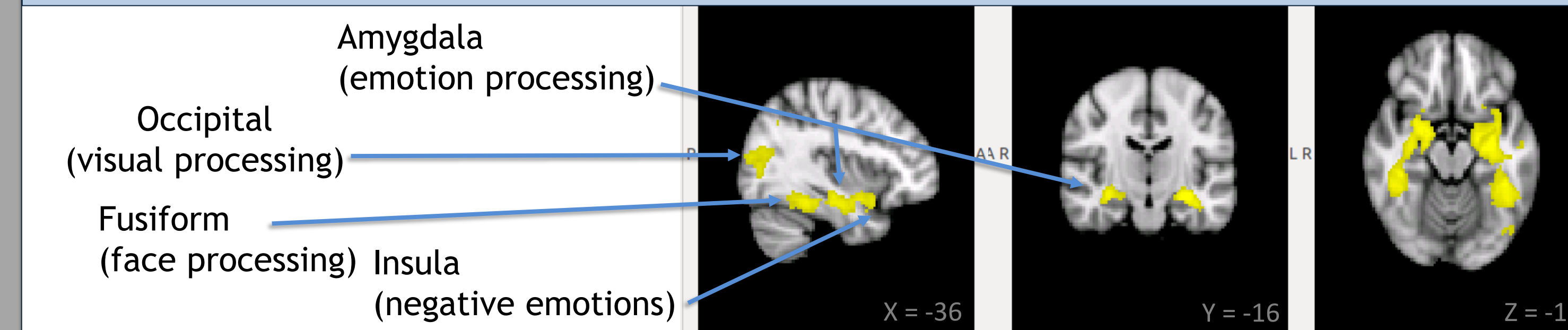
References: 1. Uchida, M., Faraone, S., Martelon, M., Kenworthy, T., Woodworth, K., Spencer, T., Biederman, J. (2014). Further evidence that severe scores in the aggression/anxiety-depression/attention subscales of child behavior checklist (severe dysregulation profile) can screen for bipolar disorder symptomatology: A conditional probability analysis. *Journal of Affective Disorders*, 165, 81-86. 2. Biederman, J., Petty, C., Monuteaux, M., Evans, M., Parcell, T., Faraone, S., & Wozniak, J. (2009). The child behavior checklist-pediatric bipolar disorder profile predicts a subsequent diagnosis of bipolar disorder and associated impairments in ADHD youth growing up: A longitudinal analysis. *Journal of Clinical Psychiatry*, 70(5), 732-740. 3. Holtmann, M., Buchmann, A. F., Esser, G., Schmidt, M. H., Banaschewski, T., & Laucht, M. (2011). The child behavior checklist-Dysregulation profile predicts substance use, suicidality, and functional impairment: A longitudinal analysis. *Journal of Child Psychology and Psychiatry*, 52(2), 139-147. doi:10.1111/j.1469-7610.2010.02309. 4. Siste, M., Massons, J., Perez, R., & Ascasso, L. (2014). Validity of the DSM-oriented scales of the child behavior checklist and youth self-report. *Psychosomatics*, 55(3), 364-371. doi:10.7326/psycosomatics2013.342. 5. Holtmann, M., Buchmann, A. F., Esser, G., Schmidt, M. H., Banaschewski, T., & Laucht, M. (2011). The child behavior checklist-Dysregulation profile predicts substance use, suicidality, and functional impairment: A longitudinal analysis. *Journal of Child Psychology and Psychiatry*, 52(2), 139-147. doi:10.1111/j.1469-7610.2010.02309.

fMRI Method

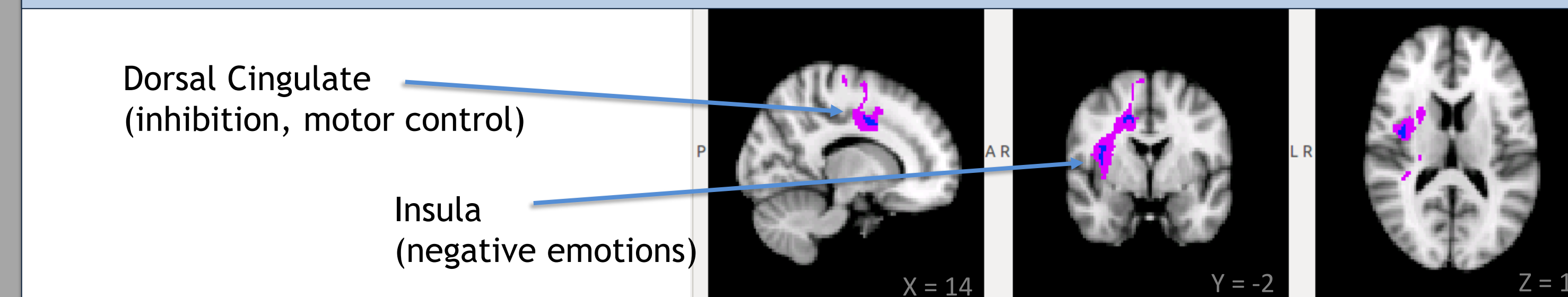
- N=14, Age: 6-16 yrs (Mean=9.55, SD=2.78)
- 3T Siemens MRI (TR = 2.2 s, TE = 30 ms, voxel size = 3 x 3 x 3.3 mm)
- fMRI processing performed by OpenfMRI pipeline (including Freesurfer, FSL, Nipype, ANTS, SPM, ART)
- Results normalized to standard brain template (MNI) for visualization
- P<0.05 corrected for multiple comparisons; cluster size > 10 voxels reported

fMRI Results

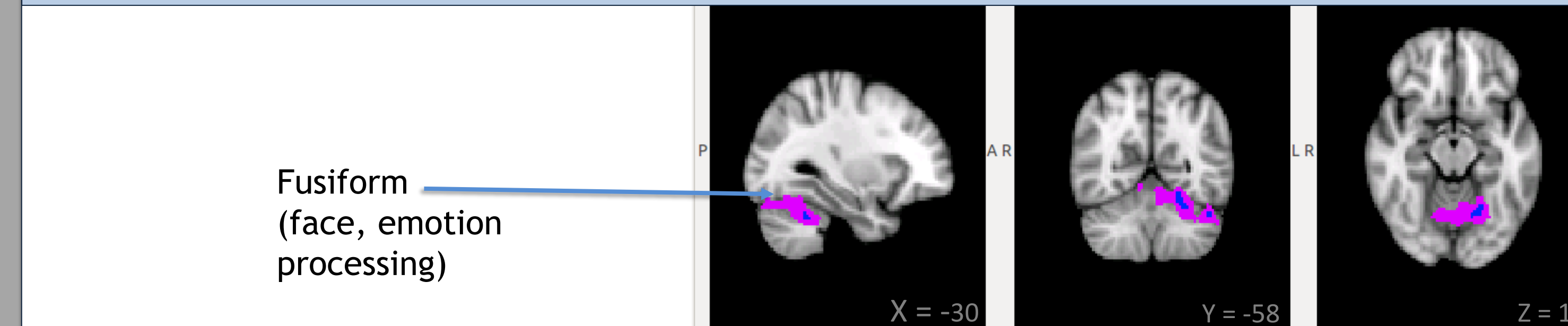
Fear > Happy Contrast



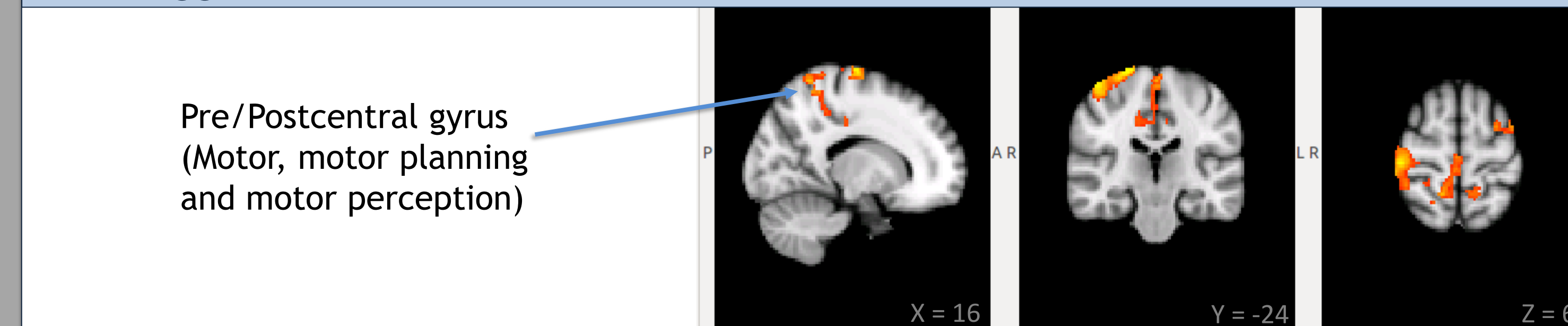
CBCL Attention and Fear



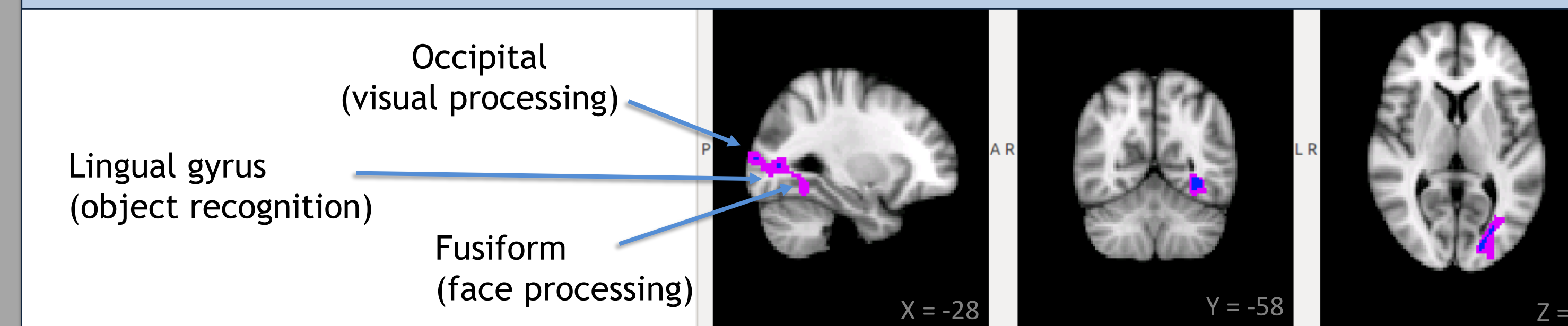
CBCL Attention and Fear vs. Neutral



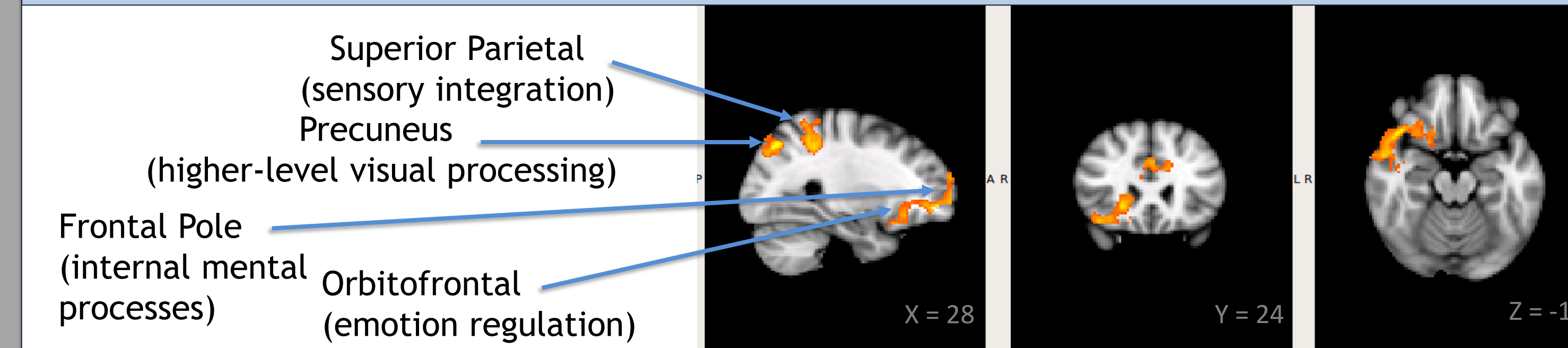
CBCL Aggression and Fear vs. Neutral



CBCL AAA and Fear



DSM Affective Problems and Fear



Initial Impressions

- Higher CBCL AAA scores (greater dysregulation) are correlated with lower functioning in areas related to emotional visual perception and behavioral regulation, accompanied with increased activity related to motor perception and execution
- In contrast, higher DSM Affective score is associated with enhanced activity in the right anterior PFC regions that are often compromised in DSM-diagnosed affective disorders, potentially related to an increased effort as a compensatory mechanism in non-disordered developmental cohort

Acknowledgements

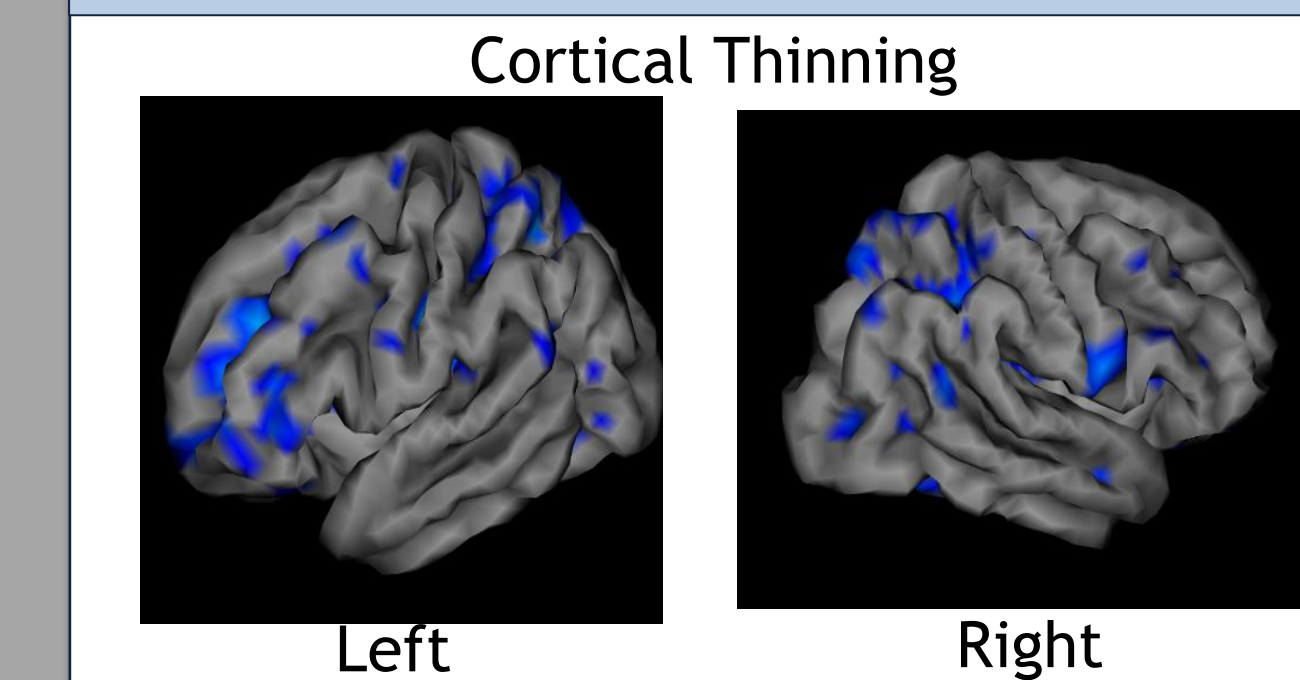
Center for Brains Minds and Machines & NSF STC Award: CCF-1231216; GabLab; Imaging Center of McGovern Institute for Brain Research; Dr. Mandana Sasanfar and MSRP; CBMM; Massachusetts General Hospital

Structural MRI Method

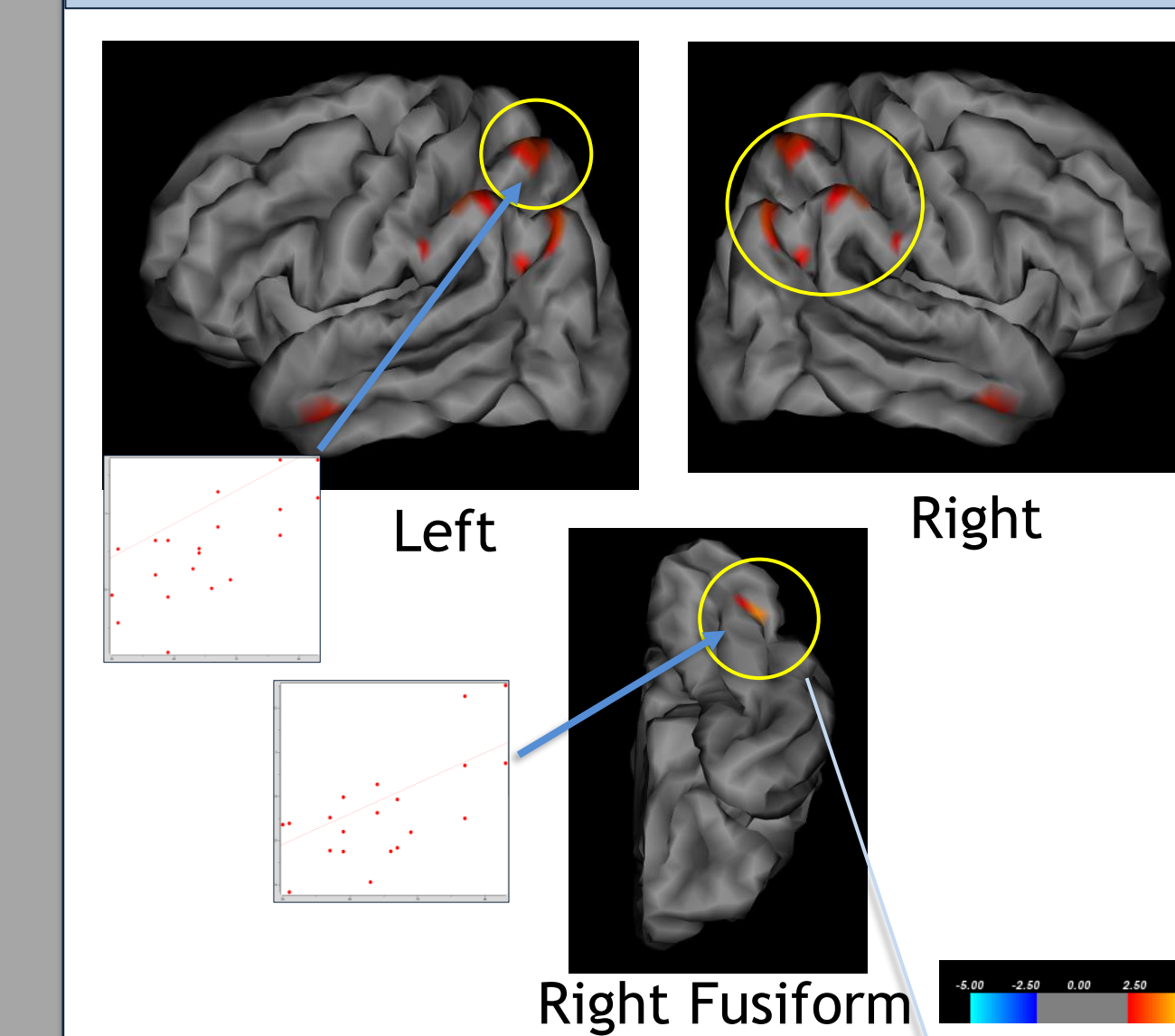
- N=20, Age: 6-16 yrs (Mean=10.05, SD=2.87)
- Standard Freesurfer Processing workflow (recon -all)
- Surface examination (<https://brainder.org>)
- Quality assessment (Qdec)
- Cortical thickness examined by whole-brain permutation tests correlating with CBCL measures controlling for Age effect (Qdec; p<.01, uncorrected)
- Subcortical volumes examined for: amygdala, hippocampus, thalamus (SPSS)

Structural MRI Results

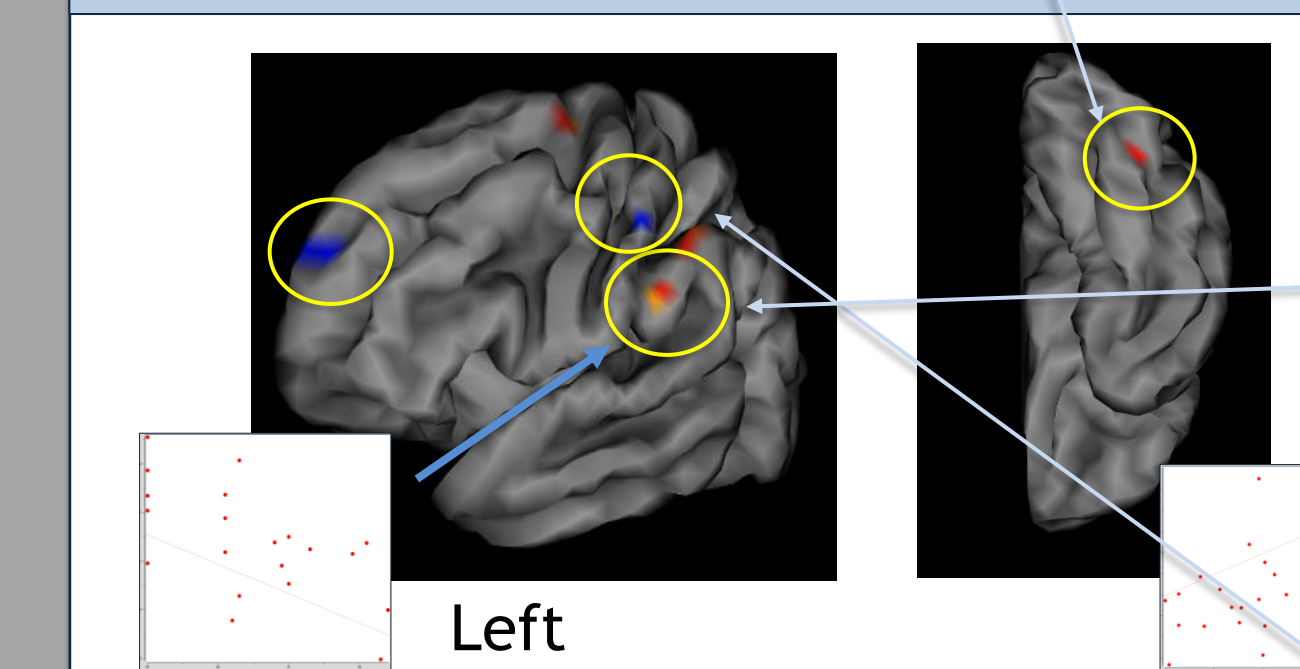
Global Negative Correlations with Age



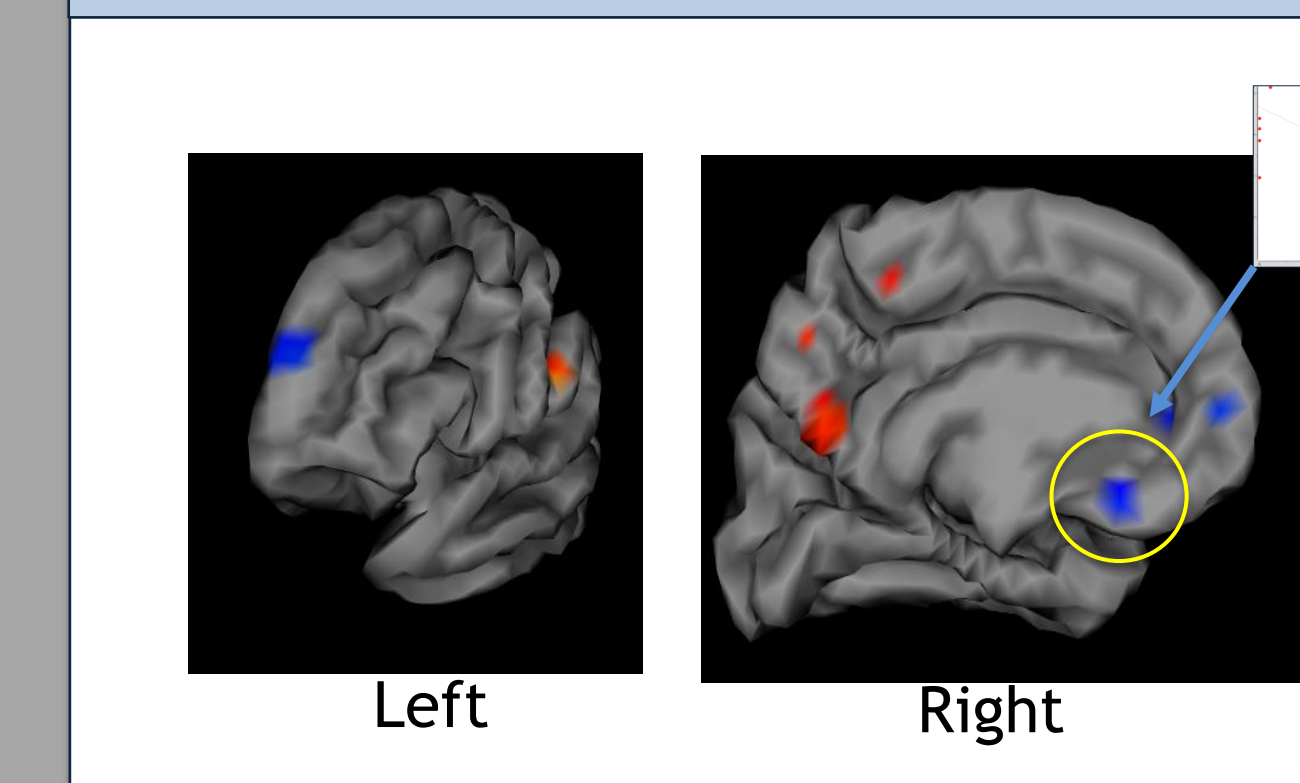
CBCL Attention Score



CBCL AAA Score



DSM Affective Score

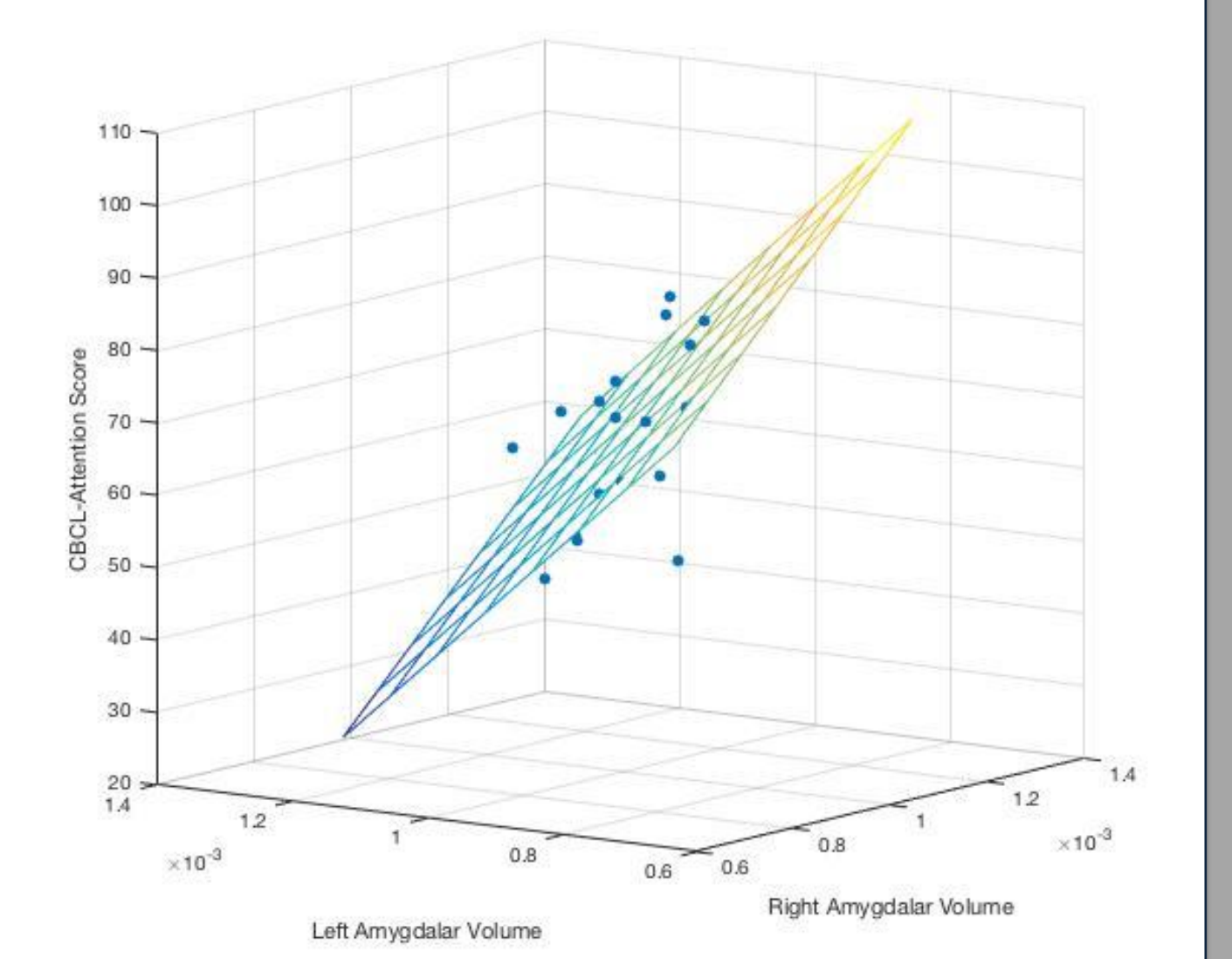


Significant Subcortical Volume

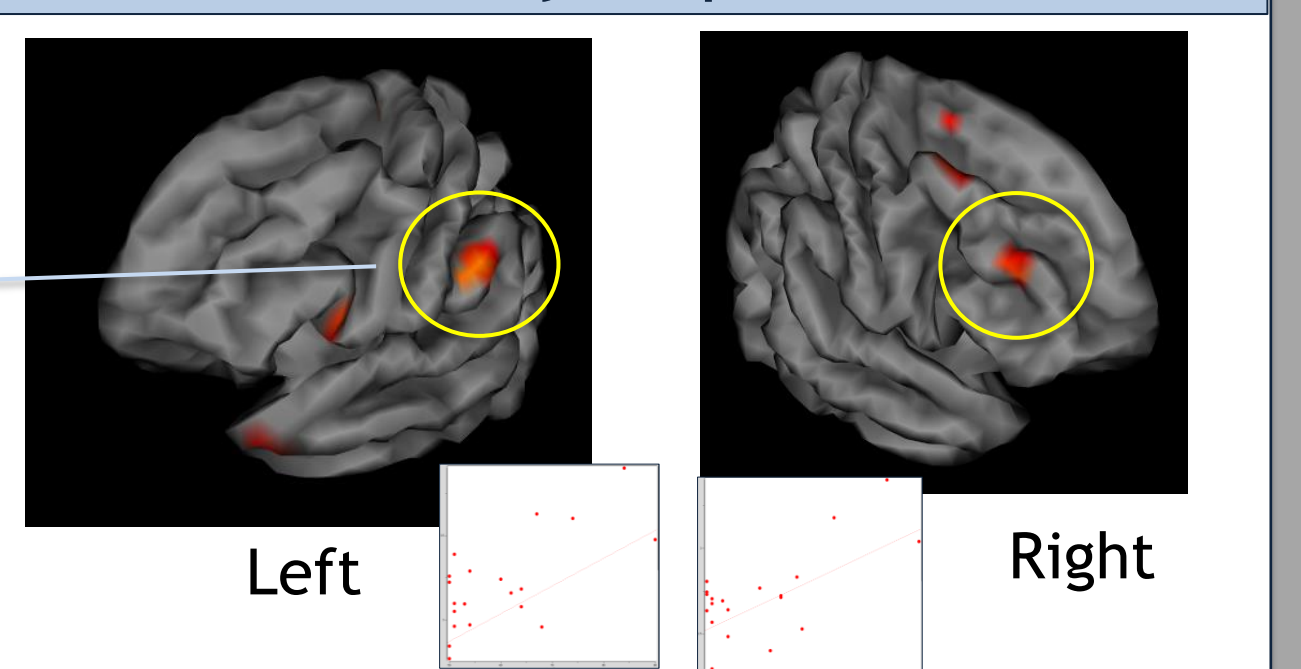
Right and Left Amygdala Volumes Predict Aggression Score (controlling for Age):

Regression Model: Aggression Score = R.Amygdala*(0.92) + L.Amygdala*(-1.093) + Current.Age*(-0.077) + 85.329 (p<0.05)

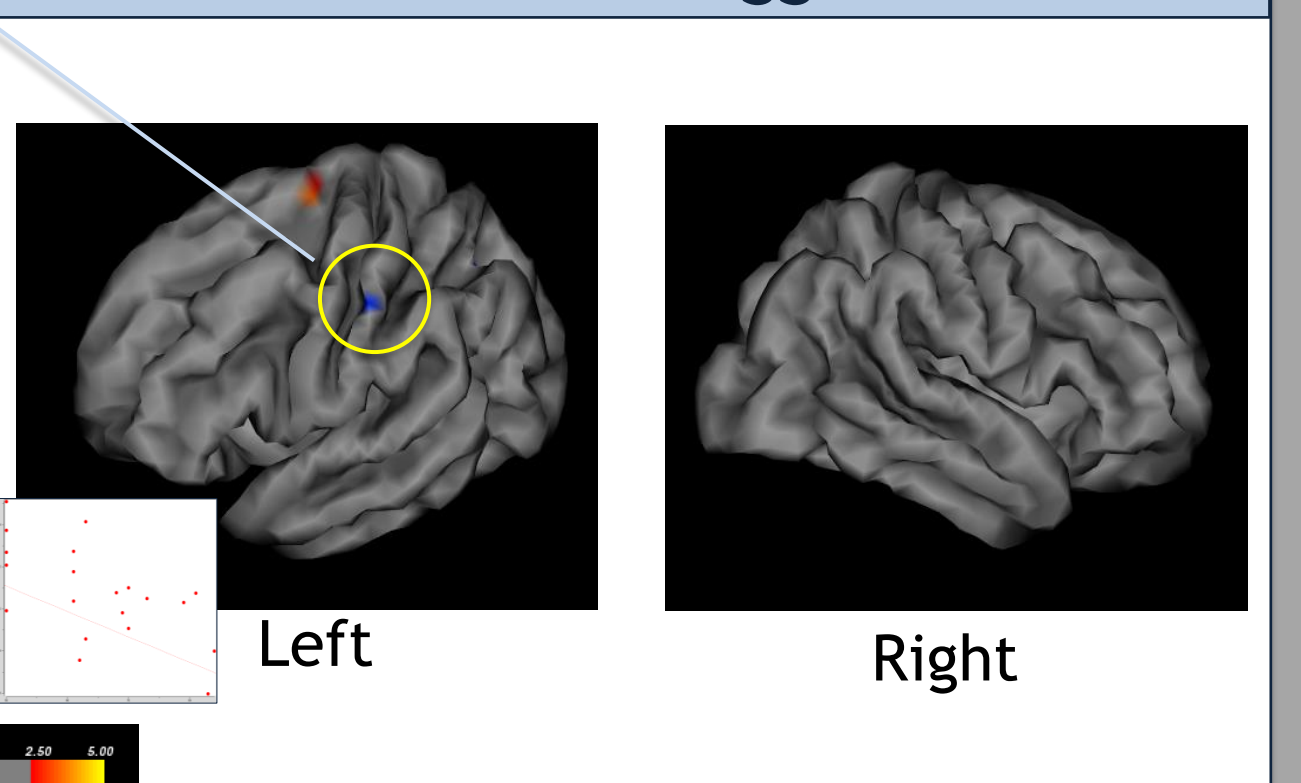
Note: Standardized scores used for beta values and corrected Amygdala volumes in this equation



CBCL Anxiety/Depression Score



CBCL Aggression Score



Conclusions

- Across analyses, higher CBCL AAA scores (risk profiles) are consistently correlated with lower functioning and greater cortical thickness (a developmentally disadvantaged profile) in regions attributable to mood-dysregulation risk factors (emotion and attentional perception, and motor control)
- Higher DSM Affective profile (diagnostic profile) is consistently associated with enhanced functioning and lower cortical thickness (an early maturational profile) in the Frontal Pole and OFC regions, likely related to a compensatory mechanism in non-disordered developmental cohort

Contributions

- Providing neurological account for emotion dysregulation and risk factors predictive of mood disorders
- Optimizing current clinical diagnostic protocols by understanding beyond behavioral observation
- Facilitating earlier identification of risk for mood disorders and development of better therapeutic intervention, prevention and treatment of affective disorders