Distinct dACC Glutamate Modulation during Inhibitory Motor Control Driven by Negative Emotional Stimuli in Trauma-Exposed Youth using $^1$H fMRS

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BACKGROUND

• Experiencing childhood trauma may contribute to pediatric psychopathology by elevating negative emotional responses and, in turn, overwhelming cognitive control$^1$.

• BOLD fMRI has implicated the dorsal Anterior Cingulate Cortex (dACC) in cognitive control, but the underlying neural processes remain unknown.

• We utilized $^1$H fMRI to investigate dynamic changes in dACC glutamate during cognitive control with and without negative emotional face stimuli to assess the impact of negative emotional processing on cognitive control in trauma-exposed youth.

We hypothesized less dACC glutamate during cognitive control with emotional face stimuli compared to squares.

METHODS

Participants: 17 trauma-exposed youth (58% female, age=11.8±0.8yrs, trauma=3.2±2.1vts).

Neuroimaging: Continuous $^1$H fMRS measurements were acquired using PRESS with OVS and VAPOR (TE=23ms, TR=4.0s, 13 measurements/task run, 4 averages/measurement, 2048 points, TA/task run=3:12min). Spectra were collected from a single voxel placed in the medial dACC (Figure 1a) and averaged to yield one glutamate level per task run using LCModel.

Trauma: sum total of DSM-5 criterion A traumas experienced, assessed using the Traumatic Events Screening Inventory, TESI.

Visual-Guided Cognitive Control Task: block designed task with “Non-Selective” (motor control) and “Selective” (motor control + inhibitory control) Response Modes, each executed with and without negative emotional stimuli, or the “Faces” and “Squares” Stimuli Conditions, respectively (Figure 1b). Baseline control condition consisted of crosshair fixation.

Statistical Analysis: Repeated measures generalized estimating equations (GEE) assessed glutamate modulation and response data by modeling main and interaction effects of response mode and stimuli condition, controlling for baseline glutamate (SAS GENMOD; SAS Institute Inc).

RESULTS - Glutamate Modulation

Figure 2: A) No main effect of Response Mode on glutamate modulation, independent of Stimuli Condition. B) Main effect of Stimuli Condition on glutamate modulation such that youth demonstrated significantly less glutamate for Faces stimuli, independent of Response Mode ($\chi^2= 4.18, p=0.04$).

RESULTS – Behavioral Response

Figure 3: A) Main effect of Response Mode on response times such that youth demonstrated increased response times during the Selective Response Mode relative to Non-Selective, independent of Stimuli Condition ($\chi^2= 11.4, p<0.01$). B) Main effect of Stimuli Condition on response times such that youth demonstrated significantly longer response times for Faces stimuli, independent of Response Mode ($\chi^2= 4.93, p=0.03$).

Figure 4: A) No effect of Response Mode on response accuracy, independent of Stimuli Condition. B) Main effect of Stimuli Condition such that youth demonstrated significantly greater response accuracy for face stimuli, independent of Response Mode ($\chi^2= 7.62, p=0.01$).

DISCUSSION

• Excitatory glutamatergic and inhibitory GABAergic neurons are highly integrated, forming an excitatory and inhibitory (E/I) balance.

• During task conditions, dynamic changes in glutamate levels (glutamate modulation) measured using $^1$H fMRI may reflect a net shift in E/I balance towards greater excitatory or inhibitory neural engagement (Figure 5).

• In the present study, we observed a significant reduction in dACC glutamate during cognitive control with face stimuli relative to squares, suggesting a net shift in dACC E/I balance towards greater inhibitory neural engagement. This effect corresponded with a significant increase in response times.

• While response times significantly increased during the Selective Response Mode, there was no corresponding change in glutamate level, indicating dACC glutamate modulation is not driven by Mode of behavioral response.

• Further research will investigate associations between glutamate modulation, trauma exposure, and pediatric anxiety.

CONCLUSION

dACC glutamate modulation during cognitive control is driven by the presence of emotional face stimuli in trauma-exposed youth.

REFERENCES
