Individual differences in GABA+ and GLX modulate brain activation during cognitive control differently in teen males and females

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Background

Research Question: Do neurotransmitters modulate brain activation during cognitive control in adolescence?

Background:

- GABA plays a role in neural sculpting during adolescence and GABAergic genes have been linked to goal maintenance (Kilb, 2012; Hatoum et al., 2020)
- PFC plays a critical role in two distinct types of cognitive control:
  - Goal maintenance: Maintaining a goal in the presence of a task-inappropriate information
  - Goal-related selection: Selecting one response from many task-relevant options

Approach: We measured levels of GABA and Glutamate as well as brain activation (fMRI) during goal maintenance and goal-related selection in a sample of 85 adolescents (47 F, 38 M; 14-22 yrs., mean age =17.2 yrs, s.d.=1.5 yrs)

Tasks

Goal Maintenance

Word-Picture Stroop:

Categorize task-relevant word (house/face) superimposed on task-irrelevant picture (house/face)

Contrast: Task vs. Fixation

Goal-Related Selection

Verb Generation:

Generate verb response to noun stimulus

Contrast: High vs. Low Selection

Low Selection: Few Verbs	High Selection: Many Verbs
scissors	**cat**
⇩	⇩
cut	**purr, meow, lick**

Spectroscopy

Neurotransmitter concentrations obtained for dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC)

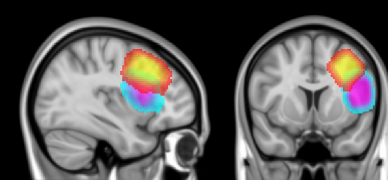
Glx (glutamate/glutamine)

- From PRESS data analyzed using LCM (Provenchar, 1993 *Magn Reson Med*)

GABA+

- From MEGA-PRESS data analyzed using Gannet (Mescher et al., *1998 NMR Biomed*; Edden et al., 2014 *JMRI*)

Neurotransmitter concentrations relative to water baseline and corrected for proportion of gray matter in each voxel



Extent of coverage for MRS voxel placement for DLPFC (warm) and VLPFC (cool) voxels. Outer extent of each voxel shows area covered in 90% of participants, while inner extent (yellow, purple) shows area covered in 75% of participants.

This work was supported by the NIMH grant R01 MH105501

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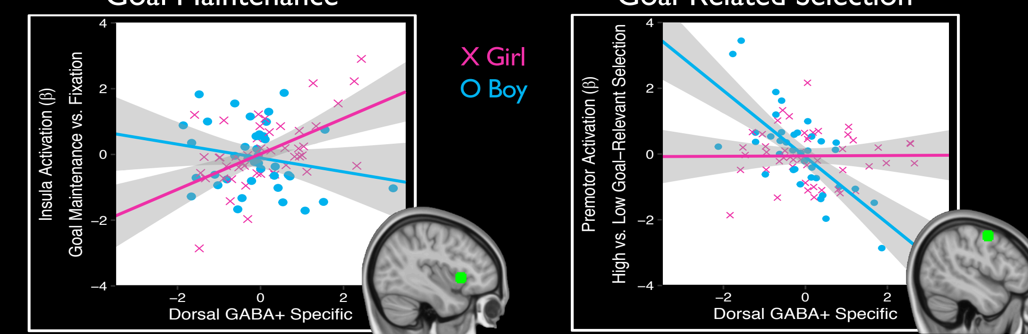
Results

Separate models were run for DLPFC and VLPFC measures. Because GABA and Glx have a common neurochemical pathway, we examined the *specific* effect of GABA and GLX by including both measures in the same model. Each GLM included the following parameters:

BOLD = GABA + GLX + Age + Gender + **Gender*GABA** + Gender*Glx

Goal Maintenance | Goal-Related Selection



- Specific to girls and significantly different from boys, individuals with higher levels of DLPFC GABA+ showed a smaller difference in activation between active goal maintenance and fixation in regions of the frontoparietal network and related portions of the anterior insula
- Specific to boys and significantly different from girls, individuals with higher levels of DLPFC GABA+ exhibited a smaller difference in activation between the difficult as compared to easy goal-related selection conditions in regions of the dorsal and ventral attention networks including premotor and inferior frontal regions (VLPFC)
- In both cases, DLPFC Glx showed weaker and opposite relationships to those observed with GABA+

Conclusions

These findings provide evidence that GABA may influence the fronto-parietal network in girls, but the dorsal and ventral attention and associated sensor-motor networks in boys.

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