Exploring Relationships of GABA and Glutamate with Negative Valence Systems

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BACKGROUND

- Dysregulation of negative valence systems (NVS) is a characteristic of mood disorders.
- Dysregulation of NVS is evidenced behaviorally by difficulties in affect processing and emotion regulation (ER), with corresponding alterations in ER neurocircuitry. [2]
- Dysregulation in the GABAergic and glutamatergic systems within ER neurocircuitry is implicated in mood disorders. [3-4]
- However, the relationship of neurometabolic dysregulation to NVS is not well understood.
- We investigated brain markers of GABAergic and glutamatergic function in a brain region involved in emotion regulation, dorsolateral prefrontal cortex (DLPFC), and their relationship to function in NVS, using self-report and behavioral measures.

METHODS

- 20 participants [14 women and 6 men; age (mean±SD): 55±2.68] with and without a mood disorder participated in this study to enrich the sample for a range of NVS function.
- MR Spectroscopy, using STEAM at 7 Tesla was used to measure GABA and glutamate levels in the DLPFC.
- NIH toolbox was used to assess self-report negative affect and to calculate a summary score
- A linguistic affective go/no-go task[1] was used to assess attentional bias by comparing number of commission and omission errors and reaction time to negative stimuli against positive and neutral stimuli.

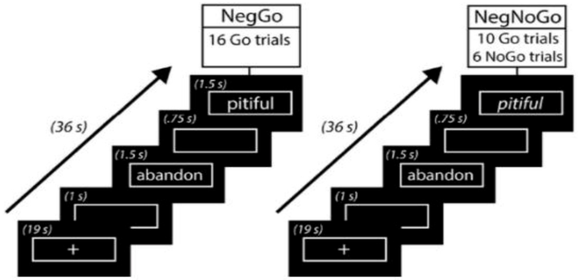

Figure 1. Example block of linguistic affective go/no-go task. 6 blocks (3 valences [positive, negative, neutral] x 2 conditions [go, no-go]) presented per run; 2 runs.

Lower DLPFC GABA is associated with higher negative affect scores and increased attentional bias toward negative stimuli.

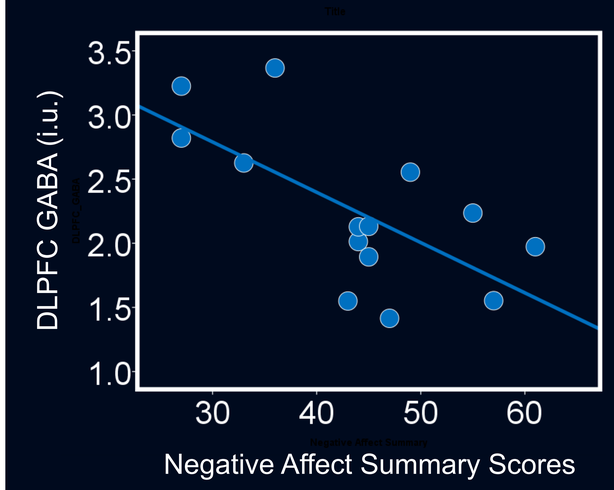

Figure 2. DLPFC GABA and negative affect summary score. DLPFC GABA levels significantly inversely correlated with the negative affect summary score (r=-.670, p=0.009).

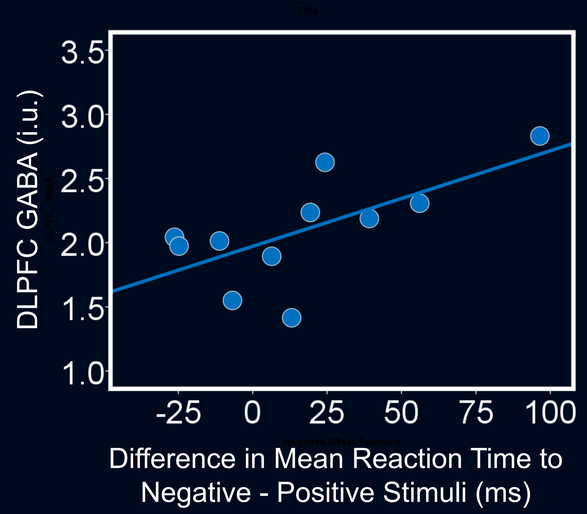

Figure 3. DLPFC GABA and reaction time. dlPFC GABA levels significantly correlated with slower reaction time to negative vs positive stimuli (r=.632, p=.027).

RESULTS

Table 1. Demographic and clinical characteristics of the sample

	Healthy Controls (N=13)	Bipolar Disorder (N=7)
Age (years)	47.31 ± 9.12	45 ± 7.64
Sex (% female)	69.2%	71.4%
YMRS	0.83 ± 2.04	0.33 ± 0.82
MADRS	3.00 ± 6.71	2.67 ± 3.72

Shown are mean ± s.d. YMRS: Young Mania Rating Scale, MADRS: Montgomery –Asberg Depression Rating Scale

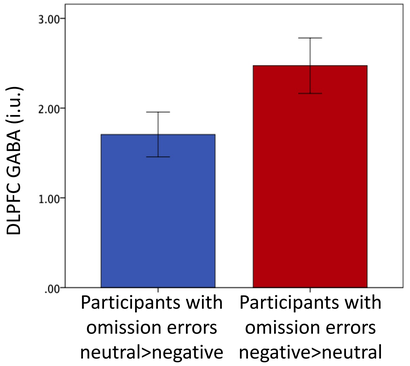

Figure 4. DLPFC GABA and omission errors. DLPFC GABA levels were significantly higher among the group who made more omission errors in response to negative versus neutral stimuli; $t(7)$=-3.9, p=.006.

CONCLUSIONS

- We did not observe a significant association between DLPFC GABA and commission errors.
- Neither did we observe a significant association when testing relationships of glutamate in the DLPFC with either negative affect scores or measures of negative affective bias.
- Our findings suggest a role for DLPFC GABA in negative valence systems functioning and is in line with studies implicating lower GABA individuals with mood disorders.
- These findings have the potential to inform clinical care regarding the use of GABAergic medications to improves outcomes in disorders involving negative valence systems.

REFERENCES

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