Relationship of Brain GABA with Circulating Progesterone

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BACKGROUND

- The GABAergic system in the prefrontal cortex of the brain is implicated in psychiatric disorders and neurodegenerative conditions such as depression.
- Preclinical studies of major depression have shown decreased $GABA_A$ receptor function in the frontal cortex and limbic areas.
- Progesterone acts as a positive modulator of $GABA_A$ receptors, contemporaneously inducing an increase in GABA levels.
- However, limited knowledge exists on the effect of circulating sex hormones on brain GABA in humans in vivo.
- We aimed to examine the relationship of circulating progesterone with regional concentrations of brain GABA.
- **Objective: Determine the association of brain GABA with circulating progesterone.**

METHODS & RESULTS

- GABA was measured using magnetic resonance spectroscopy (MRS) at 7 Tesla in the dorsal anterior cingulate cortex (ACC), ventromedial prefrontal cortex (VMPFC), and left dorsolateral prefrontal cortex (DLPFC) in 29 females.

	Female (N=29)
Age	48 (8): (36-66)
Progesterone	0.58 (1.80)
DLPFC GABA	2.36 (0.62)
ACC GABA	3.08 (1.44)
VMPFC GABA	3.44 (1.30)

- Spearman correlations were used to determine the association of brain GABA in each region with concentrations of circulating progesterone.

Figure 1. Representative voxel location (left) and MRS spectrum (right).

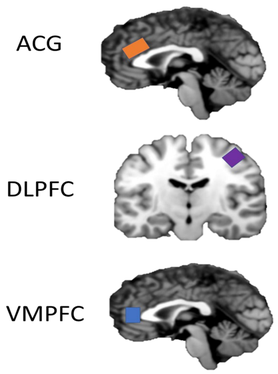
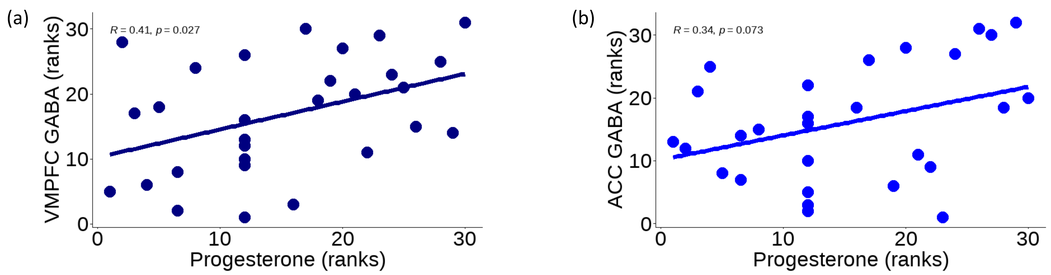


Figure 2. Relationship between a) VMPFC GABA with progesterone in females b) ACC GABA and progesterone in females.



Progesterone was positively correlated with VMPFC GABA in females.

Progesterone showed a trend in positive correlation with ACC GABA in females.

CONCLUSION

- Our study provides evidence of increased VMPFC and ACC GABA in females with higher progesterone, suggesting that circulating sex hormones may be important factors to consider in future studies examining brain GABA levels in psychiatric and other disorders.
- Further, these data suggest the interplay of progesterone and GABAergic function as a possible underlying mechanism of increased depression in women that future studies should investigate.

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