ALTERATIONS OF GABA LEVELS IN PREMENSTRUAL SYNDROME WOMEN: A PROTON MAGNETIC RESONANCE SPECTROSCOPY STUDY.

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Target audiences: psychiatrist and gynecologist.

Background: Most women of reproductive age may experience moderate to severe premenstrual symptoms, affecting their social adjustment and daily life. An increasing body of preclinical evidences has pointed to the involvement of gamma-aminobutyric acid (GABA)neurotransmitter system in the pathogenesis of premenstrual syndrome(PMS).Most studies have focused on neurosteroids and their interactions with GABA-A receptors .Research on GABA concentrations in PMS seems to be limited . The MEGA-PRESS technique is able to render the GABA peak visible and isolate it from other major metabolites[1] .Currently ,it is the most robust and most widely used method to detect GABA signals.

Purpose: The aim of this proton magnetic resonance spectroscopy (^{1}H-MRS) study was to examine whether PMS is associated with alterations in brain GABA.

Methods: 36 regularly menstruating women ,18 with PMS(23.2±1.5 years) and 18 age matched controls(23.5±1.4 years) were recruited from local medical school. Scans were performed in the late luteal phase(1-5days before onset of menses)using a 3T Philips MRI scanner. GABA signals were recorded from MEGA-PRESS sequence (TR= 2000 ms; TE =68 ms; 320 averages)(Fig.1).Spectra were extracted from the anterior cingulate cortex (ACC)/medial prefrontal cortex (mPFC) and a second voxel placed in the left basal ganglia (ltBG). Post-processing of the MRS data was carried out using AMARES within jMRUI v.4.0 software[2]. Because the signal detected at 3.02 ppm is expected to contain contributions from both macromolecules (MM) and homocarnosine, the signal is labeled GABA+ rather than GABA .Gamma-aminobutyric acid /Creatine (GABA+/Cr) ratios were determined as the primary outcome .The N-acetylaspartate /creatine (NAA/Cr) ratios and Choline/ceatine(Ch/Cr) ratios were also measured .All statistical analysis were tested using SPSS v.16.0.

Results: ACC/mPFC GABA+/Cr ratios were significantly lower (p=0.013)in PMS (0.32±0.03)compared to controls(0.34±0.03),whereas no significant difference (p>0.05)was observed in the ltBG(Fig.2) . There were no significant differences in NAA/Cr and Cho/Cr between the two groups in both regions. The lower GABA+/Cr ratios in ACC/mPFC detected in PMS remained significant after controlling for gray matter fraction .

Discussion: The lower GABA+/Cr ratios in ACC/mPFC may be due to dysfunctional GABA synthesis or due to dysfunction in enzymes involved in glutamate-glutamine cycling. The premenstrual fluctuant neurosteroids are supposed to be related to these dysfunctions ,which needs to be elucidated in laboratory studies in the future .The GABA+ alterations were observed in ACC/mPFC but not in ltBG, indicating that ACC/m PFC was more vulnerable to neurological disorders . Furthermore ,ACC/mPFC was suggested to be involved in negative emotions and in modulation of automatic nervous systems[3,4].In this regard , dysfunctions in this region may partly underlie the variety of psychosomatic symptoms in PMS .

Conclusions: In this study, we found reduced GABA+ levels existing in the ACC/mPFC of PMS women. The premenstrual GABA deficit in this region may be an important neurobiological mechanism contributing to the pathophysiology of PMS.

References:

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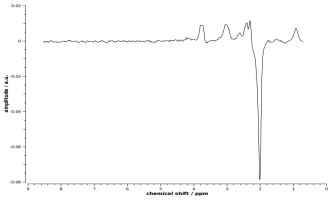

Fig.1 Representative J-edited spectrum of GABA from MEGA-PRESS method with the GABA+ peak at 3.02 ppm.

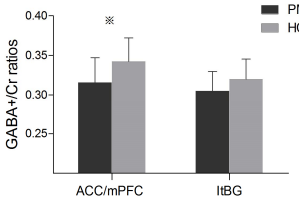

Fig.2 Comparisons of GABA+/Cr ratios in ACC/mPFC and ltBG between PMS and healthy controls. A significant decrease in ACC/mPFC was detected (※ represents p<0.05)