Increased Anterior Cingulate GABA Level Following Electroconvulsive Therapy in Patients With Major Depressive Episodes

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Introduction: Electroconvulsive Therapy (ECT) is an effective, commonly used treatment for major depressive episodes (MDE) often administered when pharmacotherapies are not efficacious or not tolerated. Even though the exact mechanism of how ECT works to relieve depression is not yet known, it is believed that ECT works by targeting the deep brain structures that control the neuroendocrine system (1). ^{1}H magnetic resonance spectroscopy (MRS) studies have shown reduced level of gamma amino butyric acid (GABA), a major inhibitory neurotransmitter, in patients experiencing and active MDE (2, 3). Reduction in GABA level at occipital and anterior cingulate cortex has also been observed in ^{1}H MRS (4). It has been shown that ECT restores the reduced GABA level at occipital cortex in depression (5). In this study we have investigated the effect of ECT in patients with acute MDE on the anterior cingulate GABA level using *in vivo* ^{1}H spectroscopy.

Methods: Adult patients experiencing a Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) defined MDE as part of either major depressive disorder or bipolar affective disorder, for whom a prior clinical decision to pursue ECT has already been made, were scanned within two weeks before their first course of ECT (pre-ECT) and again 1-2 weeks after their ECT (post-ECT). All of the procedures involved in obtaining these data were approved by the institutional review board (IRB) of Cleveland Clinic. MR scans were performed using a 3 tesla Siemens Trio scanner (Erlangen, Germany) using a 12 channel phased array head coil. Patients were scanned with a MEGA-PRESS sequence (6) having water signal-based interleaved navigator to assess and discard portion of motion-corrupted data (7). Voxels at anterior cingulate were assigned based upon a whole brain T1 weighted magnetization prepared rapid gradient echo (MPRAGE) scan having 1 mm × 1 mm in-plane resolution, with a slice thickness of 1.2 mm. The voxel size was $2 \times 2 \times 1\text{cm}^3$ for patient 1 (P1) and $2 \times 2 \times 2\text{cm}^3$ for patient 2 (P2). The frequency of the editing pulse in MEGA-PRESS (TR = 2.7 s, TE = 68 ms) was alternated in an interleaved fashion between 1.9 and 1.5 ppm to minimize macromolecule contamination. A metabolite-nulling scan was also performed (TI = 650 ms) to account for any residual macromolecule contamination. Data were acquired in a shot by shot basis, and the first four measurements were ignored during analysis in order to ensure steady state magnetization. PRESS scans with and without water suppression were performed for absolute quantification following the editing scans. For absolute quantification, the gray matter, white matter and CSF contribution to the voxel composition was performed by using the FAST segmentation algorithm (8) of the FSL software library (9) with the anatomical 3D MPRAGE as the base image, and applying a mask at the voxel location. MRUI software was used for spectroscopy data analysis (10). [GABA]/[Cr] ratio was first obtained from the editing scans following the procedure in (6). Next [Cr] was obtained from the PRESS scans as in (11). The GABA concentration, [GABA] was next determined by taking the product of [GABA]/[Cr] and [Cr].

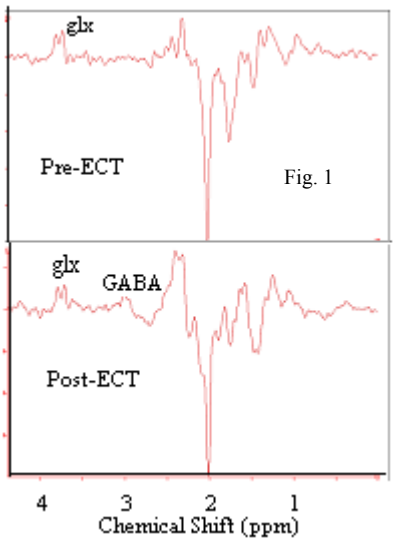

Fig. 1

[GABA]/[Cr] (Pre-ECT)	[GABA]/[Cr] (Post-ECT)	[GABA] (Pre-ECT)	[GABA] (Post-ECT)
Patient 1			
0.17±0.07*	0.36±0.20	1.70±0.70	3.35±1.94
Patient 2			
0.04±0.04*	0.21±0.05	0.32±0.32	2.33±0.55

* 90% confidence interval upper limit

Results and Discussion:
Even though patient 1's data had lower SNR (possibly due to a smaller voxel size), increase in anterior cingulate [GABA] was observed post-ECT in both patients. Fig. 1 shows the increase in GABA after treatment in P2, where almost no GABA could be seen pre-ECT. The increase in [GABA]/[Cr] and [GABA] after treatment is shown in the Table. It should be noted that the quantification of P1 is affected by low SNR. Also, in both cases, pre-ECT GABA level was below the noise level and so upper limits were estimated with a 90% confidence interval. No statistical significance in the differences in pre- and post-ECT data was calculated since this is a preliminary data with very small sample size. However, the observed increase in [GABA] observed is in line with the same results observed in occipital cortex (5). Since [GABA] is reduced in anterior cingulate of patients with MDE(4), our preliminary result suggests that ECT is indeed effective in "restoring" anterior cingulate [GABA] level in depression patients.

Conclusion:
Electroconvulsive therapy increases GABA level in anterior cingulate in patients with MDE.

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