Single voxel MEGA-edited GABA and short TE 1H MRS in hippocampus and other brain regions implicated in bruxism
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Introduction: Bruxism is a sleep related movement disorder characterized by non-functional grinding and clenching of teeth [1,2,3]. The hypothalamic-pituitary-adrenal (HPA) axis system has been identified to be involved in bruxism in recent neuroimaging studies [3,4]. A 1H MRS pilot study was conducted to establish the feasibility of gamma-aminobutyric acid (GABA) and other metabolite quantification in four brain regions implicated in bruxism: medial temporal lobe which contains the right hippocampus (rHIPP), right thalamus (rTHAL), dorso-lateral prefrontal cortex (DLPFC) and pre-supplementary motor area (preSMA) region, involved in motor planning. The right hemisphere was used because of the documented laterality in stress-regulatory components of the HPA axis.

Methods: In the absence of polysomnography, group classification was based on the initial interview, responses on a temporomandibular disorder (TMD) History Questionnaire [5] and wearing a protective night guard. 8 male bruxer subjects (confirmed by TMD questionnaire and use of protective night guard; age: 28.6 ± 3.0 years) and 9 healthy male controls (non-bruxer; age: 25.6 ± 1.9 years) were recruited. 1H MRS data was acquired on a 3 T Siemens Tim Trio MR scanner using single voxel short TE 1H MRS (TR/TE=1500/30 ms, 128 averages) and MEGA-PRESS GABA-edited MRS [6,7] (TR/TE=1500/68ms, RF editing pulse BW = 44 Hz, 256 averages for the hippocampus, 196 averages for other regions) were obtained in all VOIs. For each MRS scan, a reference spectrum was acquired without water suppression and used later for phase and frequency correction of the corresponding water-suppressed spectrum. All spectra were quantified using LCModel [8] with respectively appropriate basis sets. Only those metabolites with Cramer Rao Lower Bounds (CRLB) <20% were included and quantification results were expressed as ratio to total creatine (tCr).

Results: A significant increase was seen in NAA/tCr (p=0.002) in the rHIPP, whereas Glu/tCr (p=0.023) and Gln/tCr (p=0.021) were decreased in the rTHAL in bruxers. No significant group difference was seen in GABA+/tCr in any region, but GABA+/tCr was highest in hippocampus when averaged over all subjects and compared to the other three brain regions. The average linewidth for the single voxel spectra and MEGA-PRESS spectra obtained in all the subjects in the rHIPP was 9.3 Hz and 9.7 Hz respectively. The average coefficient of variation (%CV) for the GABA+/tCr measurements in the rHIPP for healthy and bruxer subjects was 21.1% and 28.2% respectively.

<table>
<thead>
<tr>
<th>Region</th>
<th>rHipp</th>
<th>rThal</th>
<th>preSMA</th>
<th>DLPFC</th>
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<tr>
<td>Region-wise GABA+/tCr</td>
<td>0.63±0.15</td>
<td>0.59±0.06</td>
<td>0.54±0.13</td>
<td>0.36±0.13</td>
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Table 1. Region-wise GABA+/tCr levels (mean±sd) averaged over all subjects.

Discussion: For the first time in vivo GABA+ levels were successfully measured using MEGA-editing in the human hippocampus. While medial temporal lobe is of great interest in neuroimaging studies [3,4]. Our and numerous dental and psychiatric studies, placement of VOI in the hippocampus is a particularly challenging task due to its size, location and presence of a cerebral artery. MEGA-edited GABA spectra were successfully obtained from hippocampus with good spectral quality and spectral resolution. Our finding of increased hippocampal NAA/tCr in bruxers compared to controls is similar to the reported increase in insular NAA levels in TMD subjects [9].