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 ^{1}H 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: 25.5 ± 1.9 years) were recruited. ^{1}H MRS data was acquired on a 3 T Siemens Tim Trio MR scanner using a 32-channel head coil. Fast T2-weighted MRI images were acquired for positioning of the MRS volumes of interest (VOIs). VOIs were placed in the rHIPP (11.6 ml) (shown in Fig 1), rTHAL (15.6 ml), DLPFC (16.5 ml) and preSMA (21.9 ml). Single voxel short TE ^{1}H 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).

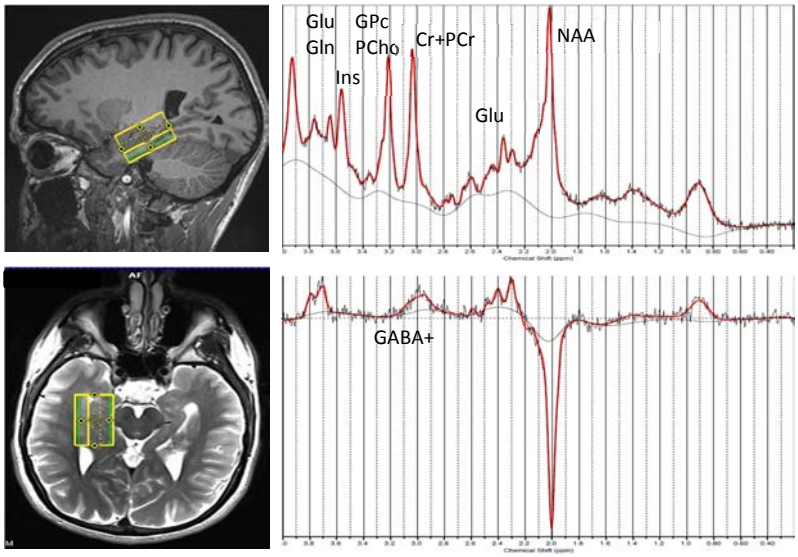

Figure 1. Sagittal and axial views showing representative VOI placement in the hippocampus (left), short TE single voxel ^{1}H spectra (top right) and MEGA-PRESS GABA spectra (bottom right).

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.

Regional average GABA+/tCr			
rHipp	rThal	preSMA	DLPFC
0.63±0.15	0.59±0.06	0.54±0.13	0.36±0.13

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 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].

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