Ultra high field MR spectroscopy of the striatum in the human brain: On the relation between striatal metabolites and performance on a search step task

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Introduction

The daily dynamic environment often poses the challenge where a planned movement needs to be interrupted in order for another action to occur. This ability to stop an initiated motor program has been studied in both humans and non-human primates using the oculomotor search step task[1,2]. During this task, the participant is instructed to make an eye movement as soon as a visual target appears. On a minority of trials, the target unexpectedly moves to another location, requiring the participant to inhibit the initial eye movement and instead make an eye movement to the new location. The processes determining the outcome of this task has been described mathematically as a race between a GO process for the initial eye-movement and a STOP process for inhibition[3,4]. If the STOP process wins the race, the eyemovement to the initial target location is successfully inhibited. In this task, inhibiting this first eye movement becomes more difficult with longer delays between the initial target presentation and the target jump because the GO process gets a bigger head start. The speed of the GO process can be calculated from overt response times, whereas the STOP process speed (target step reaction time; TSRT) can be estimated using race model logic[4]. There is evidence that the basal ganglia network is involved in successful performance on this task, by facilitating or suppressing movement-activity in oculomotor output regions via the direct and indirect pathway, respectively. Since GABAergic neurotransmission is of great importance in the functioning of this network, especially in the striatum with regards to parallel planning[5], we aimed to determine the relation between GABA availability in this region and performance on the search step task. Additionally, we also determined the relation between other striatal metabolites, namely NAA,.creatine (Cr), and choline (Cho), and performance on this task since they have also been related to general cognitive functioning in previous studies.

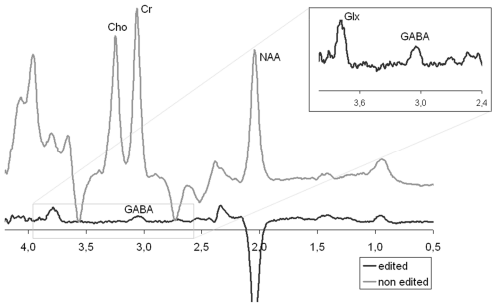

Figure 1: GABA measurement in the striatum. Edited (grey) and non-edited MR spectra are shown and a close up of the GABA resonance in the inset.

Methods

20 healthy volunteers (8 male, 12 female mean age of 31,5) participated in this study after having given informed consent. ***Saccade task:*** Saccade tasks were performed at a 3T MRI scanner during functional MRI scans (data not shown). Stimuli were displayed using Presentation software (Neurobehavioral Systems, Inc.) and presented onto an MR compatible LED screen that was viewed by the participant via a mirror on the head coil. Eye movements were recorded during scanning using an MR compatible infrared camera (Nordic Neuro Lab, Bergen, Norway). This system used a video camera mounted to the head coil, with the infrared illumination being provided by LEDs that were also mounted on the head coil. Eye position was sampled at a rate of 60Hz. Acquisition was controlled by ViewPoint Eyetracking software (Arrington Research). Stimuli presented by Presentation were digitally encoded and relayed to the ViewPoint software as triggers that were inserted into the eye movement recordings. ***MRS methods:*** GABA editing MRS in the striatum was performed at a 7T MR scanner (Philips, Cleveland, OH, USA) using a 32 channel receive dual transmit coil (Nova Medical, Wilmington, MA) driven by 2 amplifiers (4 kW each) to reach a maximum B1 of 20uT in the region of interest. RF shimming was based on phase maps. Up to 2nd order shim gradients were calculated based on B0 maps. To minimize the chemical shift displacement artefact, FOCI pulses (BW 16kHz) (hyperbolic secant (HS)) were used for refocusing. A MEGA-sLASER sequence was used for GABA editing as previously described [7], briefly, TE 74ms, TR 5000ms, NSA 64 in a voxel of 40x24x25mm. Each acquisition was frequency aligned with the singlet resonance of Cho. The acquisitions were averaged after correction and the signals of GABA, NAA, Cr, and Cho were fitted using Matlab. The signal of the water reference scan was used to correct for receive sensitivity of the coil elements, for eddy current correction, and for quantification. ***Segmentation of the MRS ROI:*** The MRS voxel was placed carefully to encompass as much of the caudate nucleus and putamen as possible excluding CSF. The MRS voxel was segmented into caudate nucleus, putamen, globus pallidus and other tissues using SPM. These values were used as covariates in the linear regression used to determine a correlation between the variables of interest.

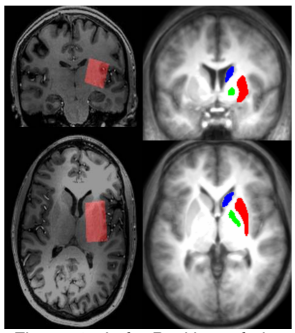

Figure 2: Left: Position of the voxel in the sbrain. Right: Segmentation of the caudate nucleus (blue), putamen (red) and globus pallidus (green) in a normalized and averaged brain.

Results and Discussion*:*

The average and standard deviation of the metabolite levels, corrected for the partial volume of caudate nucleus, putamen and globus pallidus was 12.7±1.2, 9.9±0.7, 2.5±0.3 and 1.5±0.2, for NAA, Cr, Cho and GABA respectively (based on a measured apparent T2 of water in the voxel of 42ms (n=1)). All correlations between GABA levels and performance measures (i.e. response times and TSRT) and parallel processing measures, were not significant ($p>0.05$). Also, no significant correlations with response times could be found for the other metabolites (NAA, Cr, Cho). This is in contrast to earlier studies that reported a correlation between (cortical) GABA levels and response selection related behaviour[8]. Our results suggest that neither striatal GABA availability nor striatal NAA, Cr, or Cho levels can predict the performance on a search step task in healthy participants. A reason for the negative finding might be that healthy participants do not display enough variability in baseline GABA levels. We therefore suggest repeating the experiment in psychiatric and/or neurologically impaired patient groups that display deficiencies on response selection tasks, since they might display larger variations in striatal GABA and metabolite levels, increasing the chance to detect a relation between GABA levels and response times.

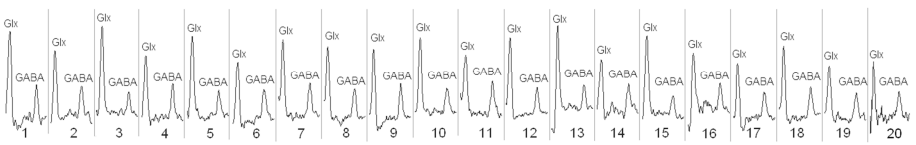

Figure 2: Signals of GABA and Glx in the edited spectra from each participant (normalized to water signal)

Conclusion:

We did not observe a relation between striatal GABA levels and performance on the search step task in healthy persons despite the fact that GABA was measured with high sensitivity at 7 Tesla and that we controlled for partial volume effects of different brain structures in the MRS voxel.

References: *[1] Hanes, DP (1995). Visual neuroscience, 12(5), 929. [2] Murthy, A (2007). Journal of Neurophysiology, 97(2), 1457.[3] Boucher, L (2007) Psychological review, 114(2), 376. [4] Logan, GD (1984) Human Perception and Performance, 10(2), 276. [5] Bhutani, N (2013) The Journal of Neuroscience, 33(24), 9985.[6] Ohrmann, P (2007) Journal of psychiatric research, 41(8), 625. [7] Andreychencko, A (2012) MRM Oct;68(4):1018 [8] Sumner, P (2010) Nature neuroscience, 13(7), 825.*