GABA, glutamate and intellectual ability

Anouk Marsman[1], Rene C.W. Mandl[1], Dennis W.J. Klomp[2], Vincent O. Boer[2], Anna Andreychenko[3], Wiepke Cahn[1], Rene S. Kahn[1], Peter R. Luijten[2], and Hilleke E. Hulshoff Pol[1]
[1]Psychiatry, University Medical Center Utrecht, Utrecht, Netherlands, [2]Radiology, University Medical Center Utrecht, Utrecht, Netherlands, [3]Radiotherapy, University Medical Center Utrecht, Utrecht, Netherlands

Target audience
Scientists and clinicians interested in the relationship between neurometabolite levels and cognitive functioning and/or measurement of neurometabolite levels *in vivo* using ^{1}H-MRS at a magnetic field strength of 7T.

Purpose
The purpose of this study was to test the hypothesis that minimizing energy resources is beneficial to intelligence in the prefrontal and occipital cortices by measuring GABA (gamma-aminobutyric acid) and glutamate (Glu) levels. A combination of higher GABA levels and lower Glu levels suggests a more efficient energy use [1]. Performing ^{1}H-MRS at an ultra-high magnetic field strength of 7T results in increased sensitivity and spectral resolution, which are particularly important when measuring Glu and GABA.

Methods
Participants: 23 matched healthy control subjects (age 27.7±5.3, M/F 16/7) participated in this study. All participants underwent a general cognitive assessment using the full Wechsler Adult Intelligence Scale (WAIS)-III [1].
MR acquisition: All investigations were performed on a 7T whole body MR scanner (Philips, Cleveland, OH, US). A birdcage transmit head coil was used in dual transmit driven by 2x4 kW amplifiers, in combination with a 32-channel receive coil (both Nova Medical Inc., Burlington, MA, US). For the assessment of Glu an sLASER sequence (TE=28ms, TR=5s, 32 averages) [2] was used (fig.1A). Non-water-suppressed spectra were obtained for quantification (acquisition time=10s, carrier frequency was set to the chemical shift of H_2O). GABA-edited experiments were conducted using a MEGA-sLASER sequence (TE=74ms, TR=4s, 64 averages) [3] (fig.1B). Voxels were located in the medial prefrontal and medial occipital lobe (fig.2). Prior to the MRS exams, second order B_0 shimming was applied using the FASTERMAP algorithm at the voxel of interest [4,5]. In order to minimize chemical shift displacement artifacts, the highest possible B_1 field was generated by optimizing the phase of both transmit channels to locally assure constructive B_1 interferences [2,6].
Spectral fitting and quantification: Fitting of the sLASER spectra was performed with LCModel-based software implemented in Matlab [7], which uses a priori knowledge of spectral components to fit metabolite resonances [8]. To correct for the contribution of gray matter, white matter and cerebrospinal fluid in each voxel, segmentation was performed using the SPM8 software package. Fitting of the MEGA-sLASER spectra was performed by frequency-domain fitting of the GABA and Cr resonances to a Lorentzian line-shape function in Matlab. GABA levels were expressed as the ratios of their peak areas relative to the peak areas of the Cr resonance. Spectra with a CRLB of 20% or more were excluded from the study.

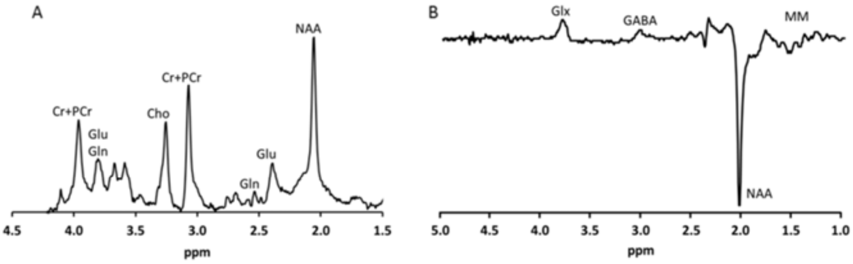

Figure 1. A: Typical sLASER spectrum. B: Typical MEGA-sLASER spectrum.

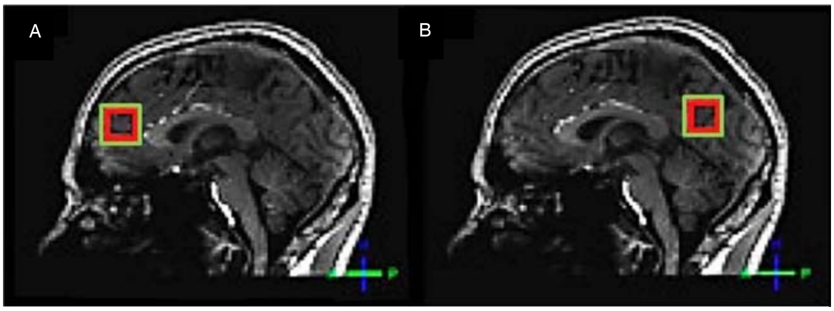

Figure 2. Voxel placement in (A) the medial prefrontal lobe and (B) the medial occipital lobe. sLASER voxels (2x2x2cm^3) are shown in red and MEGA-sLASER (2.5x2.5x2.5cm^3) are shown in green.

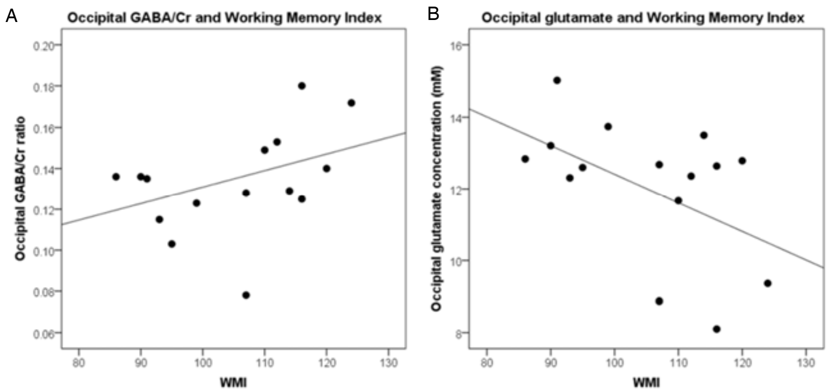

Figure 3. A: Occipital GABA/Cr ratios are not significantly correlated with WMI (r(9)=0.42, p=0.19); B: Occipital Glu concentrations are significantly correlated with WMI (r(10)=-0.79, p<0.004).

Results/Conclusion
A higher Working Memory Index (WMI) was associated with a significantly lower Glu concentration (p<0.004) and with a higher (but not significantly) GABA/Cr ratio (p=0.19), resulting in a significantly higher GABA/Glu ratio in the occipital cortex (p=0.04) (fig.3). This suggests that individuals with a higher intelligent working memory performance make more efficient use of their brains' energy resources. Also, Glu levels and GABA/Cr ratios in the occipital cortex are strongly correlated (r(7)=-0.85, p<0.01), suggesting that our findings of metabolite levels with cognitive functioning are not working in isolation but are part of a network of connective metabolites.

References
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