Diurnal Stability of MEGA-PRESS measurements of GABA concentration

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Introduction

As the principle cortical inhibitory neurotransmitter, gamma-aminobutyric acid (GABA) is the target of significant research effort in both the neuroscientific and clinical communities. Robust localised methods for measuring the concentration of GABA in the human brain in vivo are now sufficiently precise, not only to detect gross differences between patient populations and healthy controls (e.g. 1), but also to detect both individual differences between healthy subjects and task-driven changes within individuals. GABA plays a central role in the maintenance of the circadian rhythms in the brain, and animal experiments have shown circadian cortical GABA changes. However, in spite of the obvious implications for future study design, no data have been published investigating whether edited MRS measurements of GABA (plus co-edited macromolecules) vary with the time of day; this study addresses that issue.

Methods

Eight healthy volunteers were recruited for this study, with local ethics board approval. In each subject, GABA-edited MEGA-PRESS spectra were acquired in two regions at five timepoints between 7am and 8pm in the same day (as shown in Figure 1). The sensorimotor volume was centred on the ‘hand knob’ area of the precentral gyrus, aligned with the upper surface of the cortex in the sagittal plane. The visual region was centred on the median line, rotated in the sagittal plane so as to align with the cerebellar tentorium. The following experimental parameters were used: TE = 68 ms; TR = 1.8s; 16 ms editing pulse; 332 acquisitions; acquisition time 10 min. The edited GABA signal was modelled with a simple Gaussian function and a linear baseline between 2.82 ppm and 3.56 ppm, and quantified relative to the unsuppressed water signal from the same volume which was fitted with a mixed Lorentzian-Gaussian lineshape. A repeated-measures 2-way ANOVA was used to test for main effects of region and timepoint (where timepoint is treated as the repeated measure). Inter- and intra-subject variability was investigated by calculating the CV of measurements for each individual and region, and the coefficient of variation of measurements grouped across all subjects.

Figure 2: Overlay of 80 edited spectra, showing reproducible lineshape (left; data have been baseline-corrected through the points *). The plot of mean within-subject GABA concentration by region (above right) shows between-subject variability. No effect of time-of-day is seen in plots of the running mean of eight consecutive measurements (below right); shaded region represents ± 1 SEM.

Table 1: Coefficients of variation (over five measurements) for each subject and region. The column Mean shows the average of these within-subject CVs. The column Group contains the coefficient of variation as calculated across all subjects.

<table>
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<th>Subject</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<th>Group</th>
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<td>8.8%</td>
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References