In vivo GABA measurement using a PRESS-localized double quantum filter in patients with malformations of cortical development and epilepsy

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Introduction
γ-aminobutyric acid (GABA) is an important inhibitory neurotransmitter. There are reports that low initial GABA levels may be an indication for GABA-ergic drug treatment, and that an early rise in cerebral GABA may identify responders (1). We have implemented a PRESS-localized double quantum (DQ) filter for measurement of GABA concentrations in vivo, established normal ranges of GABA concentrations in controls, and studied elevation of GABA in subjects with malformations of cortical development (MCD) and epilepsy.

Methods
A pulse sequence for PRESS-localized DQF measurement of GABA on a 5x GE Signa 1.5T scanner was adapted from a previously published technique (2). Phantom calibrations were performed to optimize filter efficiency and quantify yield, so that concentrations could be estimated relative to creatine (3).

Five male subjects with unilateral MCD were studied (age 25-50) and 10 normal volunteers (4 male, 6 female, age 22-40). In patients, two 35cc voxels were studied if time permitted, one covering the malformation and one matched contralateral voxel. In controls, one 35cc mesial occipito-parietal voxel was studied. Axial T1-weighted IRP-SPGR volume images were obtained, both to guide voxel prescription and for tissue segmentation using SPM 96. The DQF spectra were acquired with TE/TR = 68/2000, scan time 17:12. Quantification was via manual integration, relative to creatine in normal-appearing tissue as well as lesions, should help to better characterize the metabolite distribution in this condition. Abnormalities in the contralateral side were almost as common as in the malformation.

Discussion
GABA has been shown to be elevated in some but not all MCD patients. The 2 patients who showed elevated GABA had large malformations, and therefore a high proportion of grey matter filling the voxel. However, the finding of increased GABA also contralaterally suggests that the elevation is a more global effect. This could be due either to more widespread abnormality than visually apparent or to medication. One patient with elevated GABA was taking topiramate, and the other gabapentin, both of which have been suggested to raise cerebral GABA levels (1); however, one patient with normal GABA level was also taking gabapentin, and most were on a combination of several drugs.

These findings agree with a recent report of elevated GABA in biopsies from MCD (4), but suggest that this may have been a result of drug treatment; no data from normal-appearing tissue was obtained. The use of spectroscopy as a non-invasive biopsy, applicable to normal-appearing tissue as well as lesions, should help to better characterize the metabolite distribution in this condition.

References

Figure 1: Conventional and DQF PRESS spectra from MCD voxel.

Results
Control mean GABA was 1.3 mM +/- 0.2. There were no differences between male and female control subjects. Three of the MCD patients had no detectable abnormality in GABA concentration, while 2 had significantly elevated GABA both in the malformation and contralaterally (Fig. 2).

In the conventional PRESS spectra, a heterogeneous pattern of metabolite abnormality was found in the lesions, with the most common findings being low N-acetyl aspartate plus NAAG (tNA) and elevated choline (Cho). No significant changes in glutamate + glutamine (Glx) or creatine (Cr) were found, but there were some decreases (and in one case an increase) in myo-inositol (Ins).