Single Voxel MR Spectroscopy Data Quality and Metabolite Signature of the Isolated Amygdala

L. Angelos[1], B. M. Nacewicz[1], A. L. Alexander[1,2], and R. J. Davidson[1,3]

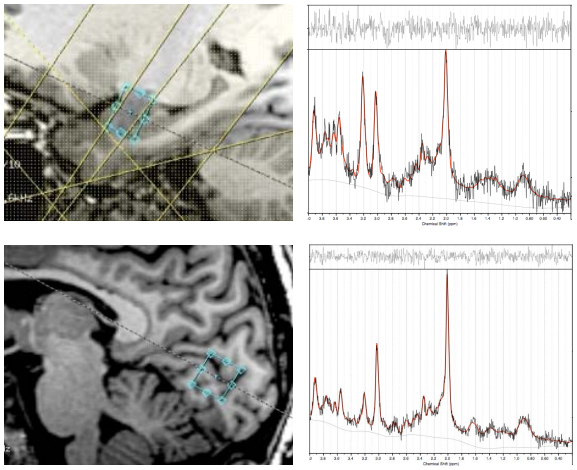
[1]Waisman Brain Imaging Laboratory, University of Wisconsin -- Madison, Madison, WI, United States, [2]Department of Medical Physics, University of Wisconsin -- Madison, Madison, WI, United States, [3]Department of Psychology, University of Wisconsin -- Madison, Madison, WI, United States

Introduction

The amygdala is an important brain structure involved in the processing of social and emotional stimuli, and its abnormal development has been linked to autism, depression, and affective disorders. As a target for MR spectroscopy, the amygdala is challenging due to its small size (about 2ml) and location in a hard-to-shim region in the medial temporal lobe. We have developed a single-voxel amygdala spectroscopy protocol that maximizes voxel volume by adapting the prescription to each individual's anatomy, and minimizes contamination and artifacts from surrounding tissue, especially hippocampus, with outer volume saturation bands. Compared to occipital cortex, a voxel location commonly used in MRS development, our amygdala data has a distinctive metabolite signature, emphasizing the need for spectroscopy protocol development focused on neuroscientifically interesting targets.

Methods

As part of a reproducibility study, we scanned 14 subjects (age 18-43, 6 males), each in four different sessions, on a GE X750 3.0T scanner with an 8-channel head coil. Each scan session included an amygdala and an occipital cortex (OCC) single-voxel spectroscopy acquisition (product PRESS, TE=35ms, TR=1.5s, 256 averages plus 16 acquisitions without water suppression, scan time 7:00). The amygdala voxel was prescribed off of two 3D inversion recovery-prepped T1 localizers: an oblique sagittal covering the right half of the brain in a plane parallel to the interhemispheric sulcus (scan time 3:55), and an oblique axial covering the whole brain and angled so the midpoint and splenium of the corpus callosum occupied the same plane (scan time 7:45). For the amygdala voxel, the MRS excitation volume was prescribed on the oblique axial localizer, and made slightly larger than each participant's right amygdala. Four saturation bands were placed to null signal from non-amygdalar tissues. The voxel was adjusted (by making it smaller or reducing the extent in the posterior/medial/inferior corner, a region of generally high field inhomogeneity) to achieve a prescan linewidth of 9Hz (0.070ppm) or less. The occipital cortex voxel was placed in a uniform region of mostly gray matter (GM), with the same voxel size and orientation as the amygdala voxel. Data was processed with LC Model, using standard water scaling and eddy current correction, and fitting to the measured TE=35ms metabolite basis spectra provided with this software package. Segmentation of brain tissue compartments (CSF, GM, WM) was done using FSL's FAST routine and the axial T1-weighted anatomical images. Metabolite concentrations were multiplied by $1/(1-f_{CSF})$ to compensate for low metabolite concentration (relative to the water reference) in the CSF portion of the voxel. To compensate for T1 relaxation, important because of our short TR, we multiplied by 1/(1-exp(-TR/T1)) with T1 values from Baker et al. (2008). Our focus is on metabolite ratios, so we present results in institutional units, not corrected for GM fraction or T2 relaxation effects (beyond the *in vitro* relaxation in the measured basis set).



Location and example spectrum of amygdala (top) and occipital cortex (bottom) voxels.

Results and Discussion

Data quality: We achieved excellent data quality in the amygdala. Relative to our occipital cortex voxel, amygdala S/N and linewidth were worse on average, but there was some overlap of these metrics in the data sets from our two voxel locations (see table, LC Model reported S/N is proportional to the NAA peak, so we compared SNR/NAA to account for metabolite concentration differences described below). Compared to single-voxel amygdala measurements by Hoerst et al. (2010), our larger voxel (2.3ml vs. 1.44ml) and shorter echo time (35ms vs. 80ms) allowed us to achieve better S/N. Unlike the Hoerst et al. study, we were able to resolve Glx with CRLB < 20% in all of 56 of our amygdala measurements.

Regional metabolite variation: As expected from the literature, our two voxels had substantially different chemical signatures. Cre was very similar, however, relative to OCC, NAA+NAAG (tNAA) was 34% lower and GPC+PCh (tCho) was 2.6 times higher in the amygdala. While our measurements at these two voxel locations had some overlap in data quality metrics and voxel composition (GM fraction), the tCho measurements did not overlap at all. These striking differences, which are clearly visible in the example spectra, emphasize the need to focus experiments on specific anatomically defined regions.

Hippocampus comparison: Focusing on tNAA/(tCho+Cre), a ratio discussed in the hippocampus MRS literature, our amygdala measurement was very similar to the amygdala measurement of Hoerst et al. (0.89 vs. 0.87), and somewhat lower than the hippocampus measurements (0.96 anterior, 1.07 posterior) presented by McLean et al. (2001). CSI studies of the hippocampus, including McLean et al., have shown a metabolite gradient, with tNAA/(tCho+Cre) increasing from the anterior to the posterior hippocampus. While this gradient has been partially attributed to large partial volume effects in the posterior hippocampus, our data suggest that the extreme chemical signature of the amygdala may be contributing to this measured gradient by decreasing, through partial volume effects, CSI measurements of tNAA/(tCho+Cre) in the anterior hippocampus.

	amygdala	OCC
voxel size (ml)	2.3 (0.2)	3.2 (0.2)
CSF fraction	0.08 (0.03)	0.11 (0.03)
GM fraction	0.76 (0.05)	0.66 (0.09)
linewidth (ppm)	0.050 (0.009)	0.039 (0.007)
SNR	9.71 (1.19)	19.5 (2.7)
SNR/NAA	1.27 (0.20)	1.72 (0.24)
	concentration (iu)	
NAA+NAAG	15.29 (2.49)	23.17 (1.66)
Cre	12.74 (1.74)	12.98 (0.90)
GPC+PCh	4.37 (0.60)	1.70 (0.17)
mI	9.27 (1.61)	7.12 (0.83)
Glu+Gln	23.08 (4.65)	21.62 (3.52)
tNAA/Cre	1.20 (0.11)	1.79 (0.13)
tCho/Cre	0.34 (0.03)	0.13 (0.01)
tNAA/(Cre+tCho)	0.89 (0.08)	1.58 (0.11)

Data quality metrics, metabolite concentrations, and ratios: average (standard deviation).