In vivo GABA T2 determination with J-refocused echo time extension at 7T

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Introduction: Spectral editing techniques can be used to unambiguously detect low concentrated J-coupled metabolites such as γ-Aminobutyric acid (GABA) from overlapping resonances such as creatine and macromolecules [1,2]. These techniques, however, have fixed and usually relatively long echo times [3-5]. Therefore, for the absolute quantification of GABA, the T2 relaxation time must be taken into account. However, to measure the T2 relaxation time, the signal intensity has to be obtained at multiple echo times, which has been shown for uncoupled resonances at 7T [6]. However, on a coupled spin system such as GABA this is challenging, because the signal intensity of the target resonances is modulated not only by T2 decay but also by the J-coupling, that strongly influence shapes and amplitudes of the edited signals depending on the echo time. This limits the sensitivity for T2 measurements. Here, we propose to refocus J-modulation of the edited signal at different echo times by chemical shift selective refocusing. In this way the echo time can be arbitrary extended while preserving the shape of the edited signal. The method was applied in combination with the MEGA-sLASER editing technique [5] to efficiently measure in vivo T2 relaxation time of GABA in the human brain at 7T.

Methods: MRS measurements were performed on a 7T MR scanner interfaced to a dual-channel volume transmit head coil and a 32 channel receiver array. A selective refocusing pulse (BW 1.8 kHz, duration 9 ms) was added to the MEGA-sLASER sequence (Fig. 1) to extend the echo time (TE) of 74 ms (optimized for GABA editing) to values between 91 and 222 ms. To refocus only the 3 ppm resonance of the GABA resonances the selective refocusing pulse was centered at 6 ppm. MRS measurements were also performed with the MEGA-sLASER at TE = 74 & 222 ms [5] without the selective refocusing pulse. Spectra were acquired in the visual cortex of 6 healthy human volunteers (TR = 4100 ms, 64 averages, 27 ml). The data was retrospectively phase and frequency corrected. The odd and even acquisitions were subtracted to measure only the GABA resonance and eliminate creatine and macromolecules resonances. In addition, the 3 ppm creatine signal was obtained from the sum of the odd and even acquisitions. The edited 3 ppm GABA signal was fitted as a doublet (14 Hz splitting) and the 3 ppm creatine signal as a singlet. The T2 relaxation times of creatine and GABA resonances were estimated with a least square fit to a single exponential decay. The data was normalized per subject to the creatine signal estimated at TE=0 ms. GABA and creatine T2 values were obtained for every subject and also from a combined dataset of all subjects. The fit error of the exponential decay was estimated using wild bootstrapping [8]. A creatine concentration of 8 μmol/g [3] was used as an internal quantification reference.

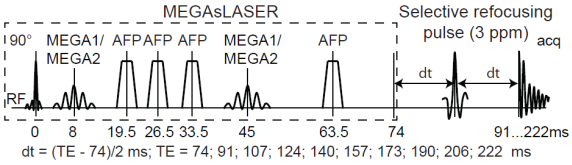

Figure 1. MEGA-sLASER sequence for GABA editing at 7T with an additional selective refocusing pulse for a flexible echo time extension.

Results and discussion: Spectra for the TE = 74, and the range of echo times from one subject are presented in Fig. 2. Note that in the spectra acquired with the MEGA-sLASER and the selective refocusing pulse, the co-edited 2 ppm NAA resonance was absent as it was outside the bandwidth of the additional refocusing pulse. The edited 3 ppm GABA and creatine signals (black) together with the fitted curves (red) are plotted in Fig. 2 (top). The results of T2-fitting are illustrated in Fig. 3. T2 values fitted individually per subject are plotted in the insets of the graphs in Fig. 3, showing one outlier (subject 3). The T2 relaxation time of the 3 ppm creatine resonance was calculated to be 104±8 ms (excluding the outlier) and 111±8 ms (including the outlier). Both values are in close agreement with the literature reported value [9]. The T2 relaxation time of the 3 ppm GABA resonance was 82±11 ms (excluding the outlier) and 92±13 ms (including the outlier). Averaged GABA concentration was determined as 1.3±0.2 μmol/g which is in the range of the previously reported values [3].

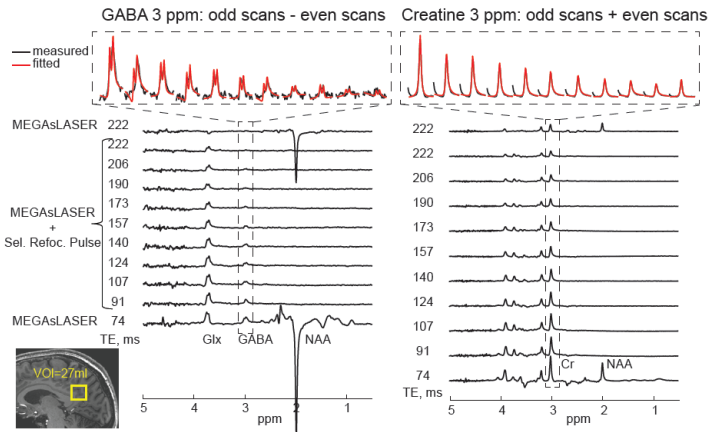

Figure 2. In vivo MR spectra obtained in one subject for the full range of echo times (74...222 ms). GABA is measured from the difference of odd and even scans (left). The creatine signal is obtained from the sum (right). Spectra at an echo time of 74 and 222 ms were acquired with a standard MEGA-sLASER without the additional selective refocusing pulse. The measured (black) and fitted (red) 3 ppm GABA and creatine resonances are shown on top.

Conclusions: The proposed method facilitates an easy and straightforward way to measure T2 relaxation times when using spectral editing techniques. It allows a dense sampling of the T2 decay curve at high sensitivity without the need for editing efficiency correction at each echo time value. The efficiency of the method was demonstrated for in vivo creatine and GABA T2 measurements at 7T, hence enabling in vivo quantification of the GABA concentration.

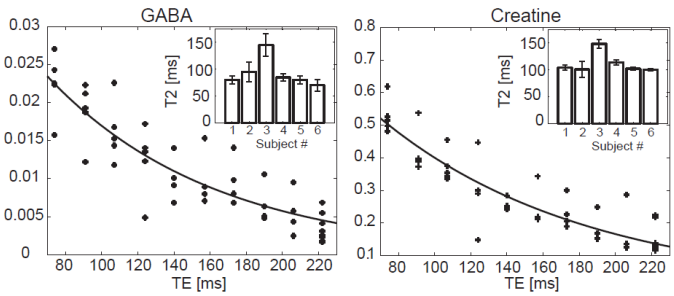

Figure 3. The combined data set of all subjects and fitted T2 decay curve for the 3 ppm GABA (left) and creatine (right) resonances.T2 values with error bounds for each subject are shown in the insets of the graphs.

References: [1] Rothman DL et al Proc Natl Acad Sci U S A 1993; [2] Mescher M et al NMR Biomed 1998; [3] Terpstra M et al MRM 2002; [4] Near J et al NMR Biomed 2011; [5] Andreychenko A et al Proc. 19thISMRM 2011; [6] Tkac I et al MRM 2001; [7] Intrapiromkul J et al Proc. 19th ISMRM 2011; [8] Zhu H et al IEEE Trans Med imaging 2007; [9] Otazo R et al MRM 2006.