Measurement of metabolite ^{1}H transverse relaxation times (T_2) in the human visual cortex over an extended echo-time range during visual stimulation at 7T

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Purpose: Previous studies, e.g.[1,2], employing ^{31}P and ^{1}H magnetic resonance spectroscopy (MRS) have reported evidence that the phosphocreatine/creatine ratio (PCr/Cr) decreases during photic stimulation consistent with the net conversion of PCr to Cr in the Cr kinase (CK) chemical reaction, resulting from increased metabolism in occipital cortex during visual stimulation [3]. Differences in transverse relaxation time (T_2) of the Cr and PCr proton resonances at 3.0 ppm were suggested to be the source of their non-monoexponential relaxation behavior and thus were considered as a potential handle for following the CK cycle [2]. In this work we employed a method we recently developed [4] for collection and analysis of multi-echo highly truncated MRS CPMG (Carr-Purrell Meiboom-Gill) spectroscopic data in order to achieve for the first time accurate T_2 measurements of total creatine (tCr), total NAA (tNAA) and choline compounds (tCho) in the primary visual cortex at 7T, and to investigate possible T_2 changes during visual stimulation. The large echo-time (TE) range employed here allowed evaluation of any deviation of the T_2 decay curves from mono-exponential relaxation, reflecting the presence of several T_2 components, as would be expected for the tCr signal at 3.0 ppm.

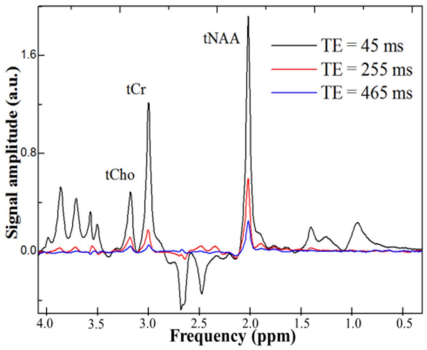

Fig.2: *Examples of spectra derived for different TE values using LPSVD.*

Methods: 6 healthy volunteers were scanned on a 7T Philips scanner equipped with a 32-channel receive coil and a quadrature transmit head coil. An initial fMRI scan (EPI, TE/TR=14/2000ms) was performed prior to the MRS studies in order to select a VOI encompassing the activated region of the primary visual cortex. Full-field visual stimulus consisted of a radial blue/yellow checkerboard flickering at a frequency of 8 Hz. A VOI of ~6cm^3 was positioned in the activated region for functional MRS acquisition (*Fig. 1*). The sequence used was based on a 8-echo PRESS-CPMG sequence with phase cycling of the PRESS as well as the multiecho part set to a CPMG sequence: 90_x-180_y-180_{-y}-acq-(180_y-acq-180_{-y}-acq)$_7$. The sequence parameters were: TE(shortest)=45ms, echo spacing=70ms, #points/echo=128, TR=4.5s, #dynamics=240). A single-echo PRESS scan was also acquired in the same VOI and for the shortest TE=45ms (BW=5000Hz, #points=2048, TR=4.5s, #averages=64). Linear prediction with singular value decomposition (LPSVD) (~20 spectral components) was used to generate priors from the short-TE fully sampled PRESS data. For the multiecho data, the priors were used to generate the components amplitudes within each echo data and FIDs were then extended to 2048 points [4] (*Fig.2*). The functional paradigm comprised 3 blocks, each of a 3 min-rest period followed by a 3 min-stimulation period. Spectra derived for each echo time during rest and stimulation were averaged in order to derive mean amplitude-TE curves of tCr, tNAA and tCho for the two conditions. Normalized signal decays were fitted to mono-exponential and stretched exponential ($S/S(0)=\exp(-(TE/T_2)^{\beta})$ curves in order to derive T_2 values of the three metabolites for rest and activation, and to evaluate deviations from mono-exponentiality.

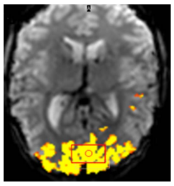

Fig.1: *Location of the VOI in the visual cortex.*

Results: The tCr signal measured as a function of TE exhibits a non-monoexponential decay pattern (β=0.69±0.04) (*Fig.3*). The tNAA and tCho amplitude-TE curves show a smaller deviation from mono-exponentiality, as indicated by the higher stretching factors β (*Tab.1*). The T_2 values of tNAA and tCr as derived from mono-exponential fits are consistent with previous findings [5], while tCho T_2 is reported for the first time at 7T (*Tab.1*). For all the metabolites, no significant changes were detected in T_2 during activation. However, an increase in the tCr signal intensity was detected during visual stimulation at long TE values (*Tab.2*) and in particular at TE=325ms, where the increase was statistically significant (p=0.01).

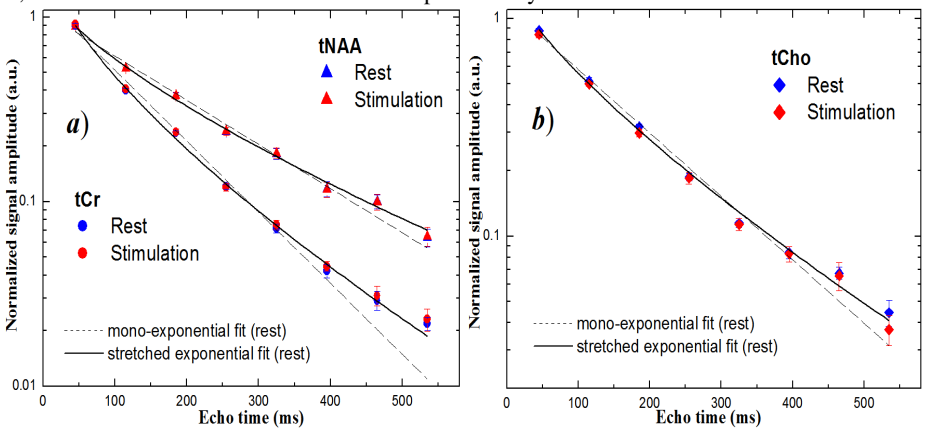

Fig.3: *Amplitude-TE curves for tCr, tNAA (a) and tCho (b) measured during rest and visual stimulation.*

	T_2 (ms,±SD) mono-exp	T_2 (ms,±SD) stretched-exp	β(±SD) stretched-exp
tCr	113±6	60±8	0.69±0.04
tNAA	181±14	119±21	0.75±0.08
tCho	148±8	102±20	0.78±0.07

Table 1

TE(ms)	S_{stim}-S_{rest}(%)	*p-value*
325	4.3±3.7	**0.01**
395	7.4±4.6	0.23
465	9.0±13	0.31
535	6.3±14	0.50

Table 2

Discussion: The deviation of tCr T_2 decay curves from mono-exponentiality is consistent with previous findings indicating that Cr has a longer T_2 than PCr [2], given that T_2 differences in the tCr peak in gray and white matter have been shown to be negligible [6]. In contrast, in tNAA and tCho the smaller deviations from mono-exponentiality could reflect differential contributions from gray and white matter [6]. The tCr signal increase during visual stimulation detected at long TE is compatible with the net conversion of PCr to Cr in the CK reaction, due to higher demand for ATP during neuronal activation, although it is expected that a larger difference would be detectable at shorter TE values, closer to the average T_2 value for Cr and PCr. The simultaneous change in Cr and PCr concentrations and their T_2 relaxation rates (BOLD effect) during activation makes it difficult to quantify these changes from bi-exponential fits, and more subjects need to be scanned to improve statistical significance.

Conclusion: Proton relaxation times T_2 of tNAA, tCr and tCho were measured for the first time in the primary visual cortex at 7T for a wide TE range and during visual stimulation. No significant T_2 changes during brain activation were detected, and the usefulness of analysis of the tCr T_2 for investigating the CK cycle needs corroboration from more subjects. In terms of other applications of this work, ischemia represents another physiological condition in which PCr may be consumed to support brain ATP levels [7]. Correct evaluation of T_2 changes during and after ischemia is necessary for quantification of metabolites under those conditions, thus providing a useful application for the method shown here.

References: [1]D.Sappey-Marinier *et al*.,JCBFM,**12,**584–592(1992). [2]Y.Ke *et al*.,MRM,**47**,232–238(2002). [3]T. Wallimann *et al*.,Biochem J, **281,**21-40(1992). [4]E.Ercan *et al*. ISMRM 2012. [5]S.Michaeli *et al*., MRM,**47,**629–633(2002). [6]S.Y.Tsai *et al*., MRM, **57,**859–865(2007). [7]H.Lei *et al*.,MRM,**49**,979–984(2003).