Functional changes in CSF volume estimated using spectroscopic water T2 decay measurement

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INTRODUCTION: Quantitative relaxometry is a well established method for assessing the volumetric voxel composition of cerebral spinal fluid (CSF) and tissue water components in quantitative magnetic resonance spectroscopy of neuro metabolites [1]. The absolute accuracy of T2 relaxometry is about 2% of the total volume, suggesting the possibility of monitoring volume redistributions of the voxel compartments due to physiological stimulation. In this study we attempt for the first time to investigate the potential of quantitative relaxometry to measure possible redistributions of brain and CSF volumes caused by manipulation of cerebral blood volume (CBV) through global (CO_2) and focal (neuronal activation) challenges.

METHODS: We studied 9 individuals (5m, 4f, 20-40 years old) in a 3T Varian INOVA scanner using a protocol consisting of 16 interleaved combinations of (i) rest, (ii) administration of 5%CO_2+air, and (iii) visual stimulation using a 10Hz reversing checkerboard. Water T2 decay curves were acquired from a 2x2x2cm PRESS-localised voxel placed manually around the calcarine sulcus in the occipital lobe (TR=12s, 12 TEs between 26ms and 1,5 s, [2]) . The amplitude of each echo was estimated using the MRUI analysis package (www.mrui.uab.es) based on AMARES fitting [3]. These amplitudes were subsequently used in a two compartmental model of relaxation to estimate the partial volume of CSF in the voxel (PVcsf, ignoring differences in water content) and the CSF and brain T2 relaxation times (Eq. 1). The model fitting was performed using in-house IDL software (ver. 6.1, www.rsi.com) by minimizing the sum of squares of residuals with an AMOEBA algorithm. We calculated fits based on running estimates from 12 consecutive TE samples and by pooling together samples selected on a per-condition basis.

$$Amp(TE_i) = S(0) \cdot \left[PV_{csf} \cdot e^{-TE_i / T2_{csf}} + (1 - PV_{csf}) \cdot e^{-TE_i / T2_{Brain}} \right] \qquad Eq.1$$

RESULTS: ***Table 1.*** *Estimates of the voxel content and their variation across the group and within subjects based on sliding selections of 12 subsequent TE samples across all physiological conditions.*

Parameter	All measurements		Repeatability [in % of intra-subject baseline]		
	Mean	SD	Min	SD	Max
S(0)	5452.au	±9.6%	-5.4%	1.7%	8.7%
PVcsf	0.107	±28.1%	-24.3%	6.6%	34.9%
T2Csf	503.0ms	±12.8%	-28.2%	6.9%	33.3%
T2Brain	61.0ms	±3.2%	-18.7%	3.1%	15.6%

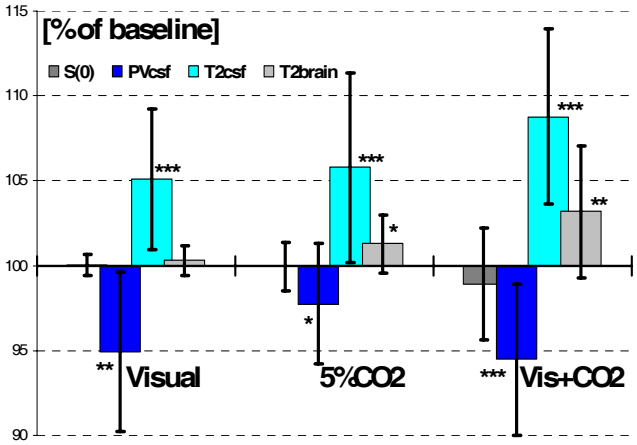

Fig.1. *Changes in the model estimates under physiological stimulation calculated from pooled data for each condition (100%=baseline values). Error bars denote SD between individually normalized responses. The statistical significance (Student T-test, paired & 2-tailed) compared to baseline is indicated by 1 to 3 stars (P=0.1, 0.05, and 0.01, respectively).*

Timecourse analyses of running estimates of PVcsf and T2 values failed to show obvious effects during stimulation periods, and comparisons of central samples (i.e. fits fully contained within each epoch) versus rest yielded no statistically significant changes (data not shown) under relatively large experimental noise (Table 1). However, when data from each condition were pooled across repeated stimulations of the same type to improve robustness of fits, we found strong effects on the T2s of CSF and brain, which increased progressively with increasing levels of vasodilatation (Fig. 1). There was a significant decrease in PVcsf of 5% during visual stimulation and a smaller trend level effect resulting from CO_2 administration (Fig. 1).

DISCUSSION: The estimated baseline PVcsf is within the expected range [1], although our T2 values are below those reported elsewhere [4], which might be a result of explicit modeling of a long T2csf component in the measured signal. The sliding 12 sample estimates, which simulate repetition of a single-shot relaxometry measurement, showed a relatively large variation due to measurement noise and transitional effects between stimulation levels, thus preventing direct observation of the effects of vasodilatation. The T2 values showed the most intra-subject variation compared to group estimates. This conforms to a likely BOLD effect in the tissue and CSF compartments arising from functional and CO_2 stimulation. This is supported by the results shown in the pooled data (Fig. 1) that show the largest effects on T2csf, probably due to extravascular BOLD effects from draining pial veins, which act on the relatively small volume of CSF. Conversely, the brain compartment is further from draining veins and is diluted by white matter which is relatively devoid of BOLD effects. The most interesting finding of the concurrent reduction of PVcsf from baseline indicates that vasodilatation affects CSF volume either directly by expanding pial vessels or indirectly by shifting the brain boundary. The larger effect of PVcsf change during visual stimulation may be explained by the greater ease of local shifts in CSF volume to neighboring sulci without a global impact on CSF volume reserve [5], as compared to the more widespread effects of CO_2 [6]. We did not quantify CBV change directly, but under the assumption that it is in the range of about 1% of the voxel volume we calculate the PVcsf change should close to zero if only brain tissue was compressed [7]. The prediction is -1% under the assumption that the CBV change is distributed between CSF and brain in proportion to their initial partial volumes. But this is still 5-fold less than observed here. To agree with the experimental data there would need to be a close-to-equal sharing of CBV change between the brain and much smaller CSF compartment, signifying the CSF's important role as a focal buffer of functional vasoreactive response.

CONCLUSION: We observed for the first time a significant functional reduction of the CSF partial volume during cerebral vasodilatation. The predicted consequent shift in brain surface may be observable in high-resolution high-field imaging, providing a new functional contrast mechanism.

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