Determination of R2* across multiple postlabeling delays in ASL and comparison with flow, arterial volume and transit times in physiological challenges

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INTRODUCTION: In arterial spin labeling (ASL) sequences with multiple postlabeling delay times, it is typically assumed that the transverse relaxation rate, R2* is consistent across the multiple postlabeling delay times, permitting accurate cerebral blood flow (CBF) quantification. To this end, we aimed to characterize R2* across the multiple time points within Look-Locker-based ASL acquisitions with dual echoes. Furthermore, R2* was used to assess the relative oxygenation of the voxels that are used for arterial input function (AIF) sampling and which contain relatively large arterial volume/vessels ("***LV***"), as compared to the gray matter ROI ("***GM***") in a ASL-fMRI dataset. Thirdly, we aimed to assess the coupling of changes in R2* with simultaneous changes in CBF, arterial blood volume (***aBV***) and the arterio-microvascular transit time (***TTam***) within the 3 conditions of Hypercapnia, Visual Stimulation, and Hypercapnia + Visual Stimulation.

METHODS: ***Experiments:*** Data from 8 healthy subjects were obtained from a previous study [1], which was performed on a Philips Intera 3.0T imager. In addition to a pure baseline state, there were 3 experimental conditions: (1) hypercapnia: subjects inhaled a gas mixture of 21% O2 and a balance of N2 and CO2 to raise their pCO2 levels by 33%; (2) visual stimulation by 8Hz reversing checkerboard; (3) hypercapnia + visual stimulation. ***MR parameters:*** QUASAR ASL: $TR/TE_1/TE_2$=3000/21/37 ms, ΔTI=200 ms, postlabeling delay time points=14, Venc=[∞, 3/6/9 cm/s], α=35°. ***Data Analysis:*** The multi-time point, perfusion-weighted data, taken from the 1st echo, were processed according to [2] and [3]. After surround subtraction of tags from controls, the crushed data yielded tissue curves, ΔM(t). Activated regions (ROIs) were determined by Spearman's Rank Test of ΔM(t). AIFs were derived from further subtraction of crushed from the non-crushed data per voxel. AIFs for the deconvolution were selected based on 2 voxels with the largest AIFs within the visual cortex. CBF values were calculated by deconvolution of the AIFs with the tissue curves. aBV values were derived from the areas under the AIFs. Transit times were taken as the difference between the start time of the AIFs and the start time of the tissue curves. Using both echoes without prior averaging/subtracting of the controls and tags, R2* values were calculated as: $R_2^*=(\ln S_1/S_2)/(TE_2-TE_1)$. Only steady state periods within each condition were analyzed. Results from the 3 different Venc levels were averaged, given insignificant differences between them. Results from 2 regions were compared – the voxels for AIF sampling (containing large arterial vessels ("***LV***")) and the ROI (containing largely gray matter ("***GM***")).

RESULTS: The R2* consistency across the time points validates the ASL requirement of similar BOLD effects within TRs of steady baseline and activation periods, as can be seen from the example in Figure 1. AIF sampling voxels ("LV") show significantly lower R2* values than in gray matter ("GM") (Table 1). Higher oxygenation reduces R2* [4]. With R2* of ~20 and assuming hematocrit is 0.44, the oxygen saturation within these voxels is estimated to be ≥0.92 [4]. R2* values were also significantly decreased with Hypercapnia, Visual Stimulation and the combined condition, in line with the resulting hyperemia. From Figure 2, the ratio of R2* to CBF change in Visual Stimulation is smaller as compared to the same changes in Hypercapnia, which is probably due to the significant increase in oxygen metabolism during visual stimulation. The relationships between changes in R2* and the vascular parameters of CBF, aBV and TTam were assessed with linear regressions. Only the relationship between R2*(GM) and CBF changes during Visual Stimulation was found to be significant. The scatterplots in Figure 3 illustrate the relationships of R2* with the vascular parameters. The linear R2*(GM) and CBF relationship in Visual Stimulation implies a tight coupling between neuronal activity, perfusion and oxygen metabolism. In the hypercapnic conditions, it is likely that individual factors, such as vascular tone and deoxyhemoglobin concentrations, account for the wide spread of responses.

CONCLUSIONS: R2* changes are tightly coupled with CBF changes, rather than arterial blood volume or transit time changes during neuronal activity alone. The presence of hypercapnia increases the complexity of the relationship. Secondly, the R2* results support the selection of the voxels sampled for the AIF and also validate the use of Look-Locker-based ASL methods for functional experiments, given relatively consistent BOLD effects across the multiple postlabeling delays.

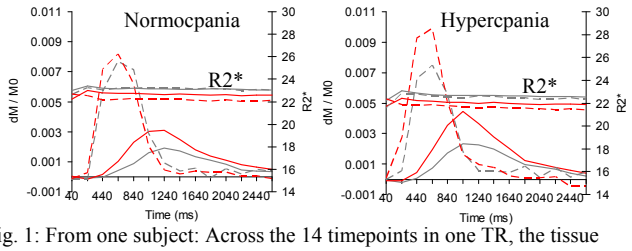

Fig. 1: From one subject: Across the 14 timepoints in one TR, the tissue curves (solid lines) from the GM ROI, the sampled AIFs (broken lines) and the corresponding R2* values from those regions. Visual baseline condition in gray, visual stimulation condition in red.

	Large vessel (LV)	Gray matter (GM)	Difference btw LV and GM
Pure Baseline	21.8±0.65	24.1±0.61	-2.22±0.68, p=0.004
Hypercapnia	20.8±0.76	22.9±0.65	-2.10±0.93, p=0.036
Visual Stimulation	21.4±0.61	23.4±0.58	-1.99±0.63, p=0.005
Hypercapnia + Vis. Stim.	20.3±0.72	22.2±0.63	-1.90±0.86, p=0.039

Table 1: R2* values (mean and SEM) by condition and region, and the differences between the regions. R2* in the 3 experimental conditions were also significantly lower than the Pure Baseline for both regions. Paired t-tests were used.

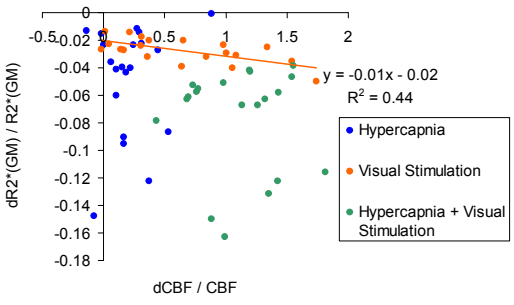

Fig. 3: Linear relationship of fractional changes of R2* with CBF is significant (p=0.002) for GM region during Visual Stimulation. The R2* relationships with aBV and TTam did not reach significance.

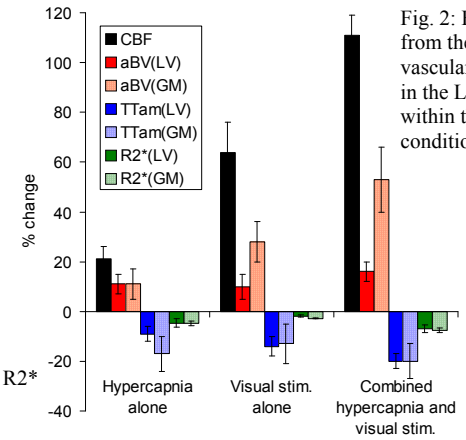

Fig. 2: Fractional changes from the pure baseline of all vascular parameters and R2* in the LV and GM regions and within the 3 experimental conditions.

REFERENCES:

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