Comparison of pulsed and continuous ASL for measurements of CBF changes induced by hypercapnia

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Introduction: Use of hypercapnia (HC) to manipulate cerebral blood flow (CBF) is an important component in MRI-based techniques for measuring metabolic and vascular reactivity in the brain [1,2]. The signal-to-noise ratio (SNR) of the ASL signal and its ability to control labeling duration are of particular concern for measurement of global flow increases such as those produced by HC, because the CBF responses are of modest amplitude and of a global nature which may cause substantial shifts in the timing of label delivery. The majority of studies measuring CBF increases during HC and other manipulations have been performed using pulsed ASL (PASL), which relies on techniques such as QUIPSS II to control label timing as required for accurate quantification [3]. Continuous ASL (CASL) provides implicit control of the labeling duration, and generally offers a higher contrast-to-noise ratio in individual flow images (although at a slightly lower imaging rate) [4]. These attributes make CASL methods attractive for measuring perfusion increases during HC. We present here a comparison of dynamic perfusion measurements acquired during a controlled HC manipulation using a PICORE/Q2TIPS PASL sequence and a pseudo-continuous ASL (pCASL) sequence [5].

Methods: Nine subjects were imaged on a 3 T scanner using a 32-channel receive-only head coil. A T1-weighted high-resolution anatomical acquisition was followed by 4 functional scans, each consisting of 5 two-minute blocks, arranged as three of resting state alternated with two of stimulation. In two runs, the stimulus consisted visual stimulation (VS), achieved with a black and white radial checkerboard flashing at 8 Hz, and baseline condition was for the subjects to view a grey screen with a fixation marker. In the other two runs, subjects underwent HC: their resting state ETCO2 was increased by 5 mmHg using a system for prospective control of blood gases described in [6]. Each of the stimulation paradigms (HC and VS) were carried out using both types of ASL, the PASL and pCASL. General PASL parameters were: TR/TE/a = 2000ms/10ms/90°. The PICORE labeling was performed on a 160 mm slab, placed 10 mm below the imaging plane, and using Q2TIPS saturation with T1/T1/T2 = 700ms/1400ms. In the pCASL acquisitions, labeling was performed over a two second period using a series of 25° Hannin pulses of 500 µs duration and separated by 360 µs gaps. These were applied along with a 6 mT/m gradient to place the labeling plane 100 mm below the center of the imaged volume. A post-labeling delay of 900 ms was used, while other sequence parameters were TR/TE/a = 3000ms/10ms/90°. The same readout was used for both types of ASL: GE-EPI with fat saturation, 4x4x6 mm3 resolution, 6x6x6 matrix, 3004 Hz/px bandwidth, employing GRAPPA and partial k-space reconstruction. Image series were first motion-corrected, spatially smoothed (6 mm FWHM 3D Gaussian kernel) and intensity normalized. The ASL signal was then isolated using linear surround subtraction and the response amplitudes estimated by performing a GLM fit. For both types of ASL, two ROI’s were defined, one including visual cortex (VC), and a second including all grey matter (GM) within the imaged volume. The VC ROI was derived from the visual activation map by thresholding it at p<0.001 and manually editing to remove activated regions outside the occipital lobe. The GM ROI consisted of the grey matter map obtained through an automated segmentation of the anatomical acquisition. The following PASL and pCASL characteristics were compared, both over GM and within VC: the temporal stability of the signal, the apparent cerebro-vascular reactivity (CVR, defined as Δ% CBF per mmHg change in ETCO2), and the percentage of voxels in a given ROI in which the HC CBF response achieved statistical significance (p<0.05 corrected for multiple comparisons). Since we can assume that all GM voxels undergo increased CBF during HC, the latter metric represents the detection power of the signal (i.e. the complement of type II error). Time-courses for PASL and pCASL were computed by averaging the signal from voxels within ROI’s and removing drift terms from the GLM fit (Fig. 1). We also computed the ROI-averaged SNR using the standard deviation of residuals and baseline flow subtraction (Fig. 2 D). The average GLM effect-size for the stimulus response was computed within the ROI, then divided by the ROI-averaged baseline (constant) term and multiplied by 100 to convert to Δ%. All ROI-averaged time courses and mean values were then averaged across subjects and results are presented as the group’s mean±SE.

Results: Fig. 1 shows the CBF response signals for PASL (left) and pCASL (right) during VS and HC in the applicable ROI’s. Both techniques yield clearly discernible visual responses (the VC-averaged Δ%CBF for PASL and pCASL are 74.83±5.39 and 81.36±3.80 respectively), but it is qualitatively clear that, overall, the pCASL signals exhibit consistently lower noise levels. Group average SNR values for GM and VC ROI’s are shown as bar graphs in Fig. 2 D and it can be seen that pCASL exhibits higher SNR, a difference which achieves statistical significance in GM. Respective SNR values for pCASL and PASL SNR in GM were 2.48±0.18 and 1.87±0.15. The corresponding SNR values in VC were 2.67±0.25 and 2.40±0.13. As seen from Fig. 2 C, PASL and pCASL are equally able to detect perfusion in both GM (93.02±2.20% detection vs. 94.68±1.16%) and VC (98.15±0.78% vs. 97.54±0.88%). From Fig. 2 A it can be seen that the ability to detect a response to HC differs, however. In VC, 55.89±7.48% of voxels achieve significant response in HC with pCASL, while 41.91±9.08% are significant with PASL. Overall, all GM, pCASL responses to HC exceeded statistical threshold in a significantly (p<0.05) higher percentage of voxels: 26.75±5.07% vs. 15.77±3.24% with PASL. As seen from Fig. 2 B, pCASL measurements of CVR were significantly (p<0.05) higher than PASL in both GM and VC. Respective CVR values measured in GM with pCASL and PASL were 4.40±0.24 and 3.03±0.61, with corresponding VC values of 7.89±0.97 and 5.29±1.05.

Discussion: Our results show that pCASL and PASL offer comparable sensitivity to visually evoked CBF responses, as well as to baseline flow. However pCASL was found to provide higher baseline SNR and improved sensitivity to CBF changes during mild HC, and indicated significantly higher values for apparent CVR. These findings tend to confirm that CASL methods offer advantages over PASL techniques for the detection and quantification of global flow changes.