Measuring Tissue Perfusion in the Human Brainstem Using Multi-Inversion Time Pulsed Arterial Spin Labelling

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Introduction The brainstem is involved in control of critical physiological processes, including cardiovascular function and breathing. Currently, arterial spin labelling studies often exclude the brainstem due to signal drop out and high levels of physiological noise. Moreover, there is likely to be a relatively large contribution of macrovascular signal to the perfusion signal in the brainstem arising from nearby arteries. The aim of this study was to demonstrate the measurement of tissue perfusion in the brainstem by separating the macrovascular and tissue perfusion signal using a two-compartment model containing both arterial and tissue components [1]. Multi-inversion time pulsed ASL (pASL) with short echo-time spiral read out was used to minimize signal drop out in the brainstem.

Methods Seven young, healthy subjects (3 female, mean age 29.6 ± 4.9 years) were recruited. Resting state perfusion measurements were made using the PICORE tagging scheme [2] with an echo-planar spiral read-out with 2 interleaves per image. Ten control-tag pairs were acquired for each of 13 inversion times (TIs): 0.1s, 0.2s, 0.3s, 0.4s, 0.5s, 0.6s, 0.7s, 1.0s, 1.3s, 1.6s, 1.9s, 2.2s 2.5s. A QUIPSSII [3] cut-off of the magnetic label at 0.7s was used for TI > 0.7s. Other image parameters were: label thickness 20 cm, 1 cm gap between label and most proximal imaging slice, resolution 3x3x7 mm^3 with a 1mm slice gap, 13 slices, echo time 3.2ms. Repetition time (TR) was minimised for each individual TI. For quantification purposes, a M_0 image was acquired with the same imaging parameters, except an infinite TR and no labelling pulse. For each TI a difference image was obtained by subtracting the 10 tag-control pairs and averaging the subtractions. Kinetic curves of the magnetic label were fitted to the average TI images with methods described by Chappell et al [1], using BASIL within the FSL toolbox v5.0 (http://fsl.fmrib.ox.ac.uk). In voxels that contained arterial signal, only the tissue perfusion curve was considered (Figure 1). Four regions of interest (ROIs) were used to analyse kinetic curves, perfusion (CBF), tissue and arterial arrival times (Δt_{tiss}, Δt_{art}, Figure 1), and arterial blood volume fraction (aBV). The ROIs (brainstem, cerebellum, occipital pole, gray matter) were registered from MNI152 Standard Space to subject space via T1 structural images of each subject.

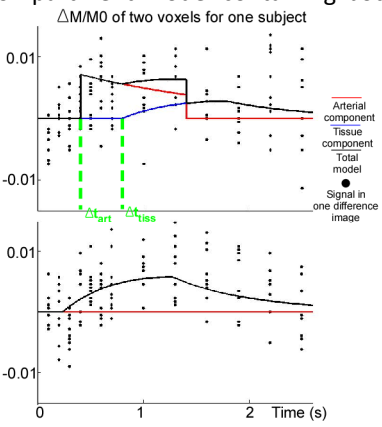

Figure 1. Examples of kinetic curves fitted by the model. Red: arterial compartment, blue: tissue compartment, black: total model. Green: Δt_{art} and Δt_{tiss}. Top; voxel with arterial signal, only the tissue curve was used to estimate CBF. Bottom: voxel without arterial signal contribution

Results and Discussion Figure 2 shows an example of CBF maps. Average brainstem CBF is significantly lower (*paired t-test, p<0.001*) than gray matter CBF (Table 1), which is expected as the brainstem contains both gray and (less perfused) white matter. As expected, the average macrovascular arterial signal contribution per voxel is larger in the brainstem than in the cerebellum and occipital pole (aBV, Table 1). Values for Δt_{tiss} (Table 1) and average tissue perfusion curves for the cerebellum and occipital pole (Figure 3) are consistent with the literature concerning similar regions [4, 5]. Higher values for Δt_{art} (Table 1) were found than previously reported values (~300 ms) [5, 6], possibly due to the use of a two-compartment model that accounts for a rapidly increasing arterial component, instead of using a single compartment model that only contains a slower increasing tissue perfusion component and thus leads to shorter arterial arrival times.

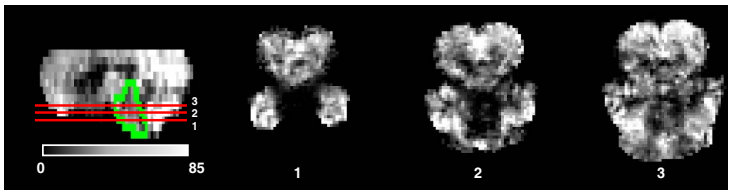

Figure 2. Example of CBF maps (ml/100 gr/min). Left: Sagittal slice, including outline of used brainstem mask in green. On the right: Axial slices 1, 2, and 3, corresponding to the red lines in the sagittal slice.

Table 1. Average parameters resulting from fitting a two-compartment model of perfusion to pASL data.

ROI	aBV (%)	Δt_{art} (ms)	Δt_{tiss} (ms)	CBF (ml/100g/min)
Brainstem	0.68 ± 0.54	438.0 ± 20.4	701.8 ± 55.6	32.1 ± 4.0*
Cerebellum	0.15 ± 0.10	381.3 ± 19.1	833.3 ± 52.8	49.8 ± 7.0
Occipital pole	0.07 ± 0.07	489.0 ± 12.1	826.6 ± 45.4	52.8 ± 12.7
Gray matter	0.40 ± 0.10	443.6 ± 7.3	701.5 ± 36.9	53.4 ± 8.4

**Significant difference between gray matter and brainstem (paired t-test, p<0.001)*

Conclusion The current study has shown that using a two-compartment perfusion model with short-echo time spiral read out pASL enables kinetic curve fitting and provides a more accurate estimate of brainstem CBF by separating the tissue signal from the macrovascular arterial signal.

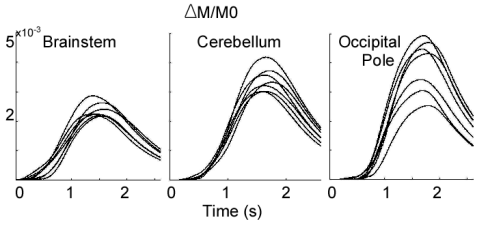

Figure 3. Regional average kinetic curves. One is displayed per subject.

References 1.Chappell, MA, et al., Magn Reson Med, 2010. **63**. 1357-65 2.Wong, EC, et al., NMR Biomed, 1997. **10**. 237-49 3.Wong, EC, et al., Magn Reson Med, 1998. **39**. 702-8 4.Gallichan, D, et al., Magn Reson Med, 2009. **61**. 686-95 5.Chen, Y, et al., MAGMA, 2012. **25**. 135-44 6.Huang, AJ, et al. *Proceedings of ISMRM*. 2011, 19, 301.