Quantitative Cerebral Vascular Response Maps: Determination with Pulsed Arterial Spin Labelling

U. Noeth[1,2,3], F. Kotajima[3], R. Deichmann[2], R. Turner[2], D. R. Corfield[3,4]

[1]Institut fuer Strahlenbiologie, GSF Forschungszentrum fuer Umwelt und Gesundheit, Neuherberg, Germany, [2]Wellcome Dept. of Imaging Neuroscience, Institute of Neurology, UCL, London, United Kingdom, [3]Clinical and Academic Unit of Sleep and Breathing, National Heart & Lung Institute, Imperial College, London, United Kingdom, [4]Institute of Science and Technology in Medicine, Keele University, Keele, United Kingdom

Introduction

Regulation of breathing and regulation of cerebral blood flow (CBF) are closely linked: changes in breathing alter the concentrations of oxygen and carbon dioxide in arterial blood, and thus the cerebral blood flow (CBF). This autoregulation mechanism can be described by the cerebral vascular response (CVR) which has been shown to be altered in different physiological and pathophysiological states, e.g. the CVR to hypoxia is lower during slow wave sleep than during the waking state [1]. This finding may be of clinical importance as the brain is particularly vulnerable to effects of hypoxia, and breathing is most prone to instability during sleep; nocturnal hypoxia is a pathological factor associated with respiratory diseases like obstructive sleep apnea [2]. Therefore, the aim of this study was (1) to determine quantitative maps of grey matter perfusion (GM-CBF) under isocapnia (isocapnic euoxia) and hypoxia (isocapnic hypoxia) using a pulsed arterial spin labelling method at 3.0 Tesla and (2) to calculate from the GM-CBF maps CVR maps which show the spatial distribution of the cerebral vascular response of GM to hypoxia in healthy humans.

Methods and Materials

Cortical perfusion was determined with the Q2TIPS sequence [3] at 3.0 T in 19 healthy male volunteers (25 ± 2 years, age range 21-28 years). Subjects breathed via a facemask attached to a breathing circuit designed to regulate F_IO_2 and to maintain the end-tidal CO_2 ($PetCO_2$) within ± 1 mmHg of a predetermined level, independent of changes in ventilation. For each subject, 50 pairs (total scan time: 4 min) of control and tag images were acquired under isocapnia (ic, $PetCO_2$ clamped) and under hypoxia (hp, subject breathing medical air with reduced O_2 content, $PetCO_2$ clamped at isocapnia level, arterial oxygen saturation (SaO_2) reduced by a value between 9 and 14%). Perfusion measurements for the two different conditions were started after SaO_2 and $PetCO_2$ were stable for 3 minutes.

Scanning parameters were: in-plane resolution 3.5 mm, 6 axial slices (4 mm each with 0.5 mm gap), TR = 2.3 sec, single slice acquisition time 66 ms, TE = 30 ms, $TI_1/TI_1stop/TI_2$ = 600ms/1200ms/1300ms. CBF was calculated from the difference signal (control-tag) ΔS [3]:

$\Delta S(TI_2) = 2 \cdot S_{0B} \cdot f \cdot TI_1 \cdot \exp(-TI_2/T_{1B}) \cdot q(T_{1B}, T_{1t}, T_{ex}, f, \lambda, TI_2)$ for $TI_1 < \tau$ and $TI_2 > TI_1 + \delta t$ and q typically near unity.

S_{0B} is the signal of fully relaxed blood, f the CBF value in sec^{-1}, T_{1B} and T_{1WM} are the longitudinal relaxation times of blood and white matter, respectively, and were assumed to be 1.5 sec [3] and 832 ms [4] at 3.0 T for quantitative calculation of CBF; τ is the time width of the tag, δt the transit delay. As there were no large arterial vessels in the tag and control images, S_{0B} was derived from the average white matter signal (S_{WM}) intensity of the control images, taking into account the differences in spin density and relaxation times. In addition, a T_1 weighted structural scan with 1 mm isotropic resolution was acquired for each subject using an MDEFT sequence [5] with optimised contrast for grey and white matter for creating a GM mask and for coregistration of the perfusion scans.

Data Analysis and Results

The structural scan was segmented to obtain a GM probability map from which a GM mask was obtained by thresholding. The quantitative perfusion images (isocapnia, hypoxia) of each subject were coregistered and resliced onto the structural scan to obtain quantitative CBF maps with 1mm isotropic resolution which were converted into quantitative GM-CBF maps by multiplication with the GM mask. CVR maps to hypoxia were calculated as follows:

$$CVR_{hp} = -10 \cdot \frac{100 \cdot (CBF_{hp} - CBF_{ic})}{CBF_{ic} \cdot (SaO_{2hp} - SaO_{2ic})}$$

Fig. 1 shows one slice of the GM-CBF map from the same subject under isocapnia (left) and hypoxia (centre) and the calculated CVR map to hypoxia (right) which shows a large regional variance. The intra-subject CBF difference between isocapnia and hypoxia was highly significant for each subject (P<0.00001, 2-tailed Student t-test) when comparing all pixels common to both maps; there was a significant CBF increase in 13 subjects (positive responders) and a significant CBF decrease in 6 subjects (negative responders). Table 1 shows the group mean CBF values ± SEM for the two subgroups with corresponding SaO_2 and $PetCO_2$ values. The mean CVR to hypoxia was 10.7 ± 2.5% CBF increase and 9.4 ± 2.6% CBF decrease per -10%SaO_2 for positive and negative responders, respectively.

	isocapnia		hypoxia		difference		P value	
responder type	positive	negative	positive	negative	positive	negative	positive	negative
CBF	41.5 ± 2.2	49.7 ± 4.7	46.3 ± 2.7	44.6 ± 3.5	11.7 ± 2.7%	-9.4 ± 2.7%	P<0.002	P<0.04
SaO_2 [%]	97.8 ± 0.2	97.7 ± 0.4	86.8 ± 0.5	87.0 ± 0.3	-11.0 ± 0.4	-10.7 ± 0.6	P<7E-12	P<0.00001
$PetCO_2$ [mmHg]	42.5 ± 0.6	43.2 ± 0.9	42.3 ± 0.5	43.1 ± 0.8	-0.2 ± 0.1	-0.2 ± 0.2	P<0.13	P<0.48

Table 1: Quantitative subgroup mean CBF, SaO_2, and $PetCO_2$ values ± SEM. CBF values are in [ml/100ml/min], CBF differences are relative in %; SaO_2 values and $PetCO_2$ values and differences are absolute values (units as indicated).

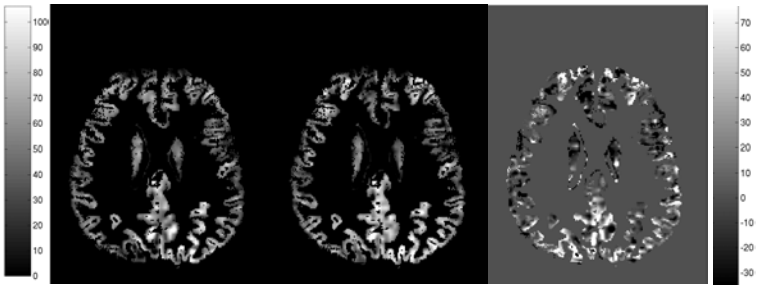

Figure 1: Quantitative GM-CBF maps for a typical subject with 1mm isotropic resolution acquired during isocapnia (left) and hypoxia (centre) and the calculated CVR map to hypoxia (right). CBF values are given in [ml/100ml/min] (left scale), CVR values in % change per -10% SaO_2 (right scale).

Conclusion and References

The method described allows the acquisition of quantitative GM-CBF maps and calculation of CVR maps due to hypoxia. The CBF increase of 10.7% per -10% SaO_2 for positive responders is in good agreement with data presented in [1], where the velocity in the middle cerebral artery was used as a measure for cerebral perfusion. The high spatial heterogeneity in the CVR maps show that different regions in GM react very differently to hypoxia. The CVR maps might thus help to identify areas which are most prone to damage in respiratory disease due to their reduced reactivity.

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