Brain Perfusion During Sleep - Determination with Quantitative Perfusion MRI and EEG with Online Artefact Removal

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Introduction

Nocturnal reduction of the oxygen (O_2) concentration in arterial blood (hypoxia) is a major pathological factor associated with cardiorespiratory diseases, imposing stress on the whole organism. The brain is particularly vulnerable to its effects. During a hypoxic insult, protection of the brain will depend on the cerebral vascular response (CVR): during wakefulness the decrease in arterial O_2 associated with hypoxia results in an increase in cerebral blood flow (CBF) in order to improve the O_2 supply. Work from our laboratory has shown that this autoregulation mechanism is altered during stage III/IV slow wave sleep: the CVR to hypoxia was lower during slow wave sleep compared to the waking state [1]. Our previous study [1] used the mid cerebral artery velocity (MCAV), determined with Doppler ultrasound, as a measure for perfusion; however, the MCAV is only proportional to CBF if the diameter of the MCA is constant; in addition, this method gives no information on the spatial distribution of the CVR. Further research on this issue requires a method for reliable brain perfusion quantification during wakefulness and sleep. This poses numerous technical problems. In this work, we present a method for the determination of quantitative GM-CBF maps during stage III/IV slow wave sleep, using a pulsed arterial spin labelling (PASL) method at 3.0 Tesla combined with simultaneous acquisition of EEG for sleep staging. We discuss technical problems arising during the study and the solutions adopted, and suggest further improvements, providing technical guidelines for the performance of similar studies.

Methods and Materials

For the determination of perfusion maps during wakefulness and slow wave sleep, the following parameters must be monitored simultaneously: (1) regional cerebral perfusion by the continuous acquisition of PASL perfusion images, (2) EEG for correct sleep staging, (3) end-tidal CO_2 ($PetCO_2$), and (4) arterial oxygen saturation (SaO_2). Cortical perfusion was determined with the Q2TIPS sequence [2] at 3 T. Subjects breathed via a facemask attached to a breathing circuit designed to monitor F_IO_2 and $PetCO_2$ using a rapidly responding gas analyser. SaO_2 was determined with a pulse oximeter attached to the index finger. For EEG acquisition, an MR compatible EEG system with an MR compatible EEG cap was used. EEG data proved to be heavily distorted by scanner noise. For online cardiac and gradient artefact removal, the clocks of the EEG system and the MR scanner were synchronized as described in [3]. For each subject, 50 pairs of control and tag images (total scan time: 4 min) were acquired while the subject was awake and during stage III/IV slow wave sleep. For the wake condition, perfusion data were acquired in the evening (at ca. 8pm) after a night of normal sleep; the scan was started after SaO_2 and $PetCO_2$ were stable for 3 minutes. For the sleep condition, perfusion data were acquired continuously for up to 4 h in the late evening (after 10pm) after a night of sleep deprivation (less than 4 h of sleep). For determination of sleep perfusion, the last 4 min (50 pairs of control and tag images) from a 7 minute period of stage III/IV deep wave sleep with no arousal showing in the online EEG and constant $PetCO_2$ and SaO_2 were selected to determine sleep CBF maps.

Scanning parameters were: in-plane resolution 3.5 mm, 6 axial slices (4 mm each with 0.5 mm gap), single slice acquisition time 66 ms, $TR/TE/TI_1/TI_1stop/TI_2$ = 2300ms/30ms/600ms/1200ms/1300ms. CBF was calculated from the difference signal (control-tag) as described in [2] and [4]. In addition, during the wake session, 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 (GM) and white matter (WM). This structural scan was segmented to obtain a GM probability map from which a GM mask was obtained by thresholding. The quantitative perfusion images (wake, sleep) of each subject were coregistered and resliced onto the structural scan and masked to include only GM to obtain quantitative GM-CBF maps. This allowed a pixelwise comparison of wake and sleep data.

Results

Nineteen subjects were studied in the wake scan, from which six withdrew from the sleep scan as they were convinced that they would not be able to fall asleep in the scanner. Of the remaining 13 subjects, seven had a sufficiently long period (7 min) of slow wave sleep during the sleep scan. Data from one of these seven subjects was excluded as a large increase in CBF from wake to sleep was judged an outlier (> 2 SD from the mean).

As anticipated slow wave sleep was associated with an increase in $PetCO_2$ and a decrease in SaO_2 (wake/sleep; $PetCO_2$: 42.6 ± 1.2 / 44.2 ± 0.9 mmHg; SaO_2: 98 ± 1 / 97 ± 0 %; mean ± SD). Fig. 1 shows one slice of the GM-CBF map from the same subject during wake (left) and sleep (right). The intra-subject CBF difference between wake and sleep was significant for each subject ($P<0.0001$, paired 2-tailed Student t-test) when comparing all pixels common to both maps. For the group of six subjects, GM-CBF fell from 65.7 ± 30.7 awake to 58.8 ± 22.8 ml/100ml/min during sleep. This reduction in GM-CBF did not reach statistical significance ($p = 0.07$) but the magnitude of the reduction is consistent with our previous report [1] using the MCAV. Fig. 2 shows the average GM-CBF values for all 6 subjects during wake and sleep together with the group mean ± SEM.

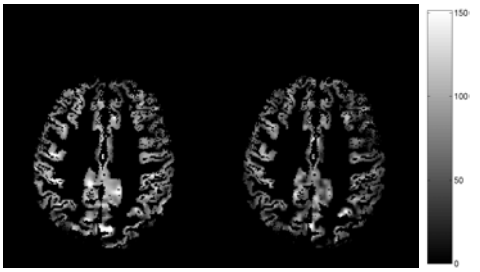

Figure 1 (left): Quantitative GM-CBF maps for one subject acquired during wake (left) and sleep (right). CBF values are given in [ml/100ml/min].

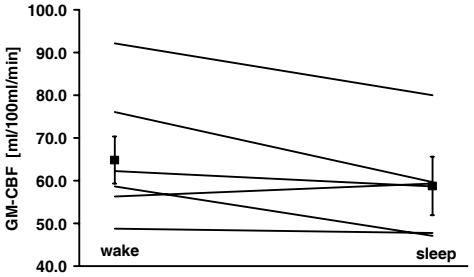

Figure 2 (right): Average GM-CBF values for all 6 subjects during wake and sleep (connected by line) with resulting group mean ± SEM.

Conclusion and References

This combination of methods enables the acquisition of quantitative GM-CBF maps during sleep. In particular, the method for gradient artefact removal from the EEG proved adequate for online sleep staging during slow wave sleep. In this study, ca. 50% of subjects had long enough slow wave sleep during the sleep scan for determination of sleep CBF. Overall, CBF was reduced during sleep, as reported in [1]. A large sleep related increase CBF was noted in one subject but the technical reasons for this outlier remains unexplained. Most of the technical problems we encountered arose from factors which potentially disturb sleep such as MR scanner noise, tight EEG cap, geometric constraint of head coil, and unfamiliar sleep environment and position (supine). Possible improvements are the use of "silent" MR sequences**,** scanners with a wider bore, slightly larger head coils (e.g. whole body systems rather than dedicated head scanners)**,** and more comfortable patient tables.

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