Appendix A – Stability of the rOxFlow technique in a flow phantom

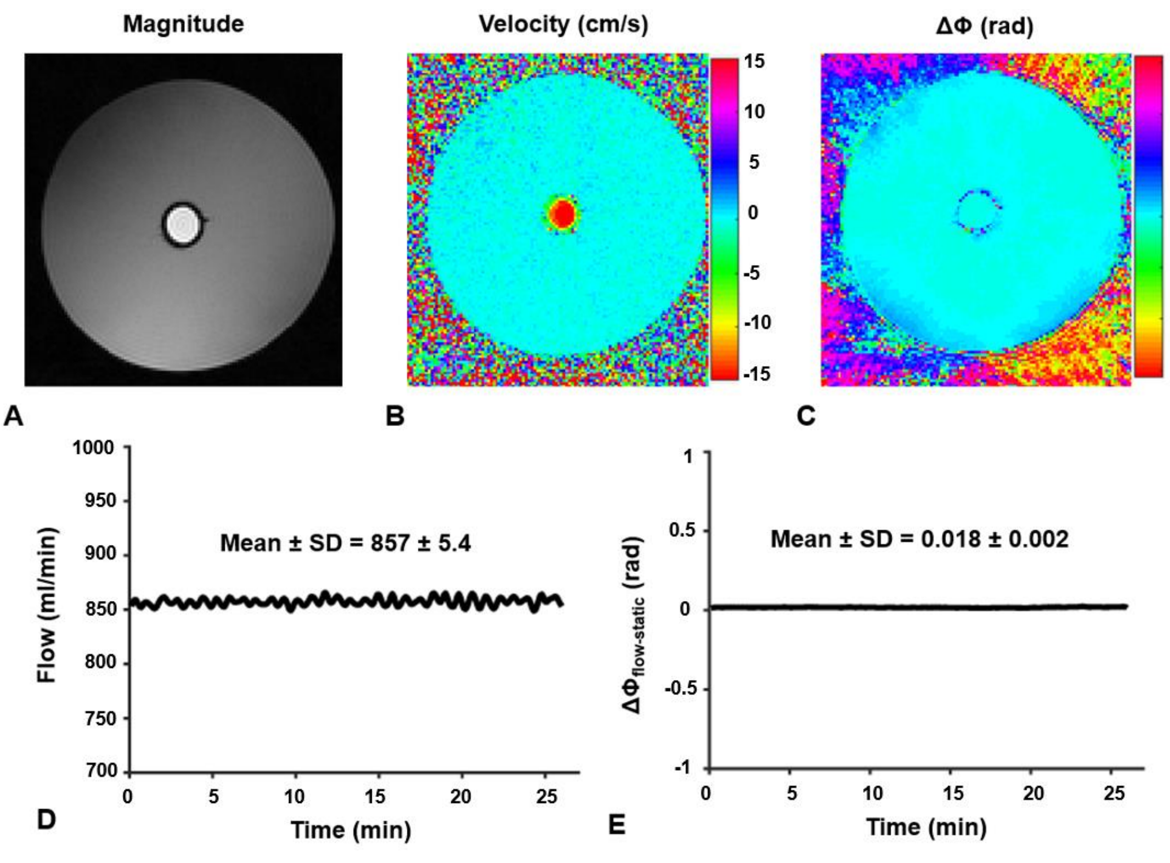

Figure A.1 – Stability of rOxFlow technique in a flow phantom experiment. *Three sets of flow phantom images (top) and quantified parameters over the time course (bottom): magnitude (**A**), velocity (**B**), $\Delta\phi$ (**C**), flow (**D**), and $\Delta\phi_{flow\text{-}static}$ (**E**). Note stable flow (except for small oscillations caused by the flow pump, CV~0.6%) and near-zero $\Delta\phi_{flow\text{-}static}$ during the experiments.*

Appendix B – Time-course of neurometabolic parameters

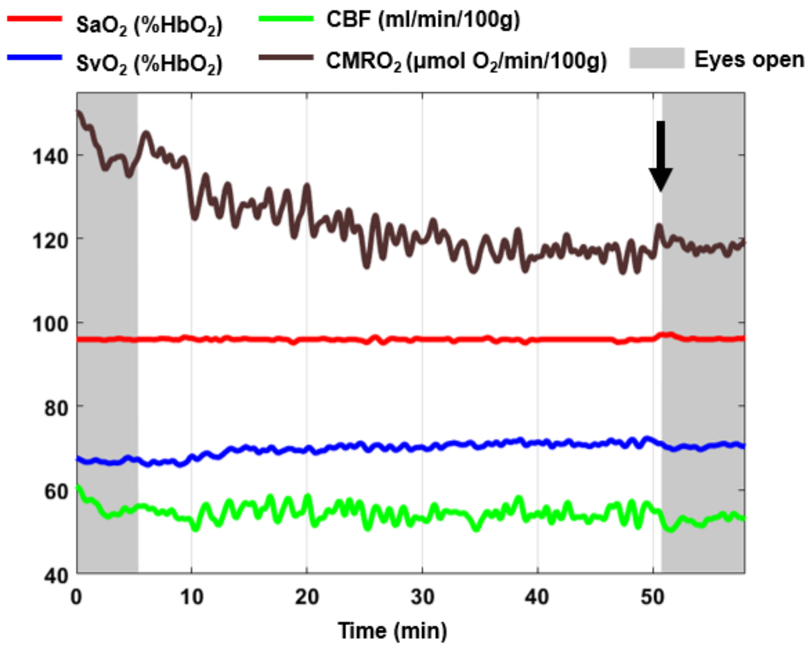

Figure B.1 – Radial OxFlow during wakefulness and drowsiness. *Metabolic parameters measured in a representative subject (F, 31 years), perceiving to have not been able to fall asleep. During the initial and final portions of the protocol the subject was awake, with eyes open (gray areas), while in the central portion eyes were closed. During the last 20 min of the eyes closed period, probably due to drowsiness, $CMRO_2$ decreased by 17% relative to the first wakefulness period. At the point indicated by the black arrow the participant was asked to provide feedback using the scanner's squeeze-ball ($CMRO_2$, cerebral metabolic rate of O_2 consumption; SaO_2, arterial O_2 saturation; SvO_2, venous O_2 saturation; CBF, total cerebral blood flow).*

Appendix C – EEG patterns and $CMRO_2$ during wakefulness and sleep

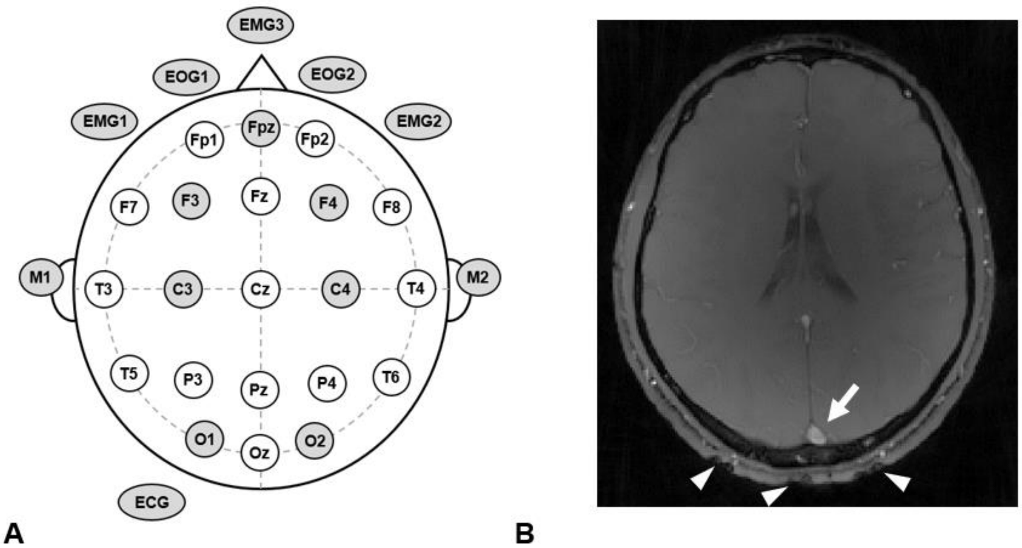

Figure C.1 - Scalp electrodes for EEG recording. A. *Sketch of the 15-channel customized MR-compatible sleep cap, with electrodes placed according to the international 10-20 system. In the schema the vertical and horizontal directions correspond to anterior-posterior, and left-right, respectively. The 15 electrodes used for recording are in gray (C=central, ECG=electrocardiography, EOG=electrooculography, EMG=electromyography F=frontal, Fp=prefrontal, O=occipital, M=mastoid process, P=parietal, T=temporal, z=midline).* ***B.*** *Gradient echo magnitude image showing the superior sagittal sinus (arrow) and three electrodes of the EEG cap (O1, Oz, O2), indicated by the white arrowheads.*

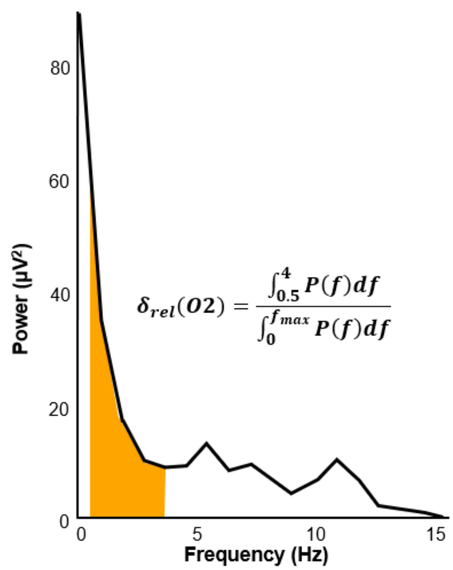

Figure C.2. *Example power spectrum derived from EEG recording of the channel O2 in a volunteer during sleep (S01 M, 40 years). The delta-band (0.5-4.0 Hz) is colored. Only the portion of the spectrum corresponding to 0-15 Hz is shown. Delta power ratio ($\delta_{rel}(O2)$ or $\delta'(O2)$) was estimated as indicated (P, power; f, frequency; f_{max}= 30 Hz).*

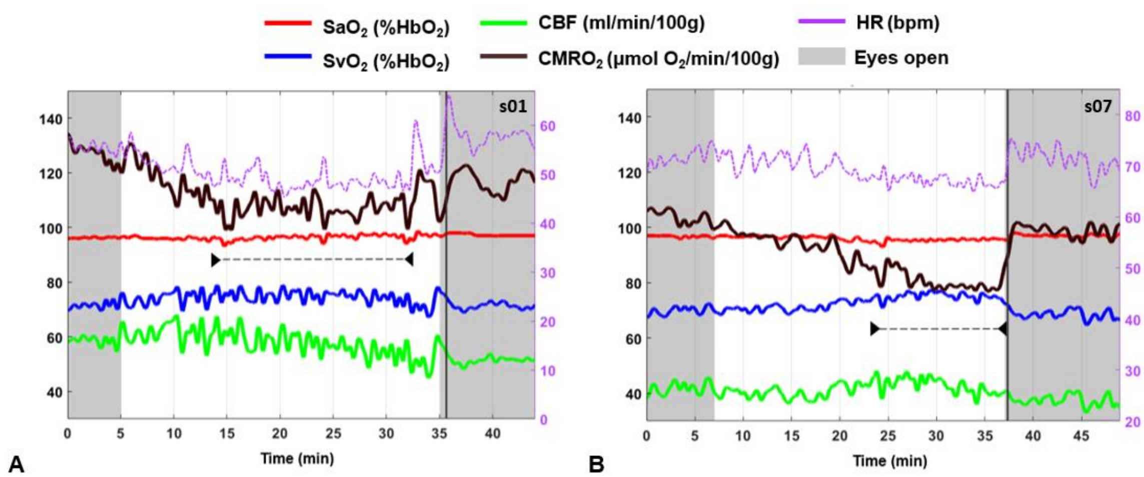

Figure C.3 ***– Concurrent EEG and rOxFlow during wakefulness and sleep.*** *Metabolic parameters measured in two subjects (**A.** S01 M, 40 years; **B.** S07 M, 36 years) who accomplished to fall asleep, according to the EEG data (arrowheads). The subjects were awake with eyes open in the initial and final parts of the protocol (gray areas). Upon awakening through vocal instructions, subjects provided feedback (vertical black line) using the scanner squeeze-ball, to indicate that they were awake (for legend see **Fig. B.1**).*

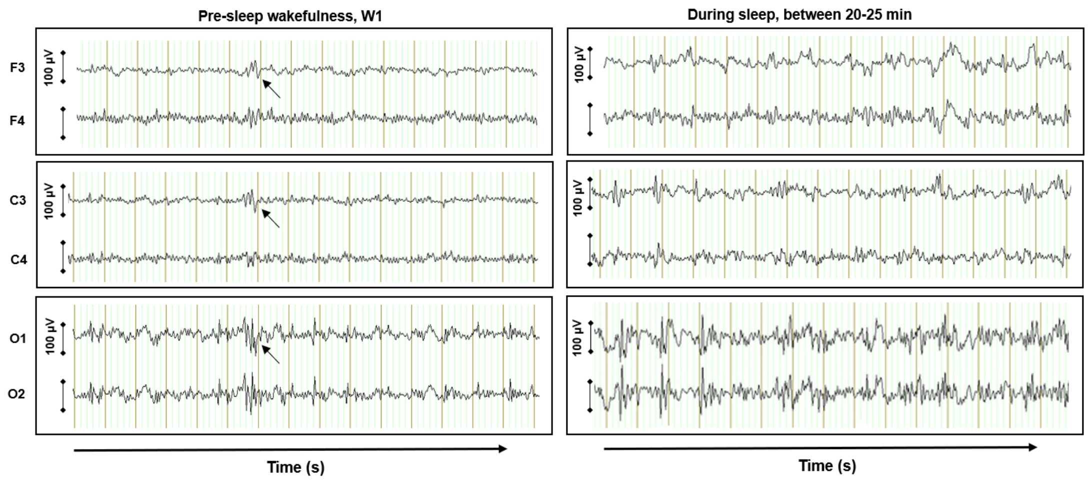

Figure C.4 – EEG patterns during wakefulness and sleep. *Brain electric activity recorded from the frontal (F3, F4), central (C3, C4) and occipital (O1, O2) electrodes, plotted versus time, in one subject (S01 M, 40 years). The EEG patterns show 15 s extracted from two distinct parts of the sleep protocol: during the first 5 min of pre-sleep wakefulness (stage W); during the central part, between 20 and 25 min, when the participant was asleep. Black arrows point to a motion artifact. Scale bar = 100 µV.*

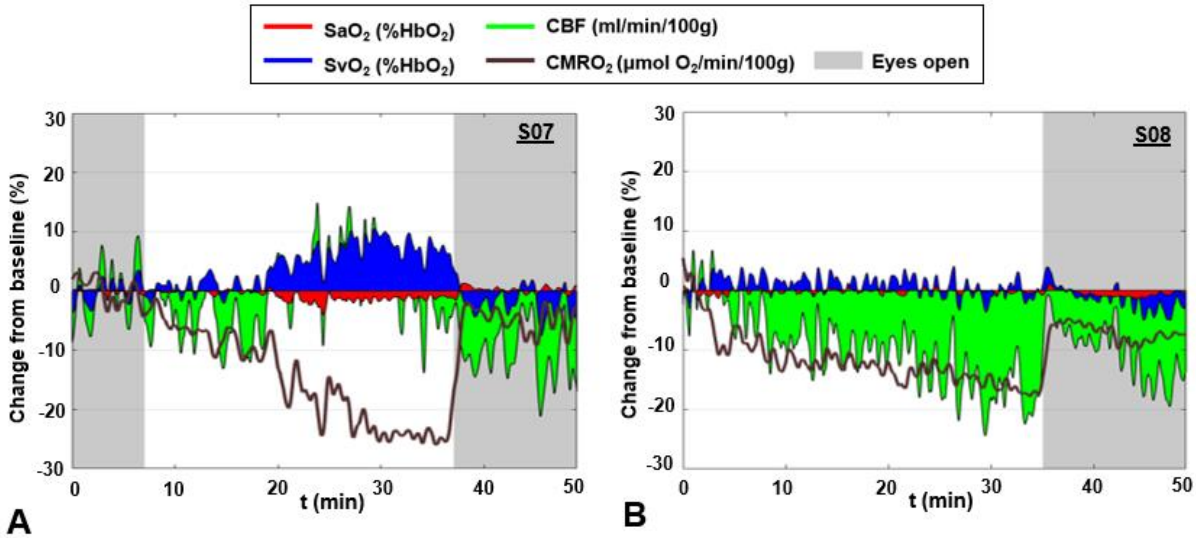

Figure C.5 – Changes in oxygen extraction and CBF during wakefulness and sleep. *Relative change of each parameter with respect to the baseline value (corresponding to the first 5 minutes of wakefulness in S07 and to the first 2.5 min in S08). In the subject of panel **A**, the lower metabolic demand is regulated by increased SvO_2 (i.e. lower oxygen extraction). In **B**, it is primarily reduced CBF.*

Table C.1 – Pearson's (r) and Spearman's (ρ) correlation coefficients between $CMRO_2$, δ'(O2), and HR, considering averages on 2.5 min time-windows.

Participant (sex, age)	$CMRO_2$ vs δ'(O2)		$CMRO_2$ vs HR		HR vs δ'(O2)	
	r/ρ	**P**	**r/ρ**	**P**	**r/ρ**	**P**
S01[a] (M, 40y)	**r= -0.82**	**<0.0001**	**r= 0.69**	**<0.0001**	**r= -0.80**	**<0.0001**
	ρ= -0.83	**<0.0001**	**ρ= 0.80**	**<0.0001**	**ρ= -0.79**	**0.0001**
S02[a] (M, 35y)	r= 0.38	0.1	**r= 0.69**	**<0.0001**	**r= 0.52**	**0.03**
	ρ= 0.38	0.1	**ρ= 0.77**	**0.0003**	ρ= 0.47	0.05
S03 (M, 22y)	r= -0.12	0.6	r= 0.24	0.1	r= 0.23	0.4
	ρ= -0.04	0.9	**ρ= 0.63**	**0.006**	ρ= 0.003	1
S04 (M, 23y)	r= -0.17	0.4	**r= -0.45**	**0.0007**	r= 0.27	0.2
	ρ= -0.17	0.4	ρ= -0.33	0.1	ρ= 0.31	0.2
S05 (M, 32y)	**r= 0.54**	**0.01**	r= -0.02	0.9	r= -0.16	0.5
	ρ= 0.55	**0.01**	ρ= -0.17	0.5	ρ= 0.04	0.9
S06 (F, 31y)	r= 0.0008	1	r= -0.20	0.2	**r= -0.56**	**0.01**
	ρ= 0.02	0.9	**ρ= -0.52**	**0.02**	**ρ= -0.66**	**0.002**
S07[a] (M, 36y)	**r= -0.73**	**0.0003**	**r= 0.66**	**<0.0001**	**r= -0.78**	**<0.0001**
	ρ= -0.49	**0.03**	**ρ= 0.73**	**0.0004**	**ρ= -0.68**	**0.002**
S08[a] (F, 24y)	**r= -0.64**	**0.002**	**r= 0.50**	**0.0003**	**r= -0.78**	**<0.0001**
	ρ= -0.74	**0.0003**	**ρ= 0.50**	**0.02**	**ρ= -0.68**	**0.001**

Notes – [a] The subject self-assessed to fall asleep during the 'eyes closed' period, and onset of sleep was confirmed by EEG for this dataset. HR = heart rate (measured in bpm); $\delta' = \frac{\int_{0.5}^{4} PSD(f)\, df}{\int_{0}^{f_{max}} PSD(f)\, df}$, PSD=power spectrum density, P=significance level.

Table C.2 – Heart rate during wakefulness and EEG-verified sleep

Participant (sex, age)	Pre-sleep (W1) [a]	'eyes closed' period (EC) [b]	Post-sleep (W2) [a]	% change EC vs W1	% change W2 vs W1
S01[c] (M, 40y)	56 (1)	48 (1)	58 (1)	-14%	4%
S02[c] (M, 35y)	69 (1)	62 (2)	67 (1)	-10%	-2%
S03 (M, 22y)	64 (2)	60 (2)	70 (4)	-6%	10%
S04 (M, 23y)	52 (1)	56 (1)	57 (1)	8%	9%
S05 (M, 32y)	53 (2)	51 (1)	53 (1)	-3%	0%
S06 (F, 31y)	63 (3)	63 (2)	62 (1)	0%	-2%
S07[c] (M, 36y)	71 (1)	66 (1)	71 (2)	-7%	0%
S08[c] (F, 24y)	68 (3)	64 (2)	66 (2)	-7%	-4%

Notes – Heart rate (HR) is measured in bpm. Standard deviations are indicated in parenthesis. [a] HR was averaged over the pre-sleep wakefulness period and over the last 5 min of the post-sleep wakefulness period, respectively in W1 and W2; [b] HR averaged over the 5 min interval at the lowest $CMRO_2$; [c] The subject self-assessed to fall asleep during the 'eyes closed' period, and onset of sleep was confirmed by EEG for this dataset.