Increased inspiratory resistance alters the cardiac contribution to the dynamic relationship between blood pressure and pial artery pulsation oscillations in healthy subjects

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Why do we talk about brain in obstructive sleep apnoea (OSA)?

OSA is associated with:

- changes in gray matter structure (volume loss or increase)
- increased free tissue water content, and altered diffusion characteristics
- elevated levels of depression and anxiety
- significant memory deficit
- increased risk of stroke

Harper RM, et al. Functional neuroanatomy and sleep-disordered breathing: implications for autonomic regulation. Anat Rec. 2012;295:1385-95.

Winklewski PJ, et al. Cerebral blood flow, sympathetic nerve activity and stroke risk in obstructive sleep apnoea. Is there a direct link? Blood Press. 2013;22:27-33.

Why does brain haemodynamic matter?

- Arterial flow is pulsatile and causes a periodic increase in blood volume entering the intracranial cavity
- Intracranial cavity has a fixed volume that is confined by a rigid skull
- Volume expansion due to arterial systolic flow must be accompanied by an equal volume reduction via the ejection of cerebrospinal fluid (CSF) and/or venous flow out of the cranial cavity (Monroe-Kellie doctrine)

Greitz D, et al. On the pulsatile nature of intracranial and spinal CSF-circulation demonstrated by MR imaging. Acta Radiol. 1993;34:321–8.

Linninger AA, et al. Pulsatile cerebrospinal fluid dynamics in the human brain. IEEE Trans Biomed Eng. 2005;52:557–565.

Why does brain haemodynamic matter?

Pulsatile CSF motion as well as the associated moderate changes in intracranial pressure are necessary for ongoing maintenance of proper brain haemodynamic

Abnormal arterial/venous pulsatility may lead to brain tissue damage and has been termed pulse wave encephalopathy

Pulse wave injury may be associated with early disruption to the structural properties of white matter

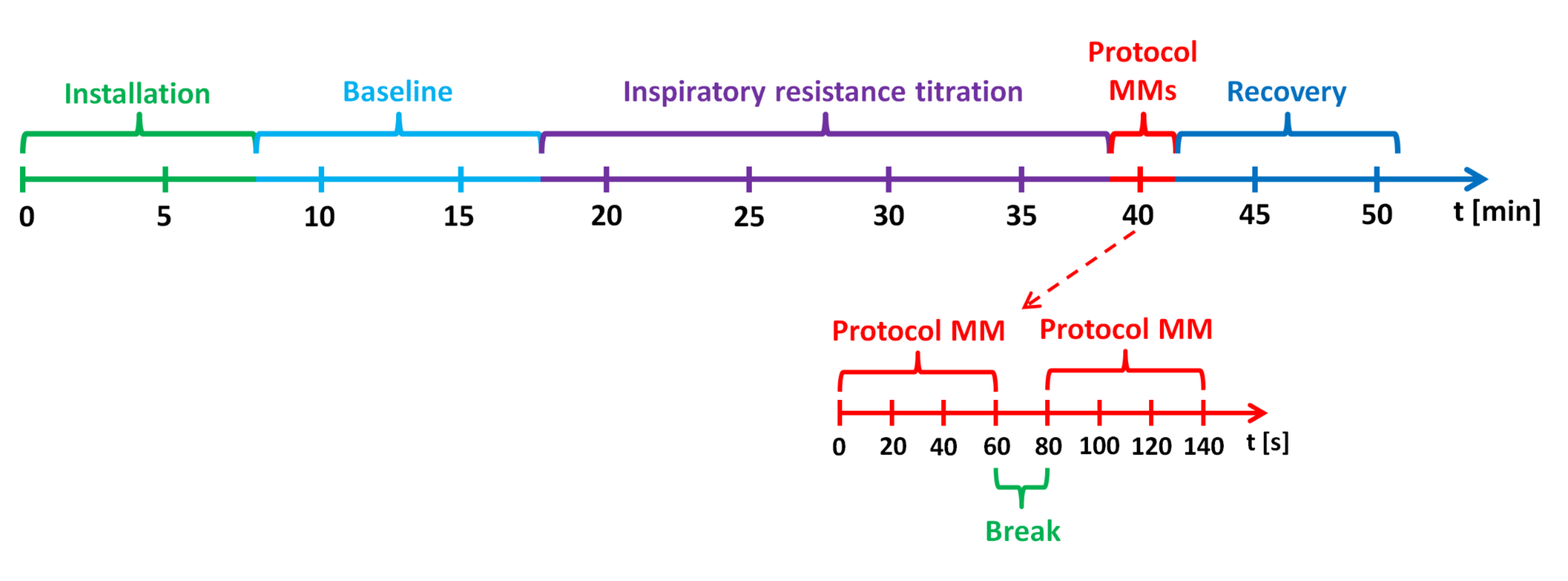
Bateman GA. Pulse-wave encephalopathy: a comparative study of the hydrodynamics of leukoaraiosis and normal pressure hydrocephalus. Neuroradiology. 2002; 44:740–748.

Jolly TA, et al. Early detection of microstructural white matter changes associated with arterial pulsatility. Front Hum Neurosci. 2013;7:782.

Methods

- 20 healthy, non-smoking volunteers
- The width of subarachnoid space (SAS) was measured using NIR-T/BSS
- Heart rate (HR) and beat-to-beat systolic (SBP) and diastolic (DBP) blood pressure were recorded using a Finometer™
- Cerebral blood flow velocity (CBFV), pulsatility index (PI) and resistive index (RI) were measured using Doppler ultrasound of the left internal carotid artery
- End-tidal CO_2 was measured using a medical gas analyzer.

Mueller manoeuvres representation of study design



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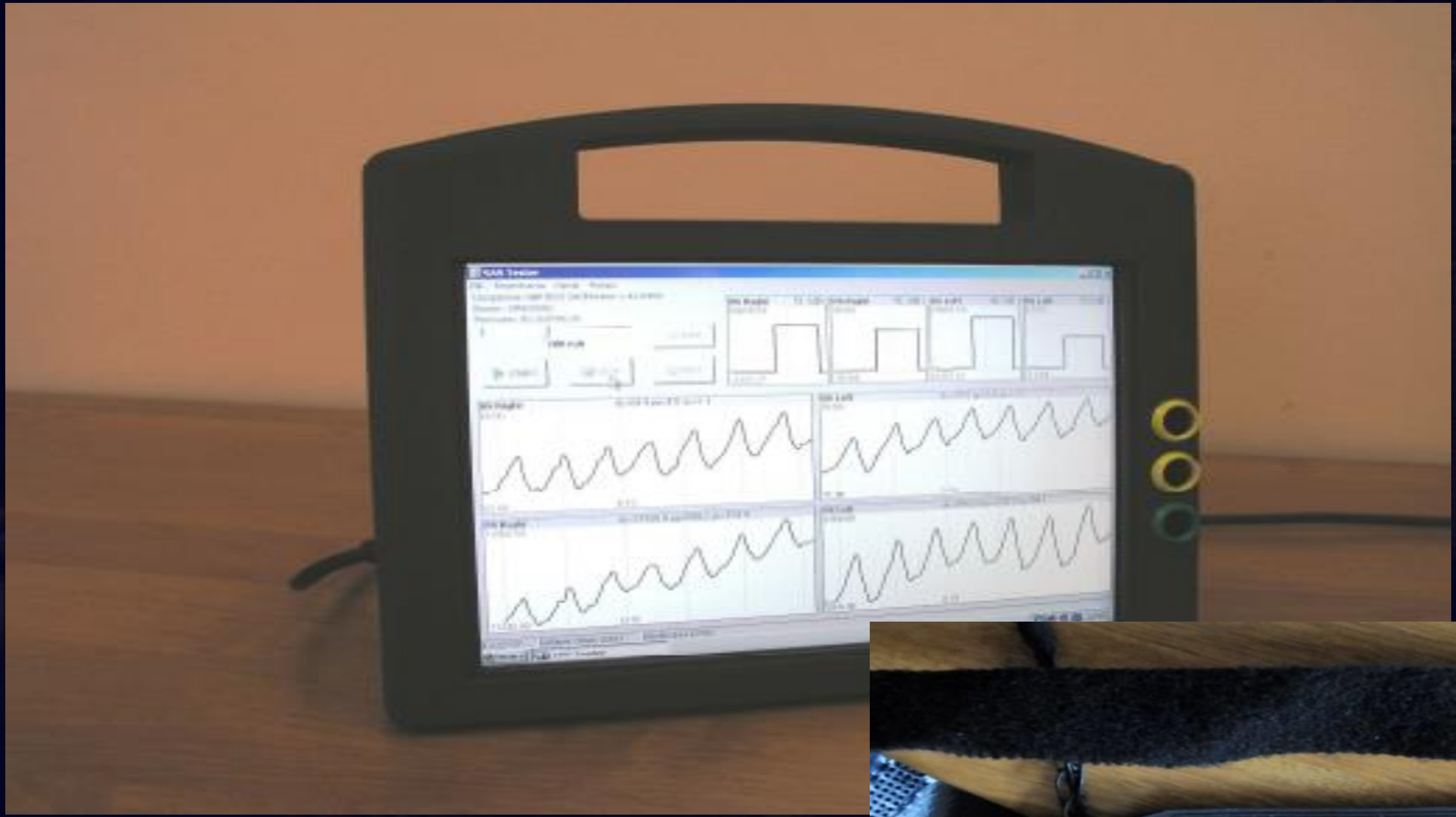
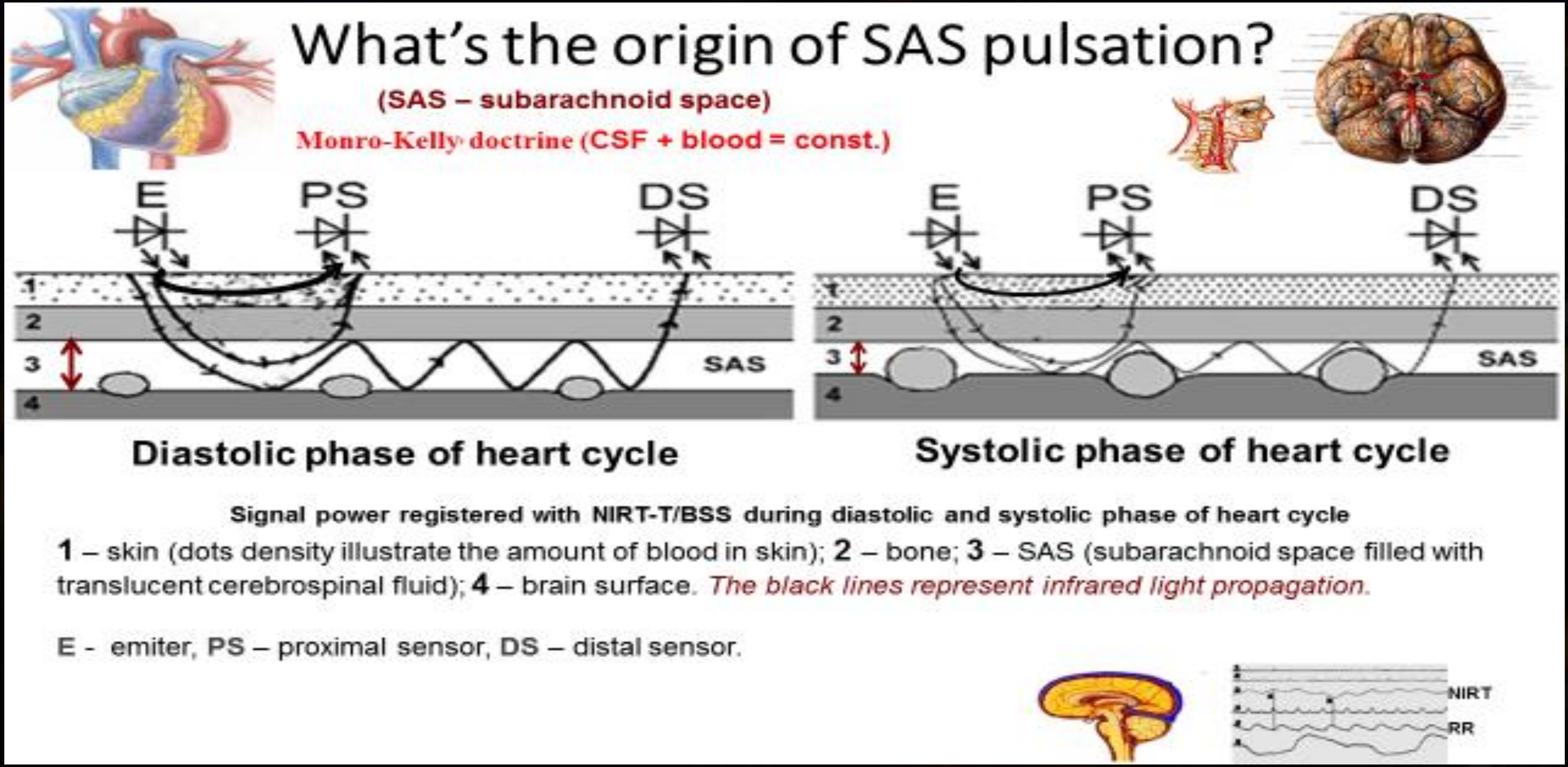
NIR-T/BSS



Pulsatile arterial flow



Methods

Wavelet transform is a method that transforms a time signal from the time domain to the time-frequency domain. The Wavelet transform is defined by the equation:

$$\mathrm{w}(\boldsymbol{s},\boldsymbol{t}) = \frac{1}{\sqrt{s}}\int_{-\infty}^{+\infty} \varphi\left(\frac{u-t}{s}\right) g(u)du$$

where $\mathrm{w}(\boldsymbol{s},\boldsymbol{t})$ is the wavelet coefficient,

$g(u)$ is the time series,

φ is the Morlet mother wavelet scaled by factor s and translated in time by t.

The Morlet mother wavelet is defined by the equation

$$\varphi(u) = \frac{1}{\sqrt[4]{\pi}} e^{-i2\pi u} e^{-0.5u^2}$$

where $i = \sqrt{-1}$

The reason for using the Morlet wavelet is its good localization of events in time and frequency due to its Gaussian shape.

Methods

We calculated wavelet coherence (WCO) and wavelet phase coherence (WPCO) to assess the relationship between blood pressure and subarachnoid space width oscillations (SAS).

WCO was used to determine the coherence of the wavelet cross-spectrum in the time-frequency domain. Following Torrence and Webster (1998) we define the wavelet coherence of two time series as:

$$w_{12}(s,t) = \frac{w_1(s,t)^* w_2(s,t)}{\sqrt{|w_1(s,t)^2|}\sqrt{|w_2(s,t)^2|}}$$

where: $w_1(s,t)$ ($w_2(s,t)$) is the wavelet coefficient for the first (the second) signal and * indicates a complex conjugate. We observed stronger coherence when the WCO value increased. A value of zero is obtained for a vanishing correlation.

To calculate WPCO we estimated phase angle of $w_{12}(s,t)$. When two oscillations are unrelated, their phase difference continuously changes with time; thus, their WPCO approaches zero. For related oscillations ther WPCO approches one.

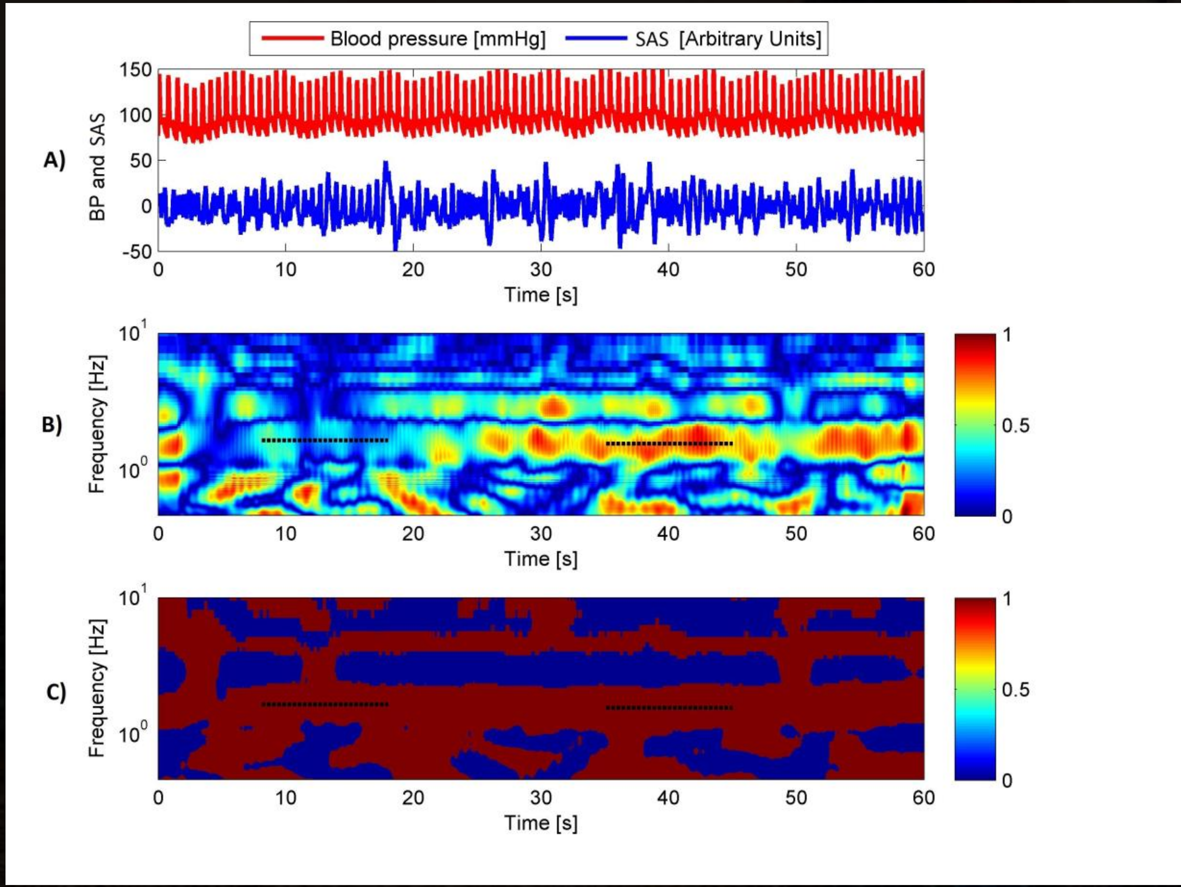
Mueller manoeuvres
WCO and WPCO

Blood pressure (red) and SAS (blue)

WCO reaches its minimum between 8 and 18 s of the MM, and later on recovers, with maximum between 35 and 45 s at cardiac frequency

WPCO remains stable at cardiac frequency

Cardiac frequency is marked with horizontal dotted lines



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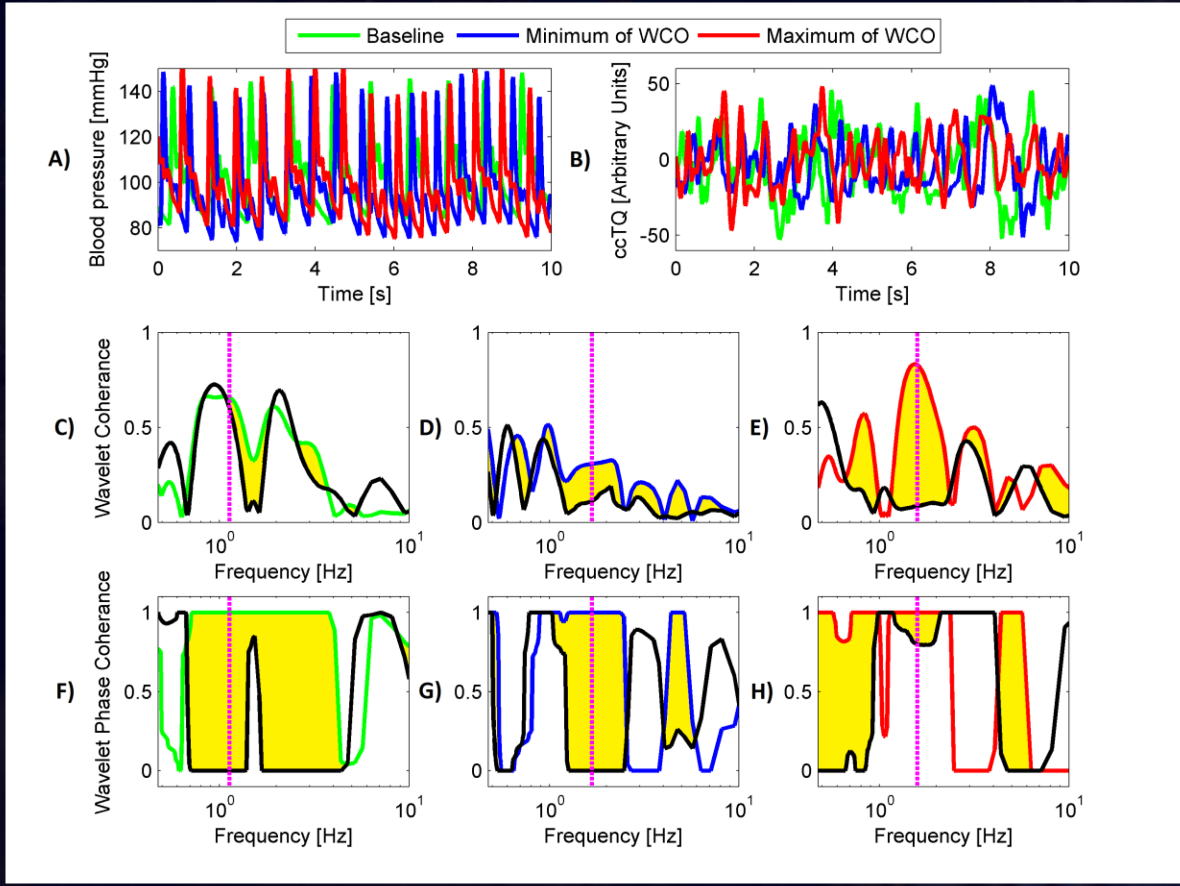
Mueller manoeuvres
Surrogates analysis

10 s signals of baseline (in green), 10 s of minimum WCO (in blue) and 10 s of maximum WCO (in red).

BP oscillations (panel A), SAS oscillations (panel B), time average of WCO (panels C, D and E) and time average of WPCO are shown (panels F, G and H).

Black lines represent time average of WCO (panles C, D, E) and WPCO (panles F, G, H) estimated for surrogate time series estimated from analysed signals. To generated surrogates we used iterative amplitude adjusted Fourier transform (IAAFT). Shaded yellow areas indicate significant coherence and phase coherence



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Mueller manoeuvres

take home messages

Mueller maneouvres are associated with large swings in cardiac contribution to the dynamic relationship between blood pressure and subarachnoid space width oscillations in healthy subjects

Impaired cardiac performance reported in Mueller manoeuvres may affect cerebral haemodynamic

Mueller manoeuvres
WCO and WPCO

Effects of a 60 s Mueller manoeuvres series on WCO and WPCO between BP and SAS oscillations at cardiac frequency. Data are presented as mean values and standard deviations (SD). The minimum and maximum correspond to WCO minimum and maximum values during the Mueller manoeuvres series.

	Baseline	Minimum	Minimum vs. Baseline (%)	Maximum	Maximum vs. Baseline (%)	Maximum vs. Minimum (%)
WCO left	0.65 ± 0.15	0.44 ± 0.30	67.7^{*}	0.67 ± 0.22	103.1^{NS}	152.3^{**}
WCO right	0.52 ± 0.18	0.28 ± 0.26	54.0^{**}	0.64 ± 0.17	123.1^{NS}	228.6^{***}
WPCO left	0.86 ± 0.36	0.85 ± 0.36	98.8^{NS}	0.78 ± 0.42	90.7^{NS}	91.8^{NS}
WPCO right	0.87 ± 0.35	0.83 ± 0.35	95.4^{NS}	0.93 ± 0.26	106.9^{NS}	112.0^{NS}

*$P<0.05$; **$P<0.01$; ***$P<0.001$; WCO – wavelet coherence; WPCO – wavelet phase coherence; left – left hemisphere; right – right hemisphere; SD – standard deviation

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