Reducing CBF Variability with Control of End-tidal Carbon Dioxide

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Introduction

As the partial pressure of CO_2 (PCO_2) in arterial blood is a potent vasodilator, changes in arterial PCO_2 lead to changes in cerebral blood flow (CBF).[1] Consequently, natural fluctuations in arterial PCO_2 (indexed by the end-tidal PCO_2 - $PETCO_2$) can have a major influence on many MR techniques, *e.g.*, cerebral perfusion or blood oxygenation level dependant (BOLD) imaging. When a subject lies at rest, there are breath-to-breath variations in $PETCO_2$, which may increase the variability of cerebral blood flow and/or volume. In fact, it has previously been shown that natural $PETCO_2$ fluctuations can significantly alter fMRI signals. This study found $PETCO_2$ fluctuations account for 8-9% of the total BOLD signal fluctuations.[2] When performing blood flow or volume sensitive imaging at 3 T, noise is predominately from physiological origins.[5] Being able to reduce CBF fluctuations due to $PETCO_2$ changes has important implications to reduce overall noise in studies of individuals. Our objective is to compare the variance in middle cerebral artery (MCA) blood velocity waveforms under conditions of naturally occurring $PETCO_2$ fluctuations and when $PETCO_2$ is controlled using end-tidal forcing [3] near resting values.

Methods

CBF was monitored by measuring blood velocity in the right MCA using a 2 MHz trans-cranial Doppler (TCD) ultrasound system. Measurements were made on 10 healthy volunteers during (1) normal air breathing and (2) controlled end-tidal gas breathing using end-tidal forcing [3]. In the second session, $PETCO_2$ was held at 1.5 mmHg above resting $PETCO_2$. Subjects breathed through a mouthpiece, and O_2 and CO_2 were continually sampled and analyzed by mass spectrometry (AMIS 2000, Innovision). End-tidal gases were identified and recorded for each breath using a dedicated computer and software.[3] One-minute periods were analyzed to obtain data over multiple cardiac cycles and to minimize slowly varying haemostatic properties. Key waveform characteristics were defined on each waveform, shown in Fig. These values were averaged across the one-minute trials for each subject, and then across the group. A variance-ratio test, modified to account for correlation, was used to examine differences between variances.[4]

Results

A strong correlation was found between normal and forcing data for all parameters. The Table summarizes the variability (standard deviation) of each waveform parameter in the two sessions and the *p*-value of the difference test. The variability of all velocity parameters, T_{DN}, and $PETCO_2$ was significantly ($p < 0.05$) reduced. The coefficient of variation of V_{CYC} was reduced from 0.86 to 0.80 with end-tidal forcing controlling $PETCO_2$. Overall there was 18% reduction in blood velocity variability (calculated from the standard deviation of V_{CYC}). Additionally, V_{MAX} decreased by 15%, V_{MIN} by 7%, V_{FWHV} by 10%, V_{REFL} by 13%, V_{DN} by 12% and Va_{MAX} by 14%.

Discussion and Conclusions

End-tidal forcing reduced the variability of most waveform parameters, specifically, the velocity parameters (markers for CBF). This effect occurs because end-tidal forcing exploits the link between arterial and end-tidal PCO_2, and therefore can be used to reduce the physiological noise due to natural PCO_2 fluctuations. Since we have shown MCA blood velocity variability can be reduced by up to 18%, this technique may have an important application to decrease physiological variability, for example, in BOLD imaging where the detected signal difference is only 3-5%. Additionally, end-tidal forcing may have application to enhance the understanding of biological and technical meanings of fMRI and oxygen sensitive imaging.

Table. Variability (quantified as average standard deviation) of $C0_2$ and waveform parameters in each session and p*-value of session differences*

Parameter	Normal	Controlled	*p*-value
T_{CYC}	96	94	NS
V_{CYC}	3.3	2.7	<0.001
V_{MIN}	3.4	2.9	<0.001
T_{MIN}	18.1	19.2	NS
V_{MAX}	4.1	3.8	0.01
T_{MAX}	12.1	12.3	NS
V_{FWHV}	3.0	2.7	<0.001
T_{FWHV1}	8.4	8.3	NS
T_{FWHV2}	50.7	51.4	<0.001
V_{REFL}	5.2	4.5	<0.001
T_{REFL}	58.4	54.1	<0.001
V_{DN}	4.2	3.7	<0.001
T_{DN}	14.1	15.1	<0.001
A_{MAX}	76.1	77.0	NS
Va_{MAX}	5.6	4.8	<0.001
Ta_{MAX}	8.6	8.8	NS
$PETCO_2$	0.85	0.68	<0.001

Parameter units: Time (T_X): ms, Velocity (V_X): cm/s, Acceleration (A_X): cm s^{-2}, and $PETCO_2$: mmHg.
NS = non-significant ($\alpha = 0.05$)

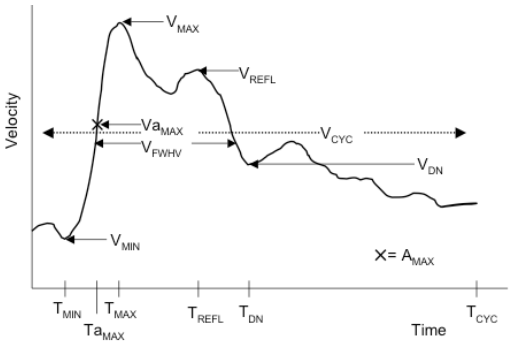

Fig: Schematic of a blood velocity waveform over one cardiac cycle with waveform parameters labeled. Waveform parameters were defined on each waveform prior to variability analysis.

References

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