MEASURING THE TIME CHARACTERISTIC OF THE BOLD CEREBROVASCULAR REACTIVITY RESPONSE TO A STEP HYPERCAPNIC STIMULUS.

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PURPOSE: BOLD MRI during manipulation of end tidal PCO2 ($P_{ET}CO_2$) can be used to measure cerebrovascular reactivity (CVR). The standard CVR approach is to measure the amplitude of the change in BOLD signal per change in $P_{ET}CO_2$. Although very robust and simple, this measure does not capture the dynamic aspect of the BOLD responses. Visual inspection reveals that the rate of BOLD signal increase is an important feature that can vary greatly throughout the brain [1] and be extremely long in vascular impaired areas. In this study, we developed a reliable method to measure the time characteristic (**τ**) of the reactivity response, voxel-wise. We then investigated the distributions of τ in patients with unilateral steno-occlusive diseases and compared them with a group of healthy subjects.

METHODS: 46 healthy subjects and 20 patients with unilateral steno-occlusive disease were imaged on a 3T MRI scanner. CVR images were acquired using BOLD MR pulse sequence during step manipulations of their $P_{ET}CO_2$ (Figure 1). Control of $P_{ET}CO_2$ was implemented by a computer-controlled gas blender (RespirAct™, Thornhill Research Inc., Toronto, Canada). T1-weighted images were acquired for co-registration and spatial normalization purposes. For the standard CVR maps, the BOLD time series at each voxel is normalized and regressed against the $P_{ET}CO_2$ waveform. The slope of the regression is the CVR measure expressed in %BOLD/mmHg (Figure 2). For the τ maps, the $P_{ET}CO_2$ is first convolved with a set of 50 exponential functions of different time characteristic, ranging from τ=2s to τ=100s in 2s increments, to obtain a set of 50 convolved $P_{ET}CO_2$ (figure 1). A Pearson correlation coefficient is then calculated between the BOLD signal and each of the 50 convolved $P_{ET}CO_2$. The maximal correlation coefficient corresponds to the convolved $P_{ET}CO_2$ that best fit the BOLD signal and its associated time characteristic (τ) is recorded. This process is applied for all voxels of the brain to obtain the **τ map** (Figure 2). Although not shown here, the amplitude A, obtained by regressing the BOLD signal with the "best" convolved $P_{ET}CO_2$ is also calculated. Additionally, in standard MNI space, we generated a map of z-score (**z-τ**) calculated as the number of standard deviations the patient's τ value is above or below the mean of the 46 healthy subjects.

RESULTS: In healthy subjects, the mean τ of grey (GM) and white matter (WM) was respectively 20.2±10.5s and 40.7±10.7s. There was no significant difference between the different vascular territories of the cortex. In the affected hemispheres of the steno-occlusive patients, the GM with positive reactivity (A>0) had a mean τ = 38.6±8.4s, which is significantly longer ($p < 0.001$) than in GM of healthy subjects. Figure 2 shows the maps of a patient with right carotid artery occlusion with some areas of steal physiology (CVR<0). In this patient, the GM of the affected hemisphere has longer τ than normal (green on the τ map) by more than 2 standard deviations (purple on the z-τ map) .

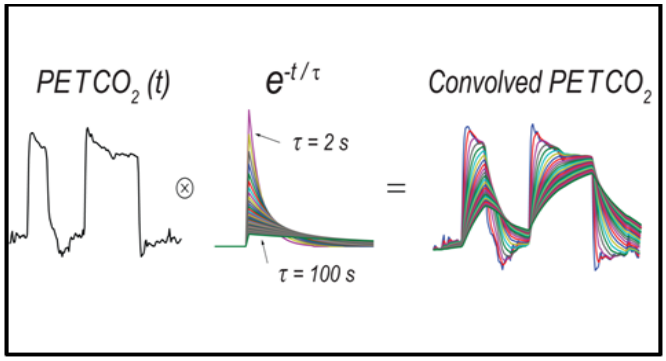

Figure 1

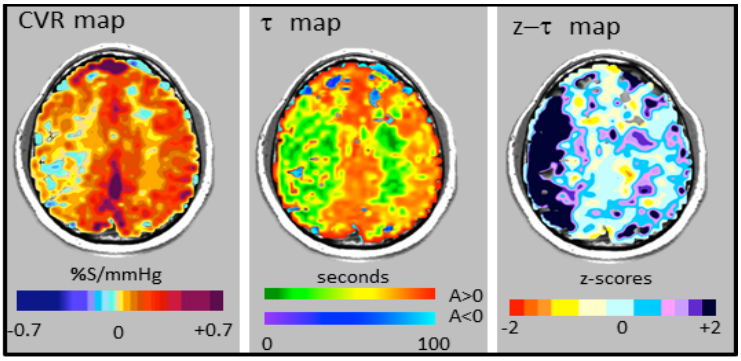

Figure 2

DISCUSSION: This method of calculating τ via the convolution of the $P_{ET}CO_2$ with multiple exponential functions has the advantage of being adaptable to any hypercapnic protocol. We observed a significant lengthening of τ in the affected hemisphere of patients with steno-occlusive diseases. However, this is only true for areas of positive reactivity (A>0). In areas of negative reactivity believed to be caused by steal physiology, τ can be complex due to the mixed effects of rapid flow diversion from steal and the influence of delayed CO_2 arrival[2].

CONCLUSION: This study benchmarks the transient response, τ, of the cerebral vasculature to a rapid change in CO_2. τ is significantly prolonged in areas of the brain with positive CO_2 reactivity, ipsilateral to a stenosis. In the future, this method could be applied for investigating a variety of diseases that affect the cerebral vasculature or alter neurovascular coupling.

REFERENCES

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