The dynamics of cerebrovascular reactivity shown with transfer function analysis

James Duffin[1,2], Olivia Sobczyk[3], David J Mikulis[3,4], and Joseph A Fisher[1,2]
[1]*Department of Physiology, University of Toronto, Toronto, Ontario, Canada,* [2]*Department of Anaesthesia and Pain Management, University Health Network, Toronto, Ontario, Canada,* [3]*Institute of Medical Sciences, University of Toronto, Toronto, Ontario, Canada,* [4]*Joint Department of Medical Imaging and the Functional Neuroimaging Laboratory, University Health Network, Toronto, Ontario, Canada*

PURPOSE: To develop a method for showing the dynamics of cerebrovascular reactivity.

INTRODUCTION: Cerebrovascular reactivity (CVR), is often defined as the increase in cerebral blood flow (CBF) produced by an increase in the partial pressure of carbon dioxide (PCO_2). The CBF response, in the absence of changes in blood pressure, is assumed to reflect the reactivity of the cerebral blood vessels, and may be used clinically to assess the health of the cerebrovasculature. With T2* used as a surrogate measure of CBF, CVR values for each voxel can be displayed using a color scale mapped onto the corresponding anatomical scan to show the distribution of reactivity, and are able to show, for example, paradoxical reductions ('steal'), which are associated with vascular pathology. However, these CVR maps only provide an estimate of the magnitude of the cerebrovascular response, and do not indicate the time course; whether rapid or slow. Here we describe transfer function analysis (TFA) of the CBF response to PCO_2 that provides not only the magnitude of the response (gain) but also the phase, which can be interpreted as indicating the speed of response, and the coherence, which can be interpreted as indicating the fidelity of the response.

METHODS: To illustrate TFA, data from standardized CVR tests were analysed for a healthy individual and a patient drawn from our database; the latter diagnosed with a known cerebrovascular disease (Moyamoya). The frequency response function, defined as the cross-spectrum of the response signal divided by the autospectrum of the stimulus signal, yielded gain and phase measures. Coherence, an indication of the causality linking the stimulus-response relationship was calculated from averages of the cross- and auto- spectra as the average cross-spectrum squared divided by the product of the stimulus and response autospectra. Welch averaging was used, dividing the time domain signals of about 500 s duration, sampled at 2 s intervals, into 50-sample segments to obtain five, 100 s segments and then overlapping them by 50% to obtain 9 averages. These calculations were implemented with a specially written program (LabVIEW, National Instruments, Texas; program available upon request). Values at a frequency of 0.01 Hz were selected to produce maps of the voxel-by-voxel gain, phase and coherence.

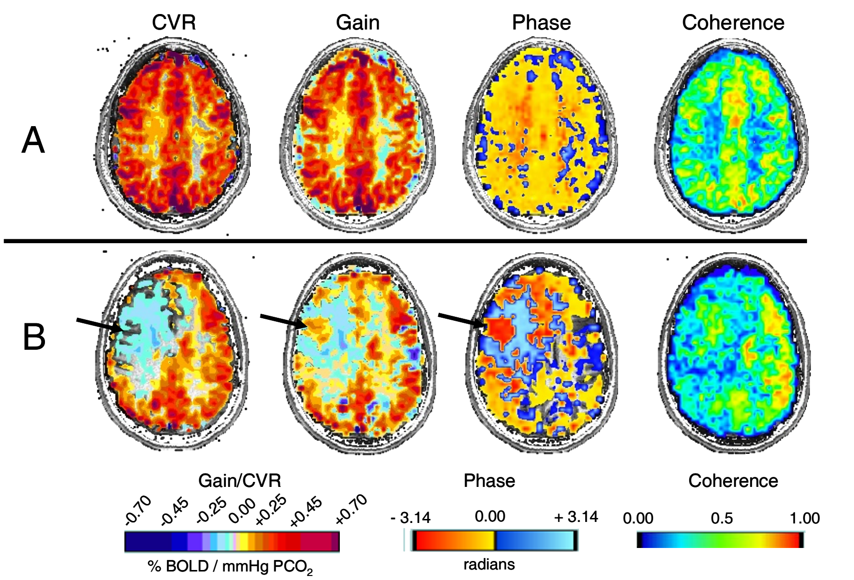

Figure 1: Maps for a 75 year-old healthy male (**A**) and an 18 year-old female with bilateral Moyamoya and a previous right STA-MCA bypass (**B**). Phase maps provide a measure of the speed of response. Negative phase signifies a positive response, fast (yellow) to slow (red). Positive phase signifies negative response, fast (light blue) to slow (darker blue). Coherence maps indicate the dependence of the BOLD signal on the PCO2 signal. The arrows show the region of a surgical extra cranial to intracranial arterial bypass, where CVR was indeterminate or negative, but gain was positive and phase indicated a markedly slowed response.

RESULTS: Fig. 1 shows the gain, phase and coherence maps for the two example individuals. We found that these maps extended the capability of CVR testing by providing a visualisation of the speed of response (phase maps). When CVR values were less than the gain, they were interpreted as due to the influence of response speed on the CVR, with slowed responses acting to decrease CVR; an effect absent in the gain maps, which provide a steady-state measure.

DISCUSSION AND CONCLUSION: This is the first application of TFA to CVR testing to provide maps identifying differences in the speed of the vasoactive response to PCO_2. These maps extend identification of cerebrovascular pathophysiology by revealing the dynamic component of CVR.