A statistical analysis to determine significant within-subject changes of BOLD MRI cerebrovascular reactivity to CO_2

Olivia Sobczyk[1], Adrian Crawley[2], Julien Poublanc[2], Kevin Sam[2,3], Daniel M. Mandell[2], David Mikulis[2], James Duffin[3,4], and Joseph Fisher[3,4]

[1]Institute of Medical Science, University of Toronto, Toronto, Ontario, Canada, [2]Department of Medical Imaging, University Health Network, Toronto, Ontario, Canada, [3]Department of Physiology, University of Toronto, Toronto, Ontario, Canada, [4]Anaesthesiology, University Health Network, Toronto, Ontario, Canada

PURPOSE: To develop a quantitative method for detecting significant within-subject changes in the cerebrovascular reactivity (CVR) over time.

INTRODUCTION: CVR is the ratio of the cerebral blood flow (CBF) response to an increase in a vasoactive stimulus. Our current measure of CVR uses the BOLD MRI signal as an indicator of the CBF response to standardized changes in carbon dioxide (CO_2). Despite uniform test conditions, there are still test-to-test differences in CVR due to variations in physiology and in the technology over time. Thus performing longitudinal studies requires the quantification of abnormal differences in CVR over time. We therefore generated a database of normal CVR test-retest variability as a normal reference to statistically score differences in CVR.

METHODS: Two standardized CVR tests were conducted in twelve healthy males (35 ± 14.3 y) within a three week period. All scans were then co-registered into standard space and a normal difference CVR map was calculated from the two time points for all voxels for each of the 12 subjects. This process generated an interval test difference (ID) atlas consisting of the mean and standard deviation (SD) of the differences for each voxel. We illustrate our concept by generating ID z-maps for a patient with moyamoya disease who had CVR tests done before and after EC-IC bypass. After co-registration to standard space, differences in CVR values for the patient were compared to the ID atlas and scored as z-values, the fractional standard deviation from the corresponding voxel of the atlas. The z-values were then color coded and superimposed on their anatomical scans to form ID z-maps.

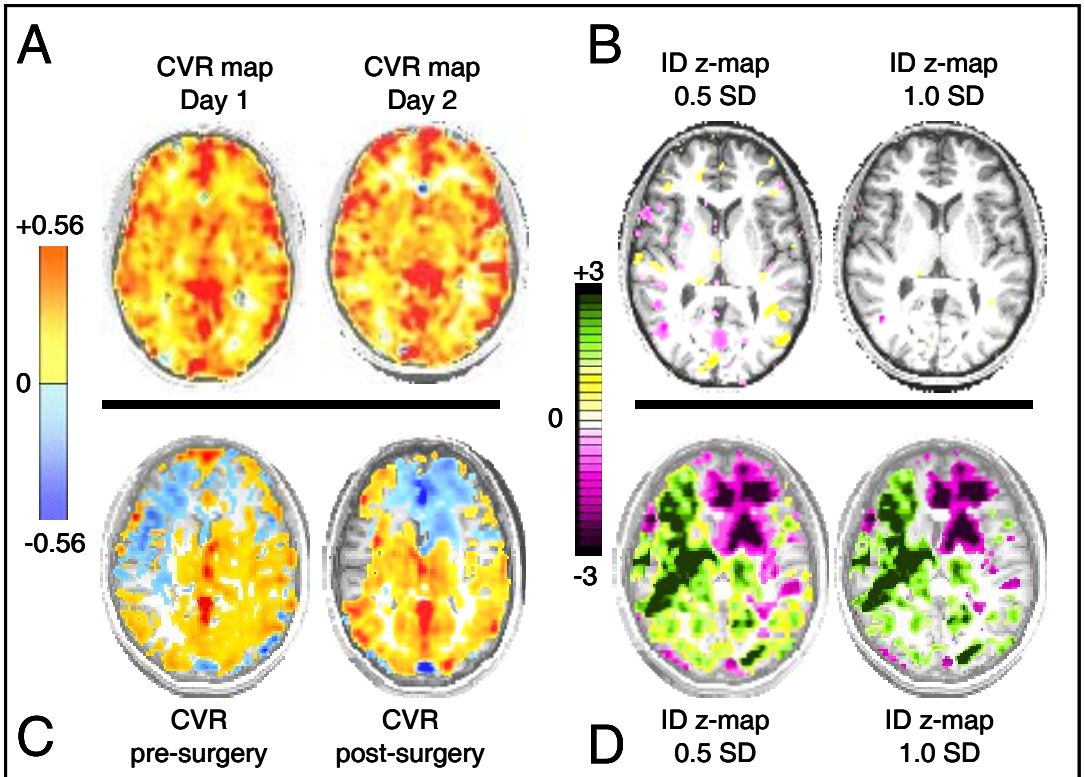

Figure 1. A&B: Normal subjects test-retest CVR and ID z-maps, show no difference between two scans. C: The post-surgery CVR map for a patient with moyamoya disease, suggests that following bypass CVR improved on the right whereas steal developed in the left MCA territory. D: The ID z-maps provide the additional information, that CVR on the right improved post-surgery while CVR on the left decreased. These changes in CVR are due to changes in the pathology of the disease that are greater than machine or normal physiology variability.

RESULTS: See Fig. 1. Indeed, the ID z-maps confirmed the improvement brought about by the EC-IC bypass surgery, and gave an indication of the extent and distribution of, changes in CVR.

DISCUSSION AND CONCLUSION: This is the first application of an atlas of normal CVR differences to identify significant differences in CVR maps over time. We used a healthy cohort and a single scanner in the expectation they would manifest a characteristic variation due to changes in physiology and scanner characteristics respectively between tests; excess variability is attributed to changes in pathophysiology. The application of ID z-maps will enable study of the natural history of cerebrovascular disease and response to treatment.