Evaluating collateral flow territory stability as a novel biomarker of recurrent stroke in patients with symptomatic intracranial stenosis

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Background: Intracranial (IC) collateral pathways provide important indicators of arterial steno-occlusion compensation, however evaluating the adequacy of these pathways is difficult with existing methods. Here, we modulated arterial partial pressure of CO2 with mild hypercapnic respiratory stimuli to evaluate the stability of cerebral blood flow (CBF) territories in IC stenosis patients as a novel marker of collateralization adequacy.

Methods: Symptomatic IC stenosis (n=20) and healthy (n=10) volunteers provided written consent and underwent noninvasive vessel-encoded arterial spin labeling. Separate magnetic labeling of the left ICA, right ICA, and vertebral arteries was performed, yielding 3 CBF territories. Scans were performed during normocapnia and hypercapnia (5% CO2) and patients were monitored for recurrent stroke for a mean 1.6 years. A graphical software package was developed **(Fig. 1A)** for data analysis. The primary study variable was the CBF territory shifting index, defined as the percent of voxels changing from normocapnia to hypercapnia; the clinical endpoint was new non-cardioembolic stroke, TIA, or silent cerebral infarct. Significance was defined as two-sided $p<0.05$.

Results: 10/20 patients experienced a clinical endpoint at or before follow-up. Shifting indices were significantly larger in patients meeting the clinical end-point (1.49±0.32) compared to controls (0.67±0.071; $p<0.022$) and patients not meeting the endpoint (0.67±0.12; $p<0.0089$) **(Fig. 1B,1C)**. Using 1 standard error above the mean patient shifting index as a threshold, sensitivities and specificities for predicting the clinical endpoint were 70% (7 of 10) and 97% (29 of 30), respectively.

Conclusion: Mild shifting of major CBF territories during hypercapnia may be elevated in IC stenosis patients at risk for recurrent stroke. This approach may provide a new marker of collateralization adequacy and risk of recurrent ischemic events.

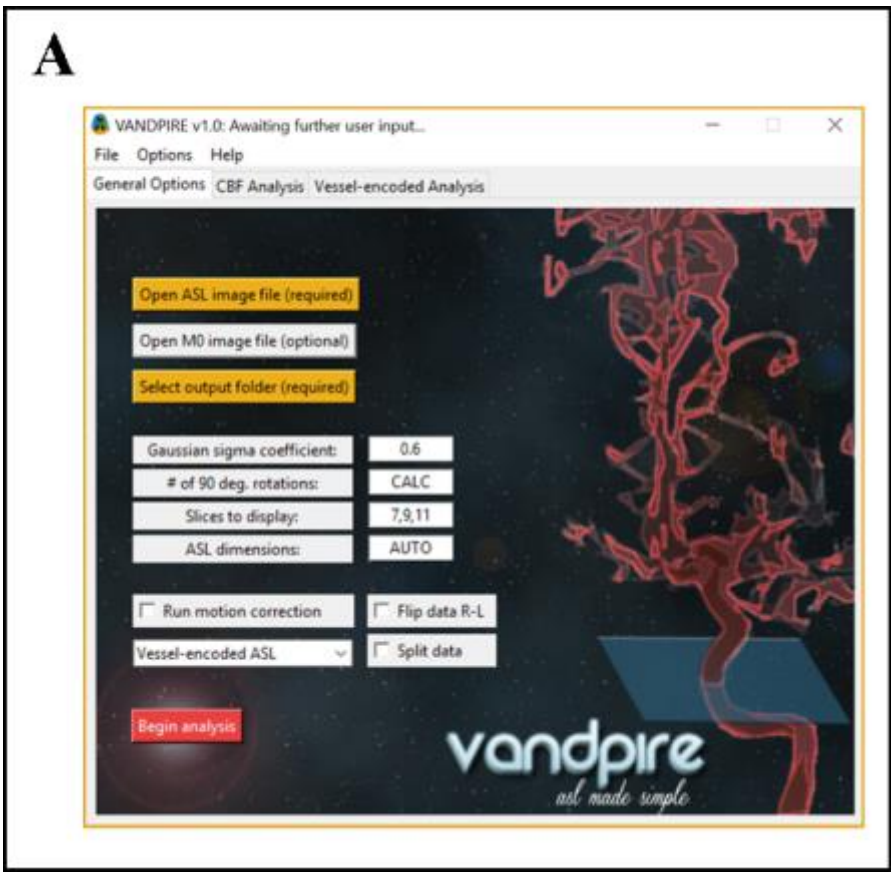

Figure 1A: Screenshot of software toolbox.

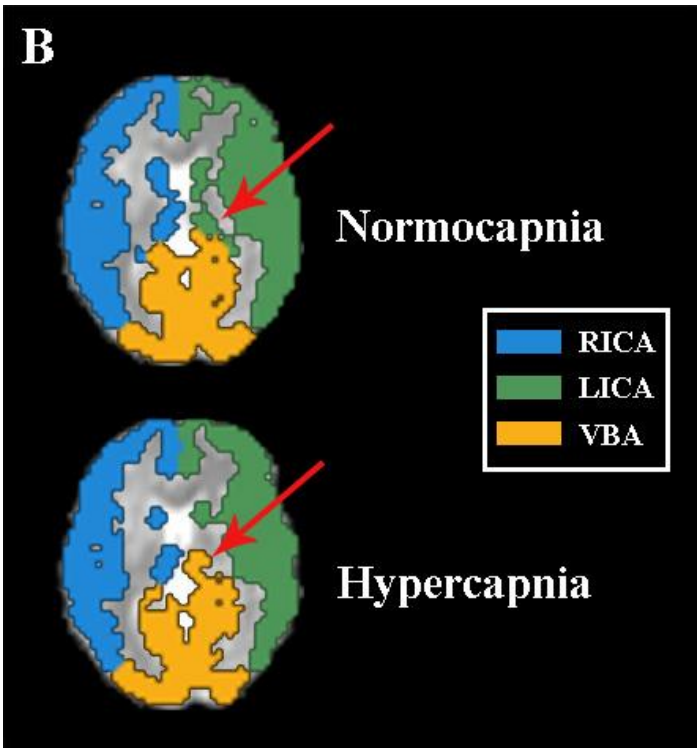

Figure 1B: CBF territory shifting in a patient with left ICA stenosis.

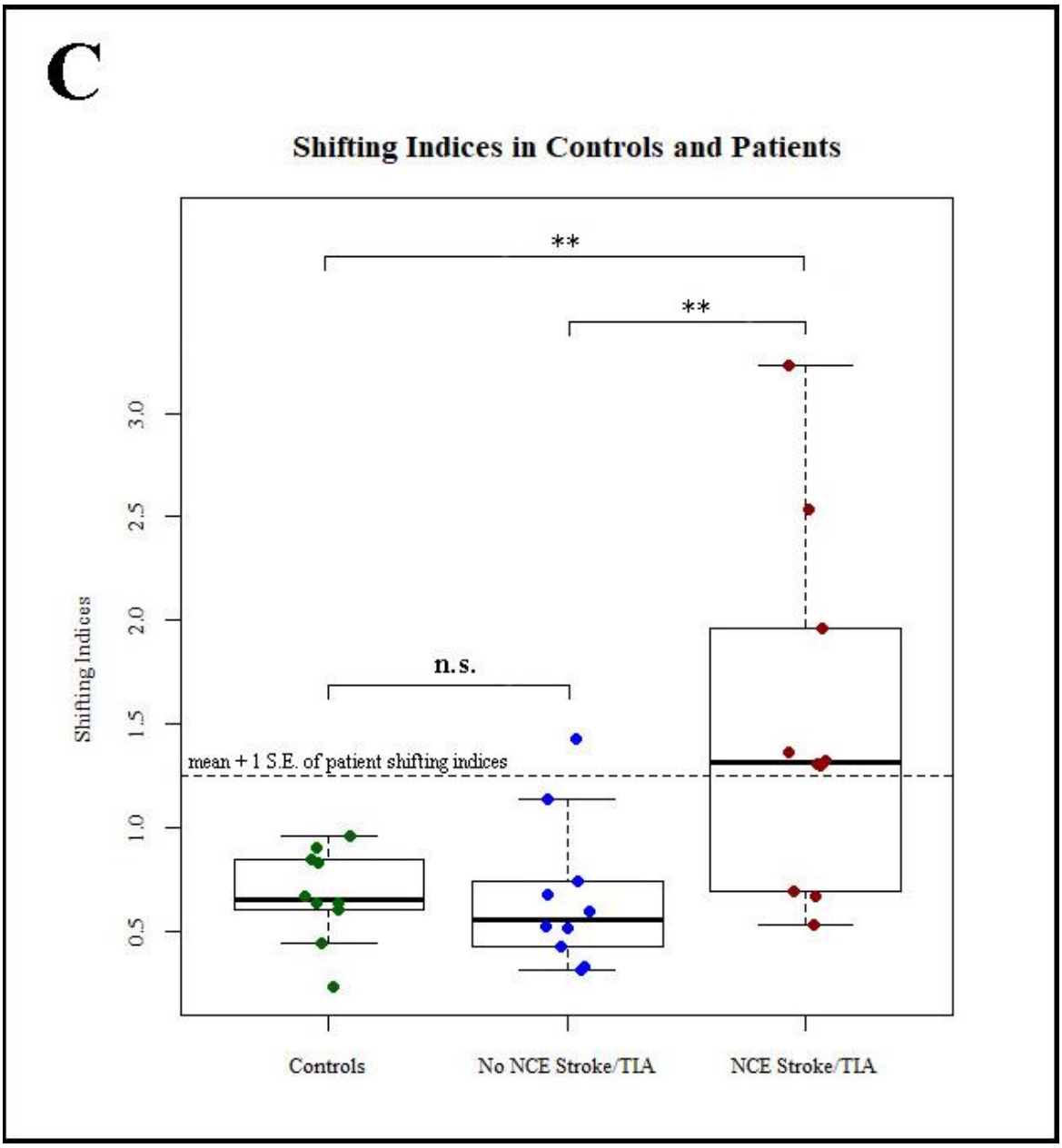

Figure 1C: Boxplots of shifting indices.