Recovery of Cerebral Hemodynamics Induces Normalization of Atypical Ipsilateral Motor Activity on fMRI
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Objective
To determine if correction of unilateral hemodynamic failure will reverse the atypical (ipsilateral) motor-related functional magnetic resonance imaging (fMRI) activity that was induced as a consequence of the hypoperfusion.

Background
fMRI studies of stroke recovery report atypical (ipsilateral) motor activation associated with movement of the hemiparetic hand. The ipsilateral activity generally disappears as motor recovery occurs. Stroke-free patients suffering unilateral critical large- vessel disease can have cognitive impairments suggestive of injury to that hemisphere that are not attributable to local lesions. We showed previously that even in the absence of stroke, uni-hemispheral impairment in cerebral hemodynamics due to large- vessel stenosis/occlusion can also induce atypical (ipsilateral) motor-related brain activity in the opposite hemisphere. We hypothesized that reversal of the hypoperfusion would result in reduced ipsilateral motor activation.

Methods
Two patients were included in this study. A 53 year old right- handed patient with right middle cerebral artery (MCA) high- grade stenosis and impaired vasomotor reactivity (VMR), as measured by transcranial Doppler with 5% CO2 inhalation, had spontaneous normalization of VMR 18 months later. A second patient, a 76 year old right- handed man with right internal carotid high- grade stenosis and impaired VMR, underwent a carotid artery stenting that resulted in normalization of VMR as measured by TOCD 3rd post-operative day. Normalization of VMR was confirmed 2 months later when the patient underwent a follow- up fMRI scan. We compared the change in fMRI motor activation pattern of the two patients to 7 healthy controls scanned twice at an interval of 3 months using voxel- wise statistical map (Brainvoyager XJ 1.1). During fMRI subjects performed a repetitive hand closure task in synchrony with the metronome in three 20- second blocks alternating with rest. Imaging was performed on a GE 1.5T magnet, imaged at 128x128 matrix, 15mmFOV, TR/TE = 1100/500, 50 slices, functional voxel dimensions 1.5 x 1.5 x 4.5 mm. Image volumes were co- registered, motion corrected and spatially normalizing corrected, subjected to high pass filter, normalized to Talairach template and modulated with a 3rd- order polynomial. The first 3 volumes of each run were excluded for signal stabilization. For all patients motion correction (3 translation planes, 3 directions of rotation) was well within the functional voxel dimensions.

METHODS cont’d.
A fixed-effects group analysis compared the blood oxygen level dependent (BOLD) activity in the 2 patients at Time 1 (baseline) and Time 2 (after normalization of VMR) with the controls. BOLD activity at Time 1 and Time 2, evaluating for a condition-by-time interaction. The interaction contrast was therefore represented as (P1-P2) – (C1-C2) whereby P1 and P2 represented the patients at Time 1 and Time 2, and C1 and C2 represented the controls at Time 1 and Time 2. All contrasts were assessed at a threshold of p<0.003, corresponding to p=0.0027 uncorrected.

ROI Analysis:
To quantitatively test our hypothesis that the atypical activation in the ipsilateral motor cortical areas decreased as a result of VMR normalization, we performed an independent region of interest (ROI) analysis among all subjects over 2 time points by computing average BOLD signal intensity (beta value) in the primary motor cortex (M1), lateral prefrontal cortex, and Supplementary motor area (SMA). We then compared the z scores of the 3 ROIs in each hemisphere at each time point to 7 healthy controls. Our results suggest that hemodynamic impairment induces a functional reorganization to the opposite hemisphere that is reversible when physiological blood flow is restored to the previously hypoperfused hemisphere. This extends our previous findings that impaired cerebral hemodynamics may be an independent variable in altering motor activity pattern. Our findings suggest that the brain is capable of dynamic and reversible reorganization in responding to physiological stressors such as hemispheric hypoperfusion.

CONCLUSION/RELEVANCE
These results have important implications for determining both the consequence of hemodynamic failure and the role of the ipsilateral hemispheres in motor function. The recruitment of alternative brain regions to share neuronal burden of the task during conditions of chronic ischemia can permit maintenance of normal neurological function. Our findings suggest that the brain is capable of dynamic and reversible reorganization in responding to physiological stressors such as hemispheric hypoperfusion.

References:

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