Better Recovery Following Stroke is Associated with Normalization of Resting-State Connectivity

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INTRODUCTION

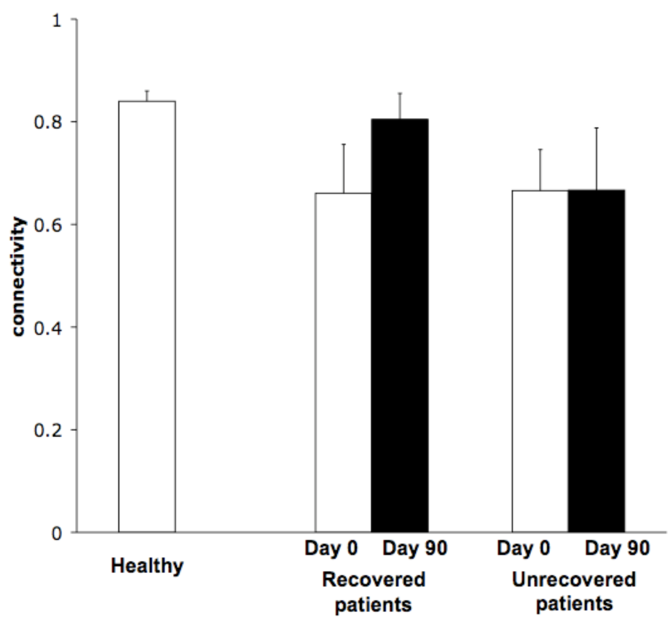
Functional magnetic resonance imaging (fMRI) of brain activity in response to a task has not emerged as a clinical tool in the assessment of acute stroke, due to logistical difficulties associated with ill patients performing tasks during imaging. fMRI studies have, however, repeatedly demonstrated that better recovery following stroke is most associated with minimum reorganization of function [1,2]. The strength of functional connections (i.e., connectivity [3]) in healthy brain has been demonstrated using fMRI by identifying strong temporal correlations between spatially distinct but functionally related regions during rest [4]. We wished to quantify the strength of resting-state connections following stroke and after recovery, to determine its potential as an index of brain function without the need for patients to perform tasks.

METHODS

Twelve ischemic stroke patients with a unilateral sensory/motor deficit (NIHSS score between 1 and 3 on scales related to the limbs) underwent two MRI sessions [0 days (< 24 hrs) and 90 days post-stroke] approved by the ethics board governing the institution. Informed written consent was obtained. During each session, anatomical images were collected, including diffusion-weighted (DWI), fluid-attenuated inversion recovery (FLAIR), and T_2 fast spin echo images (T2FSE). T_2*-weighted images were collected during rest (GRE-EPI: TE=30 ms, 24-cm FOV; twenty-seven 5-mm thick slices, 40 volumes of two shots with TR=3000 ms and 128x128 matrix size or 80 volumes of one shot with TR=1500 ms and 64x64 matrix size). Twelve healthy volunteers are also recruited as a control group. Anatomical images were acquired from healthy subjects, as well as T_2*-weighted images (GRE-EPI: TR/TE = 1500/30 ms, 24-cm FOV; twenty 5-mm thick slices, 80 volumes of one shot with 64x64 matrix size). Using anatomical images, the seed region for connectivity analysis was drawn manually to include the motor cortex of the stroke hemisphere for patients and the left hemisphere for controls. For each session, the average time series of signal intensity was recorded for the seed, and a voxel-based temporal cross-correlation was performed to determine the correlation of each voxel's time series with the seed. Connectivity was calculated as the ratio of the average of the correlation coefficients within the unaffected hemisphere motor cortex (or left for the controls) and the correlation coefficients within the affected hemisphere motor cortex (or right for the controls). That is, connectivity of the motor cortex in the hemisphere contralateral to the seed is normalized to the connectivity of the motor cortex containing the seed.

RESULTS

Eight patients were fully recovered by 90 days (NIHSS of 0 at day 90), and four did not improve or did not fully recover. As shown in the Figure, connectivity in both recovered and non-recovered patients at day 0 was significantly less than for healthy controls ($p < .05$). For stroke patients that recovered by 90 days, connectivity returned to that of the healthy controls, whereas connectivity remained decreased and unchanged for the non-recovered patients.



DISCUSSION

Our results demonstrate that resting-state connectivity is decreased after stroke, and resolves with recovery. Although recovered patients show stronger connectivity by day 90 compared to non-recovered patients, more patients are required to demonstrate a significant difference. Since resting-state connectivity is a continuous index, it may be a more sensitive index of recovery than ordinal clinical scales. Hence, connectivity has the potential to become a tool to establish the link between brain injury and regional brain function and communication, which is lacking in current clinical imaging and assessment scales.

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