Frequency Distribution of Enhanced Sensorimotor network in Stroke-recovered Rat

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INTRODUCTION: Stroke impairs neurovascular and metabolic functions and causes brain cell death, often resulting in a severe neurologic disability. Despite the apparent lack of neural regeneration after stroke, spontaneous recovery in the sensorimotor functions is commonly observed at later stages of stroke progression. Although reconstruction of the neural network is hypothesized to play the main role, the relevant stroke recovery mechanism has been poorly understood. Recently, resting-state fMRI (rs-fMRI) has emerged as an important method for non-invasively assessing evolution of neural networks. Among the rs-fMRI analysis techniques proposed, partial directed coherence (PDC) provides a promising tool to characterize the connection property, in particular, the frequency dependence of causal connectivity networks. The goal of this study was to understand relationships between the post-stroke functional recovery and reorganization of neural networks based on the causality analysis in the frequency domain.

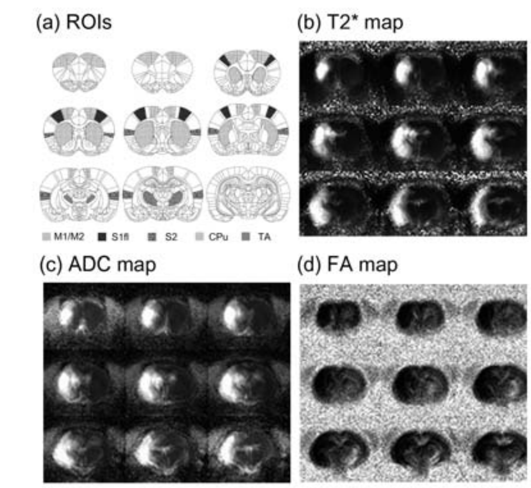

Fig 1. Region of interest (a) and stroke location and size represented on the T2* (b), ADC (c) and FA maps (d).

MATERIALS & METHODS: To maximize and demonstrate the effects of stroke recovery and associated functional reorganization, only the rats with a severe stroke (Fig. 1) were used (infarct volume > 35% of total brain). Temporary stroke was induced by 2-hour focal occlusion of the right middle cerebral artery (MCAO) by advancing an intraluminal filament up into the internal carotid artery of adult Sprague Dawley rats (n = 14, 250g to 280g). At 6 months after the temporary MCAO, MRI experiments were performed. Age-controlled normal rats were used as control group (n = 10). The rs-fMRI (Gradient EPI: TR/TE = 1000/12.89 ms; FOV = 2.5 x 2.5 cm^2; nine contiguous 1mm slices) was acquired using mechanically ventilated rats that were anaesthetized with the continuous infusion of alpha-chloralose (~30 mg/kg/h). Each rs-fMRI time course was detrended to the second order and bandpass-filtered between 0.01 and 0.5 Hz. Frequency dependent PDC values from relevant ROIs were calculated and compared using pairwise t-test between stroke and control groups.

RESULTS & DISCUSSION: A majority of rats (11/14) survived despite the large lesion involving both cortical and subcortical areas. Remarkably, these animals showed almost full functional recovery 6 months after stroke. Compared to control rats, the PDC results (Fig. 2) demonstrated the significant enhancement of the uni-directional connectivity in the contralesional hemisphere of stroke-recovered rats for causal paths such as sensory cortex (S1) → motor cortex (M1/M2), basal ganglia → cortex (M1/M2 and S1) and thalamus (TA) → cortex (M1/M2 and S1). In general, the stroke-recovery process was accompanied by the enhancement of sub-cortical → cortical causality connections. The newly emerged causal connections were also frequency-dependent, in which TA → M1/M2 showed significant difference only in the low (<0.15Hz) frequency band while TA → S1fl in the high (0.2-0.4Hz) frequency band. Such changes imply that the increased directional resting state activity in the contralesional hemisphere is associated with the long-term spontaneous stroke-recovery, possibly replacing the impaired ipsilesional brain functions. The current PDC work shows that the concomitant reshaping of the causal connectivity in the frequency-domain accompanies the stroke-recovery process.

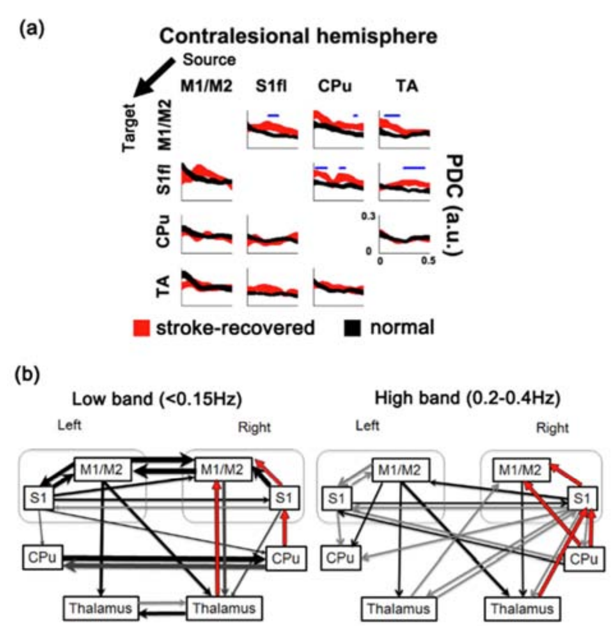

Fig 2. (a) PDC value matrices in the frequency domain - Red lines show averaged values of stroke-recovered rats with standard error (line thickness) at a given frequency while black lines are those calculated from control rats. Frequencies showing significant difference between two groups are marked with blue dots (p<0.05).
(b) Connectivity diagrams derived from PDC analyses. Red arrows show newly detected or enhanced connectivity in conralesional hemisphere from stroke-recovered group.