Changes in functional connectivity post stroke

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A dense network of cortico-cortical axonal pathways interconnects structurally segregated and functionally specialized regions of the human cerebral cortex. Functional MRI (fMRI) can be applied to study these functionally interconnected networks in the human brain (Biswal, Yetkin, Haughton, & Hyde, 1995; Damoiseaux et al., 2006; Fox & Raichle, 2007; Greicius, Krasnow, Reiss, & Menon, 2003; Lowe, Dzemidzic, Lurito, Mathews, & Phillips, 2000). When neuronal activity, as measured using functional MRI, is temporally coherent across two or more spatially segregated brain regions, those regions are assumed to be functionally connected. These fluctuations in fMRI signal are most easily measured with resting state fMRI. During resting state functional connectivity studies, brain low frequency fMRI signal fluctuations are observed as the subject lies in the scanner and is instructed to do ‘nothing’. Subjects instructed to ‘do nothing’, however, will engage in spontaneous activity (sensory, attentional, motor, memory and ‘spontaneous mind wondering’) and therefore engage different brain networks during the experiment. The observed brain networks during rest strongly overlap with the topography of multiple brain systems defined on the basis of task-related fMRI (Fox & Raichle, 2007).

By showing how damage to certain brain regions affects functional connectivity, we can learn something about the intrinsic architecture of cortical circuits involved in sensory, motor or cognitive functions (Nomura et al., 2010). Functional connectivity analysis of resting state data offers a way of inferring (abnormal) brain function, especially in sick patients, as necessary functional MRI scans can be acquired in relatively short period of time (usually less than 10 minutes) with minimal physical effort for the patient (Grefkes & Fink, 2011).

In the acute phase of stroke, over 60% of patients present with motor symptoms such as (hemi-)paresis. Recovery from motor (or language) deficits in the first few weeks to months post-stroke is predominantly driven by neuronal reorganization. Active (task-driven) fMRI experiments show such reorganization by demonstrating abnormal cortical activation patterns after stroke during movements of the affected (paretic) limb: enhanced neuronal activity in a number of areas both in the lesioned (ipsilesional) and in the healthy (contralesion) hemisphere (Chollet et al., 1991; Grefkes et al., 2008; Ward, Brown, Thompson, & Frackowiak, 2003). These findings implicate premotor cortex in the recovery of function of the stroke affected hand. Longitudinal fMRI studies early after stroke show recruitment in motor-related areas in both hemispheres, and then during the first year post-stroke a renormalization is seen in patients with good motor recovery (Ward et al., 2003).
A stroke induced lesion not only affects connectivity between cortex and spine, but also the interactions among cortical areas, even cortical areas distant from the lesion. Using resting state fMRI analysis in rodents, van Meer (van Meer et al., 2010) found a decline in functional connectivity (i.e. loss of coherence of low-frequency BOLD fluctuations) between ipsilesional and contralesional sensorimotor cortices outside the ischemic lesion. Improvements in motor function over time correlated with consolidation of interhemispheric functional connectivity. Similar data exist in humans (Carter et al., 2010).

Moreover, not only interhemispheric but also changes in the motor network within the lesioned hemisphere are important for understanding stroke deficits and their recovery (Grefkes & Fink, 2011). In healthy subjects, intrinsic coupling between motor network nodes exists during rest and involves positive interactions between intrahemispheric premotor cortex (PMC), supplementary motor area (SMA) and primary motor cortex (M1), and mostly negative (inhibitory) interactions between hemispheres (Grefkes et al., 2008). During unilateral hand movements the intrinsic coupling between PMC, SMA and M1 increases within the contralateral hemisphere and the interhemispheric inhibition also becomes stronger. In patients with stroke, there is a loss of this well balanced coupling within and across hemispheres. Movements of the paretic hand are associated with a pathological inhibition of the ipsilesional M1 exerted by contralesional M1, which does not occur in healthy subjects (Grefkes et al., 2008). This may explain why a stronger recruitment of the contralesional primary motor cortex observed during active task fMRI executed with the paretic hand is not necessarily a good indicator of efficient reorganization and functional recovery.


