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Research report

Abnormal functional networks in resting-state of the sub-cortical chronic stroke patients with hemiplegia

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ABSTRACT

The aim of this study is to identify the properties of the motor network and the default-mode network (DMN) of the sub-cortical chronic stroke patients, and to study the relationship between the network connectivity and the neurological scales of the stroke patients. Twenty-eight chronic stroke patients (28–77 days post-stroke) and twenty-eight healthy control subjects (HCs) were recruited. Independent component analysis (ICA) was performed to obtain the motor network and the DMN. Two sample *t*-tests was used to compare the differences of the motor network and the DMN between the patients and HCs. Additionally, correlations between the network connectivity and the behavioral scores of the stroke patients were studied. Compared with the HCs, the motor network connectivity of the stroke patients was significantly increased in the contralesional superior parietal lobule, but decreased in ipsilesional M1. The DMN connectivity of the stroke patients was significantly increased in the contralesional middle frontal gyrus, but decreased in bilateral precuneus, ipsilesional supramarginal and angular gyrus. Moreover, the motor network connectivity of the contralesional superior parietal lobule was positively correlated with the Fugl-Meyer assessment (FMA) score of the stroke patients. Our results showed abnormal motor network and DMN during the resting-state of the stroke patients, suggesting that resting-state network connectivity could serve as biomarkers for future stroke studies. Brain–behavior relationships could be taken into account while evaluating stroke patients.

1. Introduction

The majority of stroke survivors suffer from post-stroke motor dysfunction and cognitive impairment (Go et al., 2013). Despite the progress with rehabilitative approaches, the recovery of brain function after stroke is usually incomplete (Jin et al., 2006). To date, the underlying mechanism of the stroke is still an important and hot research topic.

Resting-state fMRI has been wildly applied as a novel approach in understanding the intrinsic state of brain activity. It is task-independent and focuses on the low frequency component of the blood oxygenation level-dependent (BOLD) signal (Shmuel and Leopold, 2008; Biswal et al., 1995). During the resting-state, spatially distinct cortical regions exhibit similar temporal properties of the spontaneous ongoing BOLD fluctuations were defined as resting-state networks, including the default mode network (DMN), motor network, central executing network, auditory network, visual network, attention network etc (Tuladhar et al., 2013). In this study, the motor network and the DMN have been chosen to analyze the abnormal brain function of the stroke patients.

Motor function has been proved to be subserved by a widely distributed brain network which is consisted of primary motor cortex (M1), lateral premotor cortex (PMC), supplementary motor area (SMA), and subcortical areas such as the basal ganglia, thalamus, and cerebellum (Middleton and Strick, 2000; Dum and Strick, 2002). A number of former studies indicated the abnormal FC between the brain regions within the motor network which subsequently affect the motor function of the stroke patients (Carter et al., 2010; Park et al., 2011). Using the region of interest (ROI)-based approaches, Carter et al. reported that patients with relatively poor hand motor function feature reduced interhemispheric M1–M1 connectivity (Carter et al., 2010). Park et al. reported increased interhemispheric connectivity between ipsilesional M1

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and contralesional thalamus, SMA and middle prefrontal cortex of the stroke patients (Park et al., 2011). Our former research also employed the ROI-based approach and found increased FC between the ipsilesional M1 and the ipsilesional inferior parietal cortex, frontal gyrus, SMA, and decreased FC between the ipsilesional M1 and bilateral M1 in the stroke patients (Zhang et al., 2016). However, few studies have used the data-driven approaches to delineate the motor network as a spatially independent pattern of coherent signals during the resting-state of the stroke patients.

The DMN, which is one of the most import sub-networks during the resting state, is comprised of posterior cingulate cortex (PCC), medial prefrontal cortex (MPFC), bilateral parietal cortices, hippocampus, and some other brain regions (Greicius et al., 2003; Raichle and Snyder, 2007; Andrews-Hanna et al., 2010). This network sustains some basic cognitive functions including the external environment monitoring, episodic memory processing, and emotional processes, which are usually spontaneous, self-referential, and independent of specific cognitive task (Cabeza and Nyberg, 2000; Donaldson et al., 2001; Alvarez and Emory, 2006). Thus functional disconnection of the DMN tends to be associated quite strongly with cognitive impairment in the neurodegenerative diseases such as Alzheimer's disease (Wang et al., 2012; Zhong et al., 2014) and Parkinson's disease (Amboni et al., 2015; Spetsieris et al., 2015). Researchers also found abnormal FC between the brain regions within the DMN of the stroke patients. For example, Tsai et al. reported significantly decreased FC in the precuneus and posterior cingulated cortex regions among stroke patients with impaired consciousness (Tsai et al., 2014). Using the independent component analysis, Tuladhar et al. reported decreased FC in the left medial temporal lobe, posterior cingulate and MPFC within the DMN in stroke patients compared with controls (Tuladhar et al., 2013). Ding et al. also found decreased FC in the PCC, precuneus, as well as increased FC in the MPFC and ipsilesional hippocampus in acute stroke patients (Ding et al., 2014). Despite of these valuable results, the relationship between the DMN change and the cognitive function of stroke patients hasn't been well explored yet.

In this study, we performed independent component analysis (ICA) to identify the properties of the motor network and the DMN of the sub-cortical stroke patients. Meanwhile, we studied the relationship between the motor network connectivity and the motor function, also the relationship between the DMN connectivity and the cognitive function of the stroke patients. Our hypothesis is that: 1) the patients will show abnormal networks compared with the healthy controls. 2) The abnormal the motor network and the DMN connectivity may be related to the patients' motor and cognitive functions.

2. Results

2.1. Behavioral data

Three stroke patients were excluded from the final analysis because of excessive head motion during MR scanning (more than 3 mm). Thus, 25 stroke patients and 28 HCs were included in the final data analysis. The demographic and clinical characteristics of the patients are described in Table 1. The two groups were well-matched for age, gender and years of education. Compared to the HCs, MMSE score of the patients were significantly decreased ($p < 0.05$).

2.2. The motor network results

One sample *t*-test results of both groups showed strong FC in bilateral M1, PMC and SMA ($p < 0.001$, corrected at the cluster level, cluster ≥ 50) (Fig. 1). Comparing with the HCs, the FC within the motor network of the stroke patients was significantly increased in the contralesional superior parietal lobule, but decreased in ipsilesional M1. ($p < 0.01$, corrected at the cluster level, cluster ≥ 20) (Fig. 2, Table 2).

2.3. DMN results

The DMN maps of the HCs and stroke patients all showed strong connectivity in MPFC, bilateral PCC, precuneus, medial temporal cortex and angular gyrus ($p < 0.001$, corrected at the cluster level, cluster ≥ 50) (Fig. 3). Comparing with the HCs, the FC within the DMN of the stroke patients was significantly increased in the contralesional middle frontal gyrus, but decreased in bilateral precuneus, ipsilesional supramarginal and angular gyrus ($p < 0.05$, corrected at the cluster level, cluster ≥ 20) (Fig. 4, Table 3).

2.4. Correlation results

The motor network connectivity of the contralesional superior parietal lobule was positively correlated with the FMA score of the stroke patients ($r^2 = 0.1748$; $p = 0.038$, uncorrected) (Fig. 5). No significant relationships between the motor network connectivity in the other brain regions and the FMA score were found, likewise no significant correlation between the DMN connectivity and MMSE score was found either.

3. Discussion

In this study, we employed the resting-state fMRI and ICA method to analyze the motor network and the DMN of the stroke patients. Meanwhile, we explored the relationship between the network connectivity and the behavioral scores of the stroke patients. The results confirmed our hypothesis that stroke patients showed abnormal functional networks during the resting-state while compared to the HCs, which were well consistent with the results of the previous studies. Also, we found motor network connectivity of the contralesional superior parietal lobule was positively correlated with the FMA score of the stroke patients.

3.1. Differences of the motor network between the stroke patients and HCs

Comparing with the HCs, the motor network connectivity of the stroke patients was significantly increased in the contralesional superior parietal lobule. The superior parietal lobule is usually connected with the postcentral gyrus above the end of the postcentral sulcus, which is involved with spatial orientation and receives a great deal of visual input as well as sensory input from one's hand (Koenigs et al., 2009; Wolpert et al., 1998). Thus, the increased FC between the contralesional superior parietal lobule and the other regions within the motor network could be a form of compensation for the weakened ipsilesional FC in the stroke patients with hemiplegia. We also found the decreased motor network connectivity in ipsilesional M1 of the stroke patients, which were consistent with the results of the previous studies using the ROI-based approach, that stroke leads to changes in interhemispheric functional connectivity (Carter et al., 2010; Park et al., 2011). Carter et al. had reported that patients with relatively poor hand motor function feature reduced interhemispheric M1–M1 connectivity (Carter et al., 2010). Wang et al. also reported abnormal FC between the ipsilesional M1 and the contralesional PMC and parietal lobe (Wang et al., 2010). The decreased motor network connectivity of M1 in our study suggested that the stroke lesions in the patients' brain not only affected the intra-hemisphere information exchange