Seed Regions and Independent Component Analysis of Resting State Brain Functional Connectivity in a Rat Model of Parkinson's Disease

Hui-Yu Wang[1], You-Yin Chen[2], Sheng-Huang Lin[3,4], and Jun-Cheng Weng[1,5]

[1]*School of Medical Imaging and Radiological Sciences, Chung Shan Medical University, Taichung, Taiwan,* [2]*Department of Biomedical Engineering, National Yang-Ming University, Taipei, Taiwan,* [3]*Department of Neurology, Tzu Chi General Hospital, Tzu Chi University, Hualien, Taiwan,* [4]*Institute of Biomedical Engineering, National Taiwan University, Taipei, Taiwan,* [5]*Department of Medical Imaging, Chung Shan Medical University Hospital, Taichung, Taiwan*

Introduction

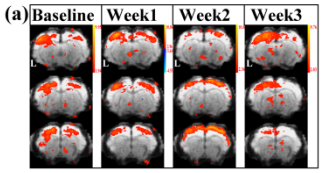
Parkinson's disease (PD) is a progressive neurodegenerative disorder that is characterized by dopamine depletion in the striatum, and it associated with predominantly motor, cognitive and affective symptoms [1]. The clinical diagnosis of PD is extremely difficult, because the symptom is similar to other central nervous disorder, such as Alzheimer's disease and Hydrocephalus [2]. The most common diagnostic methods are neurologist's inquiry and positron emission tomogram (PET) studies [3]. One consistent pathophysiological hallmark of PD is the change in spontaneous oscillatory activity in the basal ganglia thalamocortical networks [4]. Therefore, the goal of our study is to evaluate brain functional connectivity changes using frequency-specific resting-state functional MRI (rs-fMRI) in PD rat and baseline controls using three different seed regions analysis, motor cortex (M1), corpus striatum (CPu) and substantia nigra (SNr), and independent component analysis (ICA). Our results showed a PD-associated decrease in cortico-cortical and cortico-striatal functional connectivity and drops in the power content of cortical and striatal signals. Our results demonstrated that PD modulate cortical and striatal resting state BOLD signal oscillations and cortico-cortical as well as cortico-striatal network correlation.

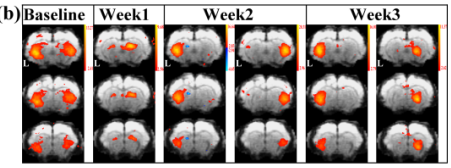
Materials and Methods

Whole brain images were acquired from five healthy rats and scanned by 7T Bruker MRI. In preparation, each rat was anesthetized with 3.5% isoflurance mixed with 800ml/min air. Before MRI experiments a short-acting tranquilizer and synthetic medicine, Domitor, was injected. It is commonly used in animal surgery and fMRI study to avoid BOLD signal contamination by isoflurance. During experiments, the temperature was maintained at ~37 ^{o}C using hot pad. The images were acquired by echo planar imaging (EPI) with the following parameters: repetition time/echo time (TR/TE) =1200ms /24 ms, image resolution = 0.3 x 0.3 x 1 mm^3, slice number = 10, number of repetition = 200, and the scan time = 4 min. The rats were scanned in the baseline and were scanned weekly after drug-induced Parkinson until third week. In data analysis, the data were first coregistered using FMRIB Software Library (FSL), and detrend, high-pass filter and smoothing were then performed. The independent component analysis was used for objective analysis with FSL, and seed regions with alphasim correction was used for subjective analysis by Resting State fMRI Data Analysis Toolkit (REST), respectively.

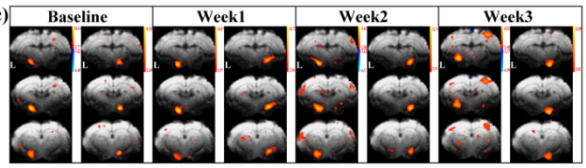
Results and Discussions

In the results of ICA (Fig.1), bilateral correlation of M1 was observed in four weeks from baseline to three week after drug-induced Parkinson, while bilateral correlation of CPu can only maintain for two weeks. There is no significant bilateral correlation of SNr in four weeks. In the power spectrum (Fig.2), the power extremely dropped in all interesting regions after drug-induced Parkinson compared to baseline, especially in M1 regions. In the results of seed regions analysis (Fig.3), we observed an overall decrease in the strength of cortico-cortical, striatum-striatal, and cortico-striatal functional connectivity in the rat brain after drug-induced Parkinson compared to baseline. In the specific frequency analysis (Fig.4), our results showed that the correlation in all of networks concentrate within low frequencies (0.01-0.04Hz), and the correlation decreased after drug-induced Parkinson compared to baseline, suggesting distinct frequency-specific features in the rs-fMRI of PD rat within these functional networks.

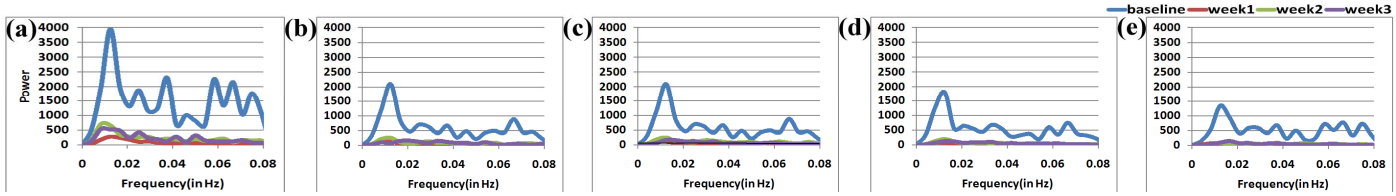




▲Fig. 1 ICA results of (a) M1, (b) CPu, (c) SNr.



▼Fig. 2 ICA power spectrum of (a) M1, (b) LCPu, (c) RCPu, (d) LSNr, (e) RSNr.



LM1: Left M1, RM1: Right M1, LCPu: Left CPu, RCPu: Right CPu, LSNr: Left SNr, RSNr: Right SNr.

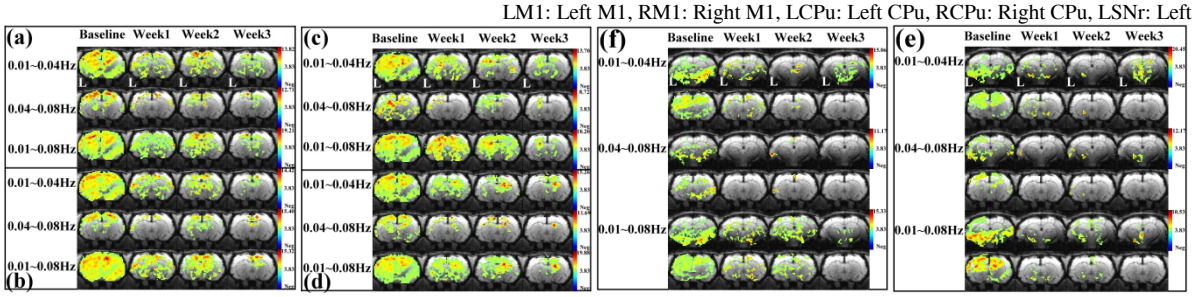


Fig. 3 Seed points of seed region analysis at (a) LM1, (b) RM1, (c) LCPu, (d) RCPu, (e)LSNr, (f) RSNr.

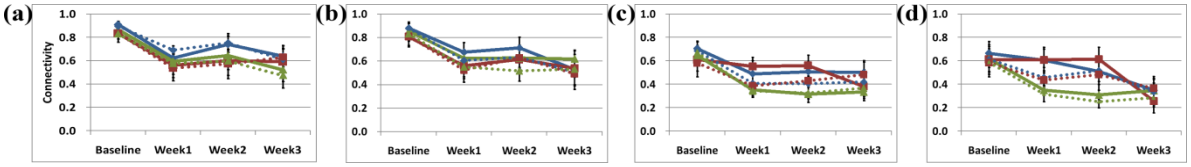


Fig.4 Correlation in all networks.

0.01~0.04Hz
0.04~0.08Hz
0.01~0.08Hz

Solid line:LM1 to LCPu
Dotted line:LM1 to RCPu

Solid line:RM1 to LCPu
Dotted line:RM1 to RCPu

Solid line: LSNr to LCPu
Dotted line: LSNr to RCPu

Solid line: RSNr to LCPu
Dotted line: RSNr to RCPu

Conclusions

Our results showed a PD-associated decrease in cortico-cortical and cortico-striatal functional connectivity and drops in the power content of cortical and striatal signals. Our results demonstrated that PD modulate cortical and striatal resting state BOLD signal oscillations and cortico-cortical as well as cortico-striatal network correlation. The rs-fMRI has great potential to be applied to further clinical research investigating the pathophysiology, progression, and treatment of PD.

References

[1] J Jankovic, J. Neurol. Neurosurg. Psychiatr. 2008; 79 (4): 368–76. [2] WR Galpern, et al., Ann. Neurol. 2006; 59 (3): 449–58.
[3] DJ Brooks, J. Nucl. Med. 2010; 51 (4): 596–609. [4] Y Kwak, et al., Frontiers in System Neuroscience 2010; 4: 14301-14325.