Comparison of the Functional Brain Connectivity Network in Night Shift Workers With and Without Shift Work Disorder: A Resting State fMRI Analysis

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Target Audience: Scientists and specialists interested in sleep studies, functional MRI, brain connectivity and neurological disorders

Purpose: We have used resting state fMRI to study the functional connectivity network in individuals with Shift Work Sleep Disorder (SWSD) as compared to the connectivity networks of asymptomatic night shift workers and daytime workers. SWSD is a circadian rhythm sleep disorder defined by clinically significant symptoms of insomnia and/or excessive sleepiness which cannot be explained by other medical conditions and can be seen in individuals whose work hours overlap with the typical sleep period. Many studies have linked health risks such as cancer, heart disease and digestive disorders to shift work[1]. Sleep deprivation and also major misalignment of circadian rhythms related to shift work can lead to deficits in the brain function and can also lead to cognitive deficits. It is possible that significant sleep disturbance in night shift workers may change the activity of neuronal connections in the brain even during the rest state. A previous study using Event Related Brain Potentials (ERPs) has shown the negative effects of SWSD on sensory memory and attention.[3]. In the current study, we have included 94 regions covering the entire brain in the connectivity network to find functional connections that might be significantly different between day and night workers and SWSD. Our results can help identify the brain regions which are most vulnerable to the night work schedule and in SWSD specifically.

Methods: Three groups of subjects were enrolled in the study: Five night shift workers with shift work disorder (SWSD), six asymptomatic night shift workers (control or SWC group) and 6 normal controls with no history of psychiatric or neurologic disorder daytime workers (NC group).Functional MRI images were acquired on a GE 3.0-T whole-body magnet using a gradient echo EPI sequence for whole-brain BOLD fMRI with an FOV of 22×22cm on a 64×64 matrix (3.4375×3.4375mm in-plane resolution), 34 slices/3.5mm slice thickness with BW/px=7.8125 kHz/px, TR/TE=2000ms/30ms. For the resting state image set, 150 volumes (five minutes) were recorded while the subjects were lying quietly with eyes open inside the scanner and using ear plugs for minimizing the noise from the scanner. Keeping the eyes open eliminates the coherent activity in the occipital cortex. High resolution (IRSPGR) images were also acquired for segmentation. Respiration and cardiac data of the subject were recorded during the scan using a pneumatic belt and pulse-oximeter, respectively. This data was used in artifact removal prior to data analysis. We previously suggested a framework for studying changes in the functional connectivity network for stroke patients using resting state fMRI images[2].The same method was applied in this study. Based on this method, Statistical Parametric Mapping (SPM8) (www.fil.ion.ucl.ac.uk/spm) was used for pre-processing the data, time-slicing correction, and realignment for correcting the motion artifact and spatial smoothing. The brain was segmented into 104 regions using the high resolution 3D IRSPGR image and the HAMMER software (University of Pennsylvania, Section of Biomedical Image Analysis, SIBA); we used only 94 of these regions in our study, excluding segments such as the ventricles which have no functional role. Next, the temporal fMRI signals from all voxels in each segmented region were averaged to represent one signal for each region and the physiological noise was removed using a linear regression model. These signals were low-pass filtered and de-trended so that only signal components with frequencies less than 0.08Hz remained for further analysis. For every subject, the correlation coefficient was calculated between the low frequency signals of each pair of these regions to create a symmetric 94×94 correlation coefficient matrix. To compare the functional connectivity between three groups, two sample t-test with significance level of 5% was performed between each of the NC/SWC, NC/SWSD and SWC/SWSD group-comparisons. This was done for every element of the correlation coefficient matrix to find node pairs that their mean value across the subjects in each group was significantly different with the mean value across subjects in the other group.

Results: The t-test revealed significant difference between the three groups (SWC/SWSD, NC/SWSD and NC/SWC). The number of highlighted links connected to each node (brain region) was summed to estimate the overall involvement of each node in the connectivity differences between the groups. Some nodes were connected to as many as 30 links with significantly different mean values across the two groups. Figure 1 shows results of comparison of these regions with the color representing the number of links connected to each region. The pattern shows the functional differences between the two compared groups. The total count of pairs in the matrix showing significant differences for SWC/SWSD, NC/SWSD and NC/SWC groups was 212, 230 and158 respectively.

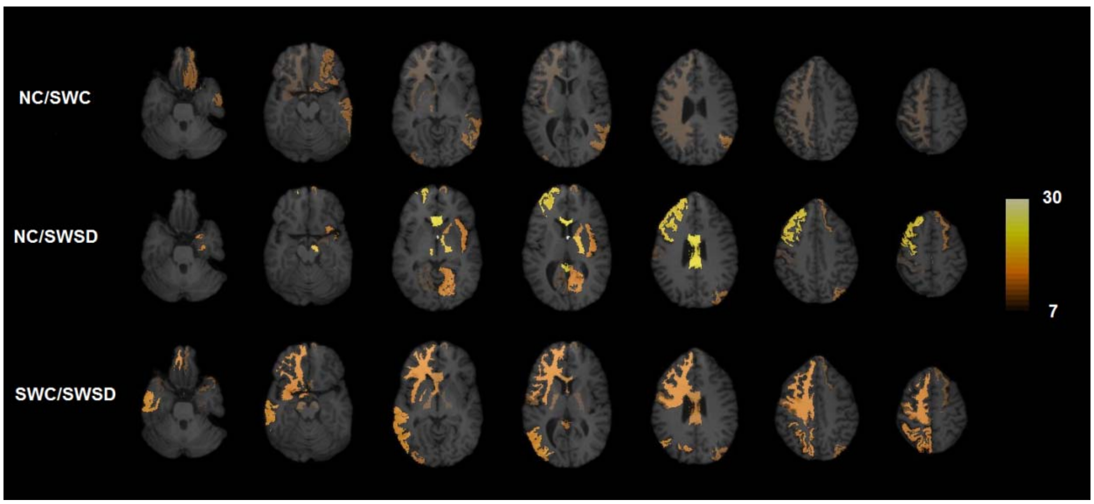

Figure 1.Maps showing regions in the brain that have been identified as nodes in the brain connectivity network with links having values that are significantly different between the two subject groups. The color of the regions represents total the number of such links connected to that region.

Discussion: The fMRI connectivity analysis in this study shows the differences in connectivity pairs between the three subject groups. There are certain connectivity links with correlation coefficient values that are statistically different between the SWSD group and SWC group. The total number of highlighted links and also the maps in Figure 1 show that while the SWC and NC groups are showing functional differences, however, the difference between the SWC and SWSD groups is much greater. This observation confirms previous findings using ERP measurements which showed that even though the patterns were different between the NC and SWC groups, they were more correlated compared to the SWSD and SWC groups[3]

Conclusions: This study shows the feasibility of using fMRI for studying the brain connectivity in individuals with SWSD. The next step, we will include other measurements such as the MSLT (Multiple Sleep Latency Test) which is a diagnostic tool for excessive sleepiness and will explore the correlation of MSLT results and fMRI connectivity results. It should be noted that the abnormal brain regions that are highlighted in this study may be either regions that are the source of the disorder or regions that are affected by complications resulting from the sleep disorder. Having larger number of subjects in each group can help achieve more significant results.

References

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