Altered Functional Complexity Associated with Structural Features in Schizophrenic Brain: A Resting-state fMRI Study

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Abstract: Power law scaling is a well-defined physical concept in complexity science that has been used to quantified the dynamic signals across temporal scales. In this research, we aim to investigate the power law scaling of resting-state fMRI signal in schizophrenic and healthy brain and to examine the potential structural properties that may correlate to the altered functional complexity. Brain imaging data of 200 schizophrenia patients and 200 age and sex-matched healthy Han Chinese was retrieved from Taiwan Aging and Mental Illness cohort. Power law scaling was extracted by Pwelch function. In schizophrenia, six brain regions with abnormal complexity were correlated to the regional structural network of grey matter volume (hub at right superior frontal gyrus) and white matter volume at right superior cerebellar peduncle and splenium of the corpus callosum. Moreover, the identified power law scaling was correlated with clinical symptom severity. Our findings suggest that a loss of scale-free brain signal dynamics affecting by brain morphometries proposed the reduced complex brain activity as one of the neurobiological mechanisms in schizophrenia. This research supports "the loss of brain complexity hypothesis" and "the dysconnectivity hypothesis of schizophrenia.", laying potential impact in psychiatry.

1 INTRODUCTION

The increasing amount of neuroimaging data has been established in recent years to understand the complex brain functions in mental disorders. To quantify the complex brain signal data, an approach that integrates mathematics, physics, and computational neuroscience is required. Studies have applied methods adopted from complexity science to more fully understand complex brain activity, as measured by resting-state functional Magnetic Resonance Imaging (fMRI). Nonlinear dynamical approaches to quantify the complexity of brain signal data may have the potential to develop brain-based imaging markers to extract fundamental features from spatial-temporal neuroimaging data at multiple levels.

Schizophrenia is a chronic and severe mental disorder that affects how a person thinks, feels, and behaves. The prevalence is nearly 1% worldwide and there have been more than 23 million people worldwide diagnosed with schizophrenia up to 2019. Base on the Diagnostic and Statistical Manual of Mental Disorders, schizophrenia patients would exhibit positive symptoms and negative symptoms such as hallucinations and delusions, disorganized speech and catatonic behavior, and negative symptoms such as the decrease in emotional range, alogia or apathy.

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The cause of such complex illness may be associated with genetic or environmental factors, however, the underlying mechanism remains unclear. Previous studies have developed models and modalities to tackle the challenge. Dr. Yang and Tsai (2013) raised the "loss of brain complexity hypothesis" based on empirical evidence (Hager et al., 2017) and clinical observation. The brain activity in healthy state performs multiscale variability, whereas the pathological brain could be associated with the breakdown of brain signal dynamics into regular or random patterns. These two types of complexity change were associated differently with psychopathology. The study using multiscale entropy analysis on the blood-oxygen-level-dependent (BOLD) signal from resting-state fMRI images of schizophrenia, Yang et al. (2015) have shown the evidence that the regular type of BOLD complexity change was associated with positive symptoms of schizophrenia, whereas the randomness type of BOLD complexity was associated with negative symptoms of the illness. the pathologic change of resting-state dynamics in schizophrenia contributes to the differences of symptoms in clinics.

The purpose of this research is to investigate a well-validated nonlinear phenomenon – power law distribution – in brain activity in schizophrenic brain. Power law is a ubiquitous principle in physics that describe the complex nature of a given system at multiple time scales, thus is implicated in modelling neuronal activity that is known to have complex behaviors. We hypothesized that the spontaneous brain activity in schizophrenia may exhibit loss of power-law characteristics compared to those observed in healthy volunteers. Based on structural MRI images, grey matter and white matter volume would be quantified to screen the possible relationships between structural properties and power law scaling for schizophrenic and healthy participants. The brain regional structural features may be associated with the abnormal functional complexity in schizophrenia.

2 POWER LAW SCALING OF THE BRAIN ACTIVITY

Power law is a distribution that indicates the relationship between two variables, where one varies as a power of the other (Figure 1). The scaling represents the frequency domain of nonlinear characteristic in a dynamic system. It is a universal phenomenon that can be observed in both social and natural contexts. For example, it is also known as 1/f signal (pink noise) in signal processing, Pareto Principle (80:20 rule) in economics (Pareto, 1897) and Zipf's Law in linguistics (Newman, 2005). In topology, signals from the system that exhibits power law behavior would organize a scale-free or small-world network (L. A. Amaral, Scala, Barthelemy, & Stanley, 2000; Bassett & Bullmore, 2017).

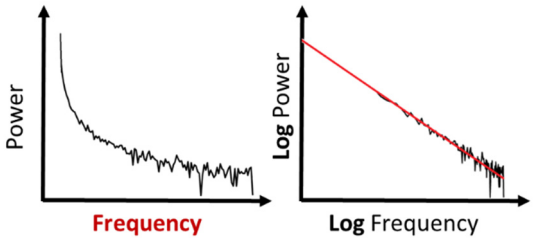

Figure 1: The typical power law distribution.

Power-law distribution as a ubiquitous principle in physics that describes the complex nature of a given system across time scales. Using power law to extract the fundamental features from spatial-temporal neuroimaging data may holds great potential to evaluate the dynamic human nervous system.

2.1 Functional Complexity in Nervous System

Power-law scaling has been observed in Nervous systems across species. In 2000, an investigation on structural neural networks of all 302 neurons on Caenorhabditis elegans (C. elegans) worm identified a power-law distribution of aging speeds in a whole nervous system (S. L. Amaral, Zorn, & Michelini, 2000). The neural networks have elucidated the nonlinear dynamical complexity in neuronal signal over a range of scales. Bystritsky, Nierenberg, Feusner, and Rabinovich (2012) presented the result in logarithm with the number of links at x-axis and cumulative distribution at y-axis. The slope (the power law distribution) in of fast aging neurons is the furthest to negative one in compare with the younger neurons, which shows the slope approximate to negative one.

Despite of the nature of C. elegans is relatively small to human nervous system, power law remains relevant to Homo sapiens. In human brain, the power-law phenomenon was also observed across different levels of the human brain, such as neuronal firing rate (Buzsaki & Mizuseki, 2014), efficacy of synaptic transmission (Mizuseki & Buzsaki, 2014), channel density (Bullmore & Sporns, 2012), or neural circuit-level networks (Marković & Gros, 2014). Eguiluz,

Chialvo, Cecchi, Baliki, and Apkarian (2005) studied the brain connectivity of fMRI data across different mental tasks. The result of average scaling taken from 22 networks in log-log plot shows a negative slope. Piekniewski (2007) adopted a similar methodology, studying the dynamic of neuronal spikes by different neuronal size groups. The result also shows similar distribution: the pattern resembles a negative slope in log-log figure with a base of 10.

The findings of power law behavior across various physiological log scale parameters provides an evidence on the existence of core phenomenon of Homo sapiens sharing properties. Transforming the information into logarithm scaling allows multi-level data to be operated by compressing large input range into a smaller manageable output.

Power law's negative slope of brain-network activity can be explained by two possible mechanisms. First is the underlying population spiking statistics (Voytek & Knight, 2015). Brain signals in logarithm with two ends of continuous distribution extending several orders of magnitude indicates that a large number of neurons spike simultaneously with a small groups of aberrant neurons spiking at different time points. In this way, the aggregate local field potential (LFP) would make the slope negative. In contrast, the units within the population spike relatively asynchronously would lead to a flatter slope (Podvalny et al., 2015; Voytek & Knight, 2015). The second underlying mechanism is the decoupling of population spiking activity from the ongoing low-frequency oscillatory neural field, which results in neural noise increasing (Tort, Komorowski, Manns, Kopell, & Eichenbaum, 2009; Voytek & Knight, 2015). Features of cortical circuits, such as redundancy and degeneracy, recurrent excitatory loops coupled with feedback and feedforward inhibition, create substrates for wide-dynamic range, log-linear computation.

Quantifying the power law scaling of neuronal signals allows the researchers to explain and evaluate the nonlinear dynamic system in the frequency domain, for which its change in complexity can be quantified rigorously via spectral analysis of resting-state fMRI signal in this research.

2.2 Bold fMRI Signal

Base on the physiological mechanism, neurovascular coupling, the fMRI technique is established base on the mechanism that the activated neuron consumes more oxygen to satisfied the energy need. The haemoglobin which carries the oxygen is paramagnetic due to the presence of oxygen ion. MR signal creating the BOLD contrast effect based on such paramagnetic state, with the contrast of oxyhemoglobin and de-oxyhemoglobin to generate the MR signal. The resting-state fMRI image is conducted base on the BOLD response in the absence of specific task. This research use complexity analysis with the resting-state BOLD signal acquired by MRI.

2.3 Quantifying Power Law Scaling

To extract the power law scaling of BOLD signals in each voxel, we first applied the Fourier Transform to the resting-state fMRI signal for each voxel to convert the time domain data into the frequency domain of the power spectrum (bin = 0.002 Hz), in order to quantify power-law scaling of the resting-state fMRI signal. Second, the data was visualized in a logarithm plot with the base equal to 10 on both axes to quantify the power spectrum across scales. Third, linear regression was deployed to derive a slope estimate, which was the scaling property of the given resting-state fMRI signal.

Figure 2 shows an example of a 30 years old healthy male's resting-state fMRI image. The 4D BOLD time series data of a voxel at (24, 14, 36 of MNI coordinate) left precuneus is acquired (A). A 3D power spectrum density was acquired after applying fast Fourier transform on the result of A (B). After transforming the signal distribution to logarithm, we use linear regression to acquire the slope of power spectrum density distribution, which is power law scaling.

The slope of the frequency scaling approaching minus one would provide evidence for the power law behavior of the given resting-state fMRI signal. Therefore, such scaling analysis will be helpful for quantifying the complex dynamics of spontaneous brain activity in order to determine the state of brain activity at the complex state of 1/f power law scaling behavior (Figure 3; left panel), reduced complexity as the slope of scaling becomes less steep (middle panel), and the brain signal to be an uncorrelated noise as the slope of scaling becomes flat (right panel).

In this research, the power law scaling is calculated voxel-wise for both schizophrenic patients and healthy participants.

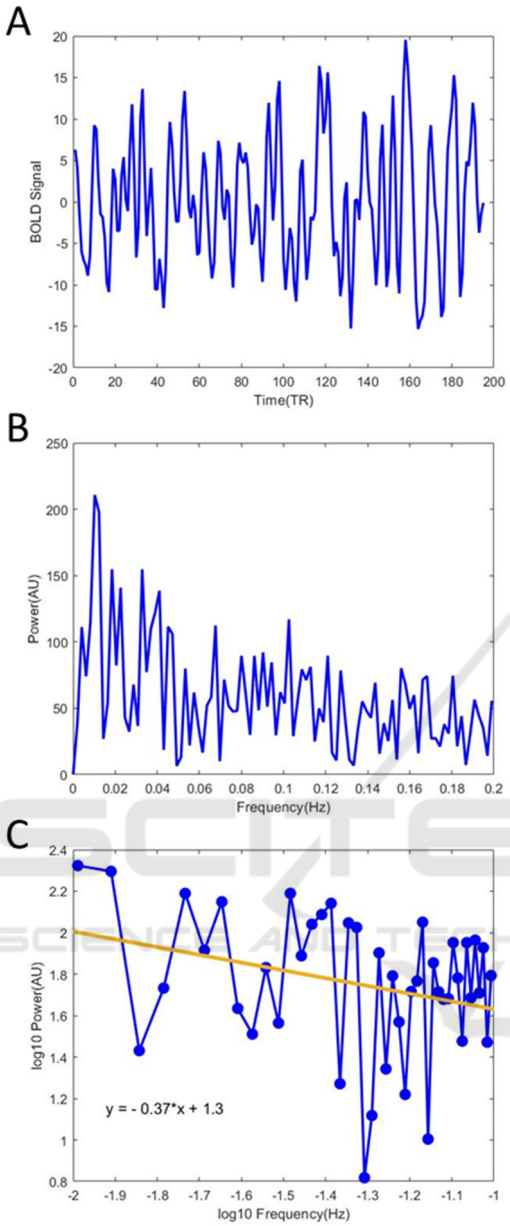

Figure 2: Quantifying power law scaling of brain BOLD signal in a voxel from real data.

3 METHODS

3.1 Study Cohort

Functional brain imaging data of 200 age and sex matched schizophrenic patients (age mean = 43.56 ± 12.64; male = 49.5%) and 200 healthy subjects (age mean = 43.56±13.41; male = 49.5%), who were right-handed Han Chinese, were retrieved from Taiwan

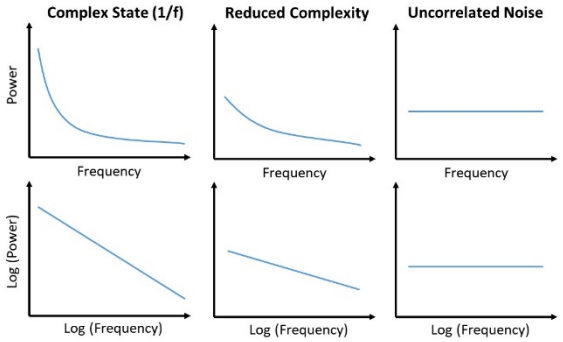

Figure 3: Power law scaling in different states.

Aging and Mental Illness (TAMI) cohort. Diagnosis of schizophrenia was screened and confirmed by two psychiatrists based on criteria given in the Diagnostic and Statistical Manual of Mental Disorders (DSM–IV-TR). The schizophrenia patients have the average onset of 28 years old and average duration of onset being 15 years, and their score of Mini-Mental State Examination (MMSE) and the Positive and Negative Syndrome Scale (PANSS) is acquired.

Written informed consent was obtained from all participants before the scanning sessions following the protocol for TAMI cohort approved by the review board at Taipei Veterans General Hospital, Taipei, Taiwan. All personal information and imaging data are de-identified for the subsequent analyses. It is worth mentioning that the TAMI cohort has recruited more than 1000 subjects so far, including a large sample of patients with healthy aging and patients covering major mental illness. All imaging data were acquired by the same 3.0T MRI Siemens Tim Trio machine with constant protocol at National Yang-Ming University.

3.2 Brain Images

3.2.1 Structure MRI and Resting-state fMRI Acquisition

The fMRI scanning was performed at National Yang Ming University on a 3.0 T MRI scanner (Siemens Magnetom Tim Trio, Erlangen, Germany). Resting-state scanning was scheduled in the morning, conducted in the darkened scanner room, and lasted approximately 10 minutes. The instruction requires the subject to relax with eyed open. The reminder was asked routinely by the technician during the scans to avoid the subject from falling asleep, otherwise, rescanning is acquired.

The MRI scanner is equipped with a 12-channel head coil. Whole-brain resting-state BOLD functional MRI images were collected using a T2*-

weighted gradient-echo-planar imaging (EPI) sequence with following imaging parameters: repetition time TR= 2500 ms, echo time = 27 ms, field of view =220×220 mm^2, voxel size= 3.4×3.4×3.4 mm3, flip angle =77°, matrix size =64×64. A total of 200 EPI images were acquired along the AC–PC plane for each run. High-resolution structural MRI images were acquired with 3-D magnetization-prepared rapid gradient echo sequence (TE= 3.5 ms, TI = 1100 ms, field of view= 256 ×256 mm^2, voxel size = 1.0 × 1.0 × 1.0 mm^3, flip angle= 7°, matrix size = 256×256). All structural MRI scans were visually reviewed by an experienced neuroradiologist to confirm that participants were free from any morphologic abnormality.

3.2.2 Resting-state fMRI Data Preprocessing

The functional and anatomical image preprocessing was performed by DPARSF and SPM12 under MATLAB9.2. The first 5 of 200 data points are routinely discarded to eliminate the time difference between actual neural activation and cerebral blood flow response. Functional images were realigned and coregistered to the subjects own anatomical images. Slice timing is adopted to correct the scanning time between slices. Segmentation is operated and all functional images are normalized to standard Montreal Neurological Institute (MNI) space. Nuisance effect is removed by constant and linear de-trend in whole brain. BOLD signal of white matter and CSF are taken as covariate regressors. Derivative 12 is adopted as head motion regression model. In addition to six rigid body head motion parameters, the first six eigenvectors of white matter signal and the first six eigenvectors from CSF were regressed out by linear regression for each voxel. The band pass filtering is set 0.01 to 0.1 Hz. Moreover, fast Fourier Transform (fFT) is operated to extract power law spectrum from each voxel of functional resting images with customized pwelch code in MATLAB. Finally, Gaussian smoothing with 8 mm full width at half maximum (FWHM) is applied to all functional data by SPM 12. The structural properties were quantified by T1 image. the Automated Anatomical Labeling (AAL) and International Consortium for Brain Mapping (ICBM) were used for the measurement of regional GMV and white matter volume.

3.3 Software

The resting-state fMRI images preprocessing was operated by DPARSF_V4.3_170105 (Data Processing Assistant for Resting-State fMRI; Yan) (Yan, Wang, Zuo, & Zang, 2016) and SPM12 (Statistical Parametric Mapping, Department of Imaging Neuroscience, London, UK) under MATLAB 2017a (Version 9.2). Statistical analysis was conducted by SPM12 and MATLAB. Brain image results are reviewed presented by BrainNet Viewer (Version 1.53, Beijing Normal University, China) and MRIcron (Georgia Tech Center for Advanced Brain Imaging, the Georgia state, USA).

3.4 Statistical Analysis

T-test is applied to compare the relationship of brain structural parameters and signal complexity between interested groups. The significance of voxel-wise comparison p value is set <0.05 correction for multiple comparison by family-wise error (FEW) method. Pearson correlation is operated to access the relationship between power law scaling and grey and white matter volume. The structural network will be conducted by Pearson correlation with Bonferroni correction. In schizophrenia group, the correlation between abnormal power law scaling in identified key brain regions and the score of the PANSS was analysed. To control possible confounding, age and sex of all participants are covariates.

3.5 Experimental Design

In this research, we focus on validating power law phenomenon in dynamic human brain activity. The purpose of the first study is to fundamentally understand how power law spectrum of the resting-state BOLD signal varies in different brain morphological tissues in schizophrenic and healthy participants. The association between abnormal power law scaling and the clinical severity measured by PANSS in schizophrenic patients is examined. The second study aims to understand how grey matter change (such as local or global volume decreased) would effect on power law of dynamic BOLD signal. In study 2, we firstly access the brain regions where both power law scaling and grey matter volume (GMV) show significance between groups. Following we use Pearson correlation with Bonferroni multiple-comparison correction to investigate the correlation between power law scaling and GMV in the identified brain region. In addition, we select the brain regions which show high GMV correlation to the identified regions to conduct the structural network. The third study aims to screen the possible association between white matter volume and power law scaling. Such study design will allow

us to integrate structural and functional results to identify basic principles of multi-scale neuronal dynamic and inter-individual variability in mental illness patients and healthy groups, uttering a comprehensive meaning from a broader view.

4 RESULTS

4.1 Power Law Change of rs-fMRI in Different Anatomical Regions

The t-test was used to compare the power-law scaling between schizophrenic patients and healthy adults, with the extent threshold k = 35 voxels. Parametric images were assessed for cluster-wise significance using a cluster-defining threshold of FWE $p < 0.05$. The result visualization is shown in Figure 4, presenting the distribution of voxel-wise t-value across the brain. In Figure 4, red color indicates positive t value whereas blue color represents more negative t value. The swift of power-law scaling of resting-state fMRI signal indicates the state change in the brain system. The results reveal that schizophrenic patients, with the average onset of 28 years old and average duration of illness being 15 years, have significantly four more positive power-law scaling and two more negative power-law scaling than healthy adults at anatomical clusters.

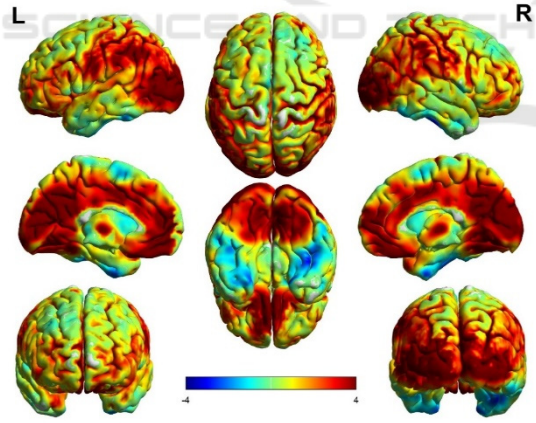

Figure 4: The t-map visualization of different power law scaling observed in schizophrenic and healthy participants.

The four more positive clusters included left precuneus (k = 17,555; peak coordinate (mm) = -18, -66, 18; t = 7.72), with sub-cluster at left middle occipital gyrus (peak coordinate (mm) = -21, -93,18 ; t = 6.97), left medial dorsal nucleus (k = 183; peak coordinate (mm) = -6,-15, 3; t =5.99), right inferior frontal gyrus (k = 160; peak coordinate (mm) = 42, 21, 30; t = 4.26), and right middle temporal gyrus (k = 48; peak coordinate (mm) = 51, -39, -3; t = 3.93). All these four clusters have p (FWE-cor) < 0.001 at voxel level. The equivalent k = 37 of left Insula reached threshold of k = 35, however, at cluster level, the uncorrected p remained marginally significant. On the other hand, healthy adults demonstrated significantly higher power-law scaling than schizophrenic patients in two regions: right putamen (k = 60; peak coordinate (mm) = 18, 6, -3; t = -3.11) and left putamen (k = 44; peak coordinate (mm) = -18, 9, 3; t = -3.11).

Two anatomical clusters presenting more negative power-law scaling in schizophrenic patients are right putamen (k = 60; peak coordinate (mm) = 18, 6, -3; t = -3.11) and left putamen (k = 44; peak coordinate (mm) = -18, 9, 3; t = -3.11). These two clusters have p (FRD-cor) < 0.001 at the voxel level.

4.1.1 Correlation of Power Law Scaling and Clinical Severity in Schizophrenia

The Pearson correlation between the abnormal power-law scaling and score of PANSS is calculated. Interestingly, significant correlations with p-value < 0.05 were found in the key regions where the slope of power-law scaling was more positive in schizophrenic patients. The positive correlation was found between the power-law scaling slope in left precuneus and score of item G5 (mannerisms & posturing, r = 0.15, p = 0.04) and left thalamus and score of item N3 (passive/apathetic social withdrawal, r = 0.17, p = 0.02). Negative correlations were found between right middle frontal gyrus and score of item P4 (r = -0.15, p = 0.03) and right middle temporal gyrus and score of item P4 (excitement, r = -0.15, p = 0.03).

Pearson's correlation is used to evaluate the relationship between the dosage of antipsychotic drugs and power-law scaling of resting-state fMRI signals in the identified brain regions. The antipsychotic dosage was transformed into chlorpromazine (CPZ) equivalence dosage based on empirical studies (Danivas & Venkatasubramanian, 2013; Gardner, Murphy, O'Donnell, Centorrino, & Baldessarini, 2010). There was no significant correlation between CPZ dosage and the power-law scaling in six brain regions.

4.2 Grey Matter Structural Correlates of Power Law Scaling

Healthy adult and schizophrenic patients have significant difference in total grey volume (t = 4.76;

$p = 0.00$) and MMSE score ($t = 3.53$; $p = 0.00$). The total grey volume is 634.96 cm^3 (*S.D.* = 79.60) in healthy adult and 616.75 cm^3 (*S.D.* = 69.66) in schizophrenic patients. The mean MMSE score is 28.00 (*S.D.* = 4.72) and 26.43 (*S.D.* = 4.17) in healthy and schizophrenia participants, respectively.

4.2.1 Candidate Brain Regions Identification

Across all AAL regions, we identified the candidate brain regions where both groups showing significance in GMV and power law scaling. The results of t- test showed that schizophrenia patients and healthy participants have significant difference of power law scaling in 66 AAL regions and difference in GMV in 81 AAL regions with significant level less than .05. Sixty-one candidate brain regions were identified where both group showing significant difference in GMV and power law scaling based on AAL atlas.

The relationship between GMV and power law scaling in the candidate brain regions was examined with Pearson correlation. With Bonferroni correction for multiple comparison ($p < 0.00056$), schizophrenic brain showed significant correlation between GMV and power law scaling in 32 AAL regions. On the other hand, healthy participants had significant correlation of GMV and power law scaling in two AAL regions, right superior frontal gyrus (dorsolateral part) and left inferior occipital gyrus. Moreover, the found significant correlation coefficient were negative for schizophrenia and positive for healthy brain. As a result, right superior frontal gyrus (AAL4) was the key region where power law scaling and GMV show significant correlation in both groups, where the correlation coefficient is -0.22 (p=0.000019) in schizophrenic brain and 0.17 (p =0.000213) for healthy brain.

4.2.2 The Possible Structural Network Contributing to Abnormal Complexity

With the dorsolateral part of right superior frontal gyrus (AAL4) as the hub, we then explored the possible structural network that may support the functional complexity change. The grey matter structural network is defined by the Pearson correlation of GMV in AAL brain regions. In table 3, the result shows the top 10 most correlated brain regions to AAL4 for healthy and schizophrenic brain. As the result, top 1 to top 5 identified satellite regions were the same for both groups with the same order. The GMV AAL4 is highly positively correlated to the GMV of AAL 3 (left dorsolateral part of superior frontal gyrus), AAL 6 (right orbital part of superior frontal gyrus), AAL 5 (left orbital part of super frontal gyrus) and AAL 20 (right supplementary motor area). The top five ranking correlated regions are organized a cluster at superior frontal gyrus in healthy and schizophrenic patients. The top 6 to 10 correlation ranking to AAL 4 regions are shared for both groups: AAL 10 (right orbital part of middle frontal gyrus), AAL 9 (left orbital part of middle frontal gyrus), AAL 1 (left precentral gyrus), AAL 16 (right orbital part of inferior frontal gyrus) and AAL 19 (left supplementary motor area), organizing another cluster linking to the hub.

The most different structural connections to AAL4 between schizophrenic and healthy brain is calculated. The connection difference was quantified by subtraction of each Pearson correlation coefficient between groups. The result shows in Figure 5. Schizophrenia and healthy brain shown most correlation difference (Difference > 0.1) to right superior-frontal gyrus at bilateral superior temporal gyrus, bilateral lenticular nucleus (pallidum) and bilateral thalamus.

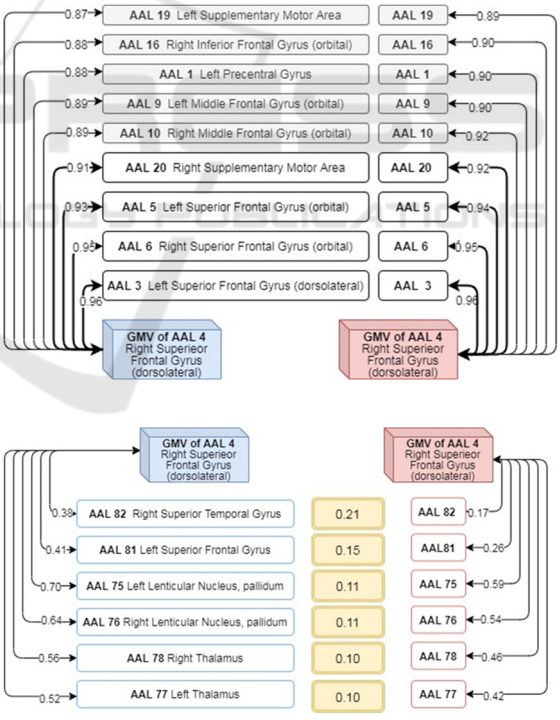

Figure 5: The Structure Network of Right Superior Frontal Gyrus (Blue for Healthy; Red for Schizophrenia).

4.3 White Matter Structural Correlates of Power Law Scaling

Thirteen ICBM regions showing significant different white matter volume between schizophrenic and healthy brain were identified. Pearson correlation with multiple comparison correction was used. The results showed no significant correlation for healthy participants. For the schizophrenic patients, ICBM 13 (right superior cerebellar peduncle) and ICBM 15 (splenium of corpus callosum) showed the most negative correlation (r = -0.15 to -0.32; $p < 0.038$) at the brain regions where power law scaling shows significant difference between groups and that may correlate to GMV in schizophrenia.

5 DISCUSSION

The key findings in this study include (1) the difference in power law scaling behavior in different anatomical regions indicates that patients with schizophrenia are associated with the abnormal complexity of spontaneous brain activity in grey matter; (2) the identified brain regions with abnormal complexity found in schizophrenic patients are correlated to psychotic symptoms such as mannerism and posturing, excitement, and passive or apathetic social withdrawal; (3) The abnormal functional complexity in schizophrenia may be stemmed from the structural network of GMV, with the hub at the dorsal lateral part of right superior frontal gyrus.

The study findings indicate that spectral density of resting-state fMRI signals in healthy volunteers exhibit a higher power in lower frequency bands and lower power in higher frequency bands, compared to schizophrenic patients, and such scaling behavior is more close to 1/f characteristics in healthy volunteers than that observed in patients with schizophrenia. These findings suggest that schizophrenic patients may have a loss of 1/f power law scaling which indicates a possible loss of scale-free brain signal dynamics. Our findings may link to the underlying pathophysiology of schizophrenia. For example, the more negative power law scaling in putamen may indicate over-activity of dopaminergic neurons, which is associated with cognitive dysfunction in schizophrenia.

From the perspective of complexity science, signals observed in a dysfunctional system may show random or regular behaviors. Change in power law scaling toward a flat slope indicates a loss of multi-scale complexity, which is possibly associated with a lack of thinking or behavioral flexibility commonly observed in psychotic patients. Additionally, flattened power law scaling observed in schizophrenic patients may also indicate an increased noise of information flow in the neuronal systems, which may be associated with abnormal structural or functional connectivity.

The findings provide the evidences supporting the disconnection hypothesis raised by Friston and Frith (1995). By analysis the data from schizophrenic patients, the functional complexity is effected by brain structures. The altered functional complexity, quantified by power law, representing the discontinuity in time-series. Such dysconnectivity is significantly correlated to grey matter and white matter structure.

There are two limitations of this study. The use of linear model on power spectrum may overlook certain dynamics. Due to relatively short resting-state fMRI time series, the frequency resolution of power spectrum may be limited by the use of Fourier transform. In the future, longer scanning time or higher sampling rate at data acquiring may be considered to increase the spatial resolution. The results from white matter volume may be validated by the use of Diffusion Tensor Images.

6 CONCLUSIONS

The application of complexity science in neuroscience has overcome common concerns of typical statistic methods, and has presented insights complementary to traditional biological knowledge. The power law phenomenon is emerged based on the integration of various biological mechanisms across temporal and spatial levels, supporting the nonlinear behavior of neuronal activity in human central nervous system. Based on frequency domain, power law scaling plays a role to differentiate schizophrenia and healthy brain by analyzing resting-state brain imaging signal. The results of this study support “the loss of brain complexity hypothesis,” (Yang & Tsai, 2013) and the “dysconnectivity hypothesis of schizophrenia” (Friston & Frith, 1995), suggest the reduced complex brain activity as one of neurobiological mechanisms in schizophrenia. Such abnormal functional brain complexity proposing the power law scaling as a ubiquitous principle of governing brain signal dynamics, which serves a great potential clinical impact in psychiatry.

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