氏名	Steven M.A. Carpels
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論文題目	Analysis of the Functional Connectivity Patterns in the Brain of Mental Disorder Patients and Epilepsy Patients using Wavelet-crosscorrelation Analysis and Graph Theory
論文審査委員	（主査）教授　水野（松本）　由子 （副査）教授　竹村　匡正 （副査）教授　原口　亮

学位論文の要旨

A lot of recent studies have shown that analyzing functional connectivity in the brain may be useful to study and understand brain function, as well as help in the diagnosis of epilepsy and mental diseases. In this thesis, engineering theory and engineering methodology were applied to the field of clinical neurophysiology. The main purpose of this thesis is to examine the functional connectivity and changes in connectivity patterns in the brain derived from EEG data, and to use wavelet-crosscorrelation analysis and graph theory analysis in order to make the pathology clear in the diseased brain. Connectivity patterns, information transfer in the brain, and changes in brain activity were examined in the alpha band in healthy individuals, mental disorder patients and epilepsy patients. After constructing functional networks, the spatial distribution of the constructed functional networks was analyzed based on graph theory to further characterize the connectivity in the healthy brain and in the diseased brain.

As described in chapter II, the first goal of this dissertation was to investigate and compare the functional connectivity in the brain between healthy individuals and individuals suffering from mental diseases in the alpha band. In some individuals, alpha waves appear in broad regions of the brain, and this is considered abnormal electroencephalography (EEG). This phenomenon is known as diffuse alpha pattern. The EEGs of 10 healthy individuals and 10 neuropsychiatric disorder patients with the diffuse alpha pattern were analyzed using wavelet–crosscorrelation analysis. Five epochs of 2 seconds were analyzed for each subject. Wavelet–crosscorrelation coefficients (WCC) were calculated for frequencies in the alpha band for all epochs in each subject. This study wanted to examine how the functional connectivity in the alpha band between the parts of the brain is different between healthy individuals and mental disorder patients with the diffuse alpha pattern. Wavelet-crosscorrelation analysis was used to visualize the connectivity pattern and the connectivity strength between the brain of healthy individuals and mental disorder individuals. It was hypothesized that

the connectivity strength between the parts in the brain could be different between these two groups of subjects. The novelty of this study is abstracting the alpha band to visualize and make the connectivity pattern and connectivity strength clear in the healthy brain and the diseased brain. The results showed that the WCC values were higher in the patients with diffuse alpha, as well as a different connectivity pattern between the healthy individuals and the patients. The results suggest that the connectivity strength in the entire brain, as well as along the sagittal and coronal orientations may be stronger in the brain of the patients than in the healthy individuals in order to compensate for a less time-efficient information transfer.

The study in chapter III aims to compare the functional brain networks derived from electroencephalography (EEG) of 10 patients suffering from epilepsy with 10 healthy subjects based on graph theory to analyze the spatial distribution of the functional network in the brain. This study compared the interictal functional network of the brain of epilepsy patients during epileptiform discharge with during non-discharge. Five epochs per healthy subject, and ten epochs (during epileptiform discharge and non-discharge) per patient were selected and analyzed using wavelet–crosscorrelation analysis. The clustering coefficient, characteristic path length, small-worldness, and nodal betweenness centrality were calculated using graph analysis. The results showed that in the patients, Wavelet-crosscorrelation Coefficients (WCC) were significantly higher, and clustering and path length were significantly lower during discharge compared with the healthy subjects, along with alterations in the hub regions. The functional connectivity strength and the functional network configuration in the brain of the epilepsy patients were altered compared to the healthy subjects. Even though in the patients, the functional connectivity and small-worldness of the brain did not show significant differences between discharge and non-discharge, the centrality and the spatial distribution of the hub regions were different between during epileptiform discharge and during non-discharge. The results showed a loss of small-world topology in the functional brain network of epilepsy patients. A more random topology was found during discharge and non-discharge, therefore network indices may aid to distinguish epilepsy patients from healthy individuals, and diagnose epilepsy with a higher sensitivity. The nodal betweenness centrality index may aid to distinguish EEGs at the time of epileptiform discharges from EEGs at the time of non-discharges. The novel finding of this study is that a very short characteristic path length was found which causes the brain in epilepsy patients to synchronize too much, resulting in epileptic seizures to occur easier (seizure-prone state).

The results of both studies show that the functional connectivity differs between healthy individuals and neuropsychiatric and epilepsy patients. Performing graph theory analysis in addition to wavelet-crosscorrelation analysis provides further characterization of the functional network and information transfer in the brain. Combining WCC or other connectivity measures with network measures could make the pathology in the brain clear by revealing failing network characteristics of individuals suffering from brain disorders. This could lead to a deeper understanding of how the information transfer between brain areas fails, and may reveal the causes of brain dysfunction. The study in chapter III revealed a facilitation of synchronization in the epileptic brain due to more random topology, potentially explaining the cause of seizures. The value of this dissertation is that these results could aid in the future diagnosis and treatment of neuropsychiatric diseases and epilepsy, as well as predict a potential brain disorder or a potential patient.

論文審査の結果の要旨

本論文は、ヒトの健常脳、及び疾患脳における脳波を用いた脳内の機能的結合とネットワークに関して、時系列解析を用いて明らかにすることを目的として行った研究について、記したものである。博士論文は次の章より構成されている。

Chapter I は、Introduction について記述している。

Chapter II は、健常脳と疾患脳で、脳波の α 帯域の出現部位や機能的結合が異なることを示した研究について記述している。10 人の健常者と、10 人の神経精神疾患で、脳波において diffuse alpha pattern が見られた場合について、比較した。方法論として、時間周波数解析手法である Wavelet–crosscorrelation coefficients (WCC)を用いた。その結果、疾患脳においては、健常脳と比較して、脳皮質の広範囲で、WCC 値が有意に高値を示した。

Chapter III は、健常者とてんかん患者において、脳波のグラフ理論を用いて、脳機能ネットワークの空間的分布が異なることを示した研究について記述している。10 人の健常者と 10 人のてんかん患者で、WCC から求めたクラスタリング係数、特徴的経路長、スモールワールドを比較した。その結果、てんかんの異常波出現中には、健常者と比較して、WCC 値は有意に高値を示し、クラスタリング係数及び特徴的経路長は、有意に低値を示した。

Chapter IV は、これまでの研究で得られた主要な知見に基づき、本論文の総括をまとめた。

本博士論文より得られた一連の研究から得られた知見は、脳の疾患により、脳内の機能的結合性や情報伝播が変化することを定量的に示したことである。加齢や神経変性による脳の疾患を、脳波の時系列解析により、早期に発見することが可能であることを示すことができたことは、本論文の成果である。

以上を総合した結果、本審査委員会では、本論文が「博士（応用情報科学）」の学位授与に値する論文であると全員一致により判定した。