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Neuronal Impairment and Instability

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Abstract

The scalp potentials originate in neuronal activity in the brain cortex, and neuronal abnormality causes scalp potential abnormality. As a measure of scalp potential abnormality, the normalized power variance, NPV, of EEG signals is introduced, where its mean m and standard deviation σ are defined for each of 21 EEG channel over a group of normal controls. When an NPV value of a subject to be tested is larger or smaller than m ± σ, neurons contributing to generation of the scalp potentials are regarded as abnormal, namely hyperactive or hypoactive. Similarities are observed between the abnormality map and the corresponding regional cerebral blood flow reduction map measured by SPECT.

1. Introduction

Increase of demented population is a serious social concern, but we have no effective method of blocking this trend. Only way we can do is in the early detection of cortical neuronal impairment and application of proper brain rehabilitations especially designed for blocking progression of Alzheimer's disease (AD). AD is a slow process and it takes 30 years or so until the syndrome appears after onset of neuronal impairment of neurons in cortices including hippocampus and others in the vicinity of it. Neuronal impairment, for instance, in the hippocampal cortex results in its atrophy, which can be detectable by MRI volumetry measurement or by regional cerebral blood flow (rCBF) reduction measured by SPECT examinations. To block or delay the onset of AD, an early detection of neuronal impairment should be effectively done by regular (annual) examinations on senior normal people. SPECT and MRI examinations are not appropriate for screening the mild cognitive impairment (MCI) because the instruments are too expensive and SPECT injects radioactive materials into blood.

Therefore, it is desired to develop a diagnostic tool, which can be used for the screening of MCI. Such a tool should satisfy the following requirements: to be *inexpensive*, *without radioactive materials*, *with high sensitivity* and *high reliability*, and *easy to operate*. Musha et al. have developed a *diagnosis method of neuronal dysfunction* (*DIMENSION*), which sensitively detects impairment of cortical neurons through distortion of the scalp potential distributions of the spontaneous EEG alpha component caused [1]. The scalp potentials generated by electric generators distributed uniformly on the cortical surface are well approximated by scalp potentials generated by a single equivalent electric current dipole [2,3], and the goodness-of-fit is called *dipolarity* which is close to unity in. Partial impairments of cortical neurons distort the potential distribution, and dipolarity is lowered. This phenomenon is observed with the EEG alpha component with 3 Hz bandwidth. Such a dipolarity value is sensitive to neuronal impairments.

With the alpha component the dipolarity value varies with twice the period of the alpha rhythm because of variation in the signal-to-ratio. Therefore, about 20 dipolarity peaks are observed per second. We just pick up peak values, and the mean and the standard deviation are named D_α and D_σ. With progress of AD, D_α decreases and D_σ increases. These two variables are markers for neuronal impairment caused by AD. This is a principle of DIMENSION.

estimates the mean values of dipolarity peaks, D_α, of the spontaneous EEG alpha component with bandwidth 3 Hz over 5 minutes in a rest state with closed eyes together with its standard deviation D_σ. In a normal subject, D_α is close to unity and D_σ is close to zero. This result suggests that cortical neuronal activities over cortical surface layers are uniform and stable. In an AD patient, on the other hand, cortical neuronal activities are impaired in mosaic way and the D_α value decreases and the D_α value increases.

Theses two variables are found to be good markers for impairment of cortical neuronal impairment, and we have obtained *Brain Function Diagram* as shown in Fig.1. Most of the normal subjects are in the normal region with 10% of false negatives, while most of moderately severe AD patients are in the impaired region with 10% of false positives; when the state to be tested is in the intermediate sub-normal region, repeated test will clarify whether or not the subject test is normal or not depending which direction the state shifts.

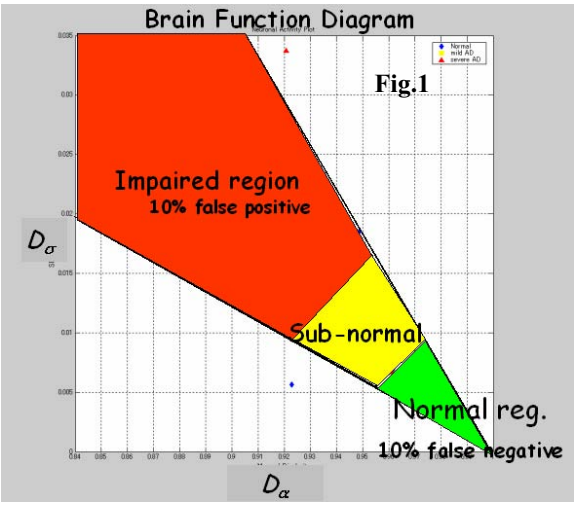


Fig.1

DIMENSION specifies a degree of global neuronal impairment but does not show if the subject is in AD or other neuronal disorders. We have developed a new diagnosis tool that allows differentiation of neuronal disorders. This is a topic of the present presentation.

2. Neuronal Impairment and EEG Power variance

Information transfer between neurons is carried by action potential impulses, which is accompanied by scalp potential fluctuations. Power of EEG is defined as its mean squared values. The scalp potential is always defined in reference to a potential on a reference electrode; currently we take it on the right eye lobe. The mean power level of the scalp potential depends on individuals but it has no positive meaning in the present study. What matters is power variance that is normalized to the mean squared power, and it is named normalized power variance *NPV*.

We have a database for 25 very mild AD (age: 71.9 ± 10.2; MMSE: 26 ± 1.6), 33 moderately severe AD (age: 72.9 ± 7.5; MMSE: 15.3 ± 6.4), and age-matched normal controls (age: 71.7 ± 8.3; MMSE: 28.5 ± 1.6). EEG recordings were made on 21 electrodes arranged on the scalp according to the International 10-20 standard. NPV values on channel j were calculated over a group of normal controlsfor 5 min and the mean and standard deviation were denoted as $\langle NPV\rangle_j$ and σ_j. If a measured $NPV_j > > \langle NPV\rangle_j + \sigma_j$, neuronal activities related to this channel are judged to be more unstable than normal controls or *hyperactive*, while if $NPV_j > < \langle NPV\rangle_j - \sigma_j$, it is more inactive than normal controls or *hypoactive*.

3. Z-score map of neuronal abnormality

There are two different kinds of abnormality in neuronal activity. These abnormalities are mapped on the brain surface or the scalp surface in terms of remoteness of NPV_j from the corresponding normal controls where the remoteness is expressed in terms of σ_j, which is called a z-score. The z-score map averaged over the group of moderately severe AD patents is shown in Fig.2a where red and blue areas refer to hyperactivity and hypoactivity, respectively. Fig.2b shows a regional cerebral blood flow reduction map measured by SPECT (Single Photon Emission CT) averaged over the groups of very mild AD and moderately severe AD patients of our database. We can find similarities between them. It turns out that cerebral blood flow reduction areas include both of the hyperactive and hypoactive areas. This is a main difference between SPECT and our Neuronal Abnormality map.

4. Dynamic neuronal abnormality map

It seems from the SPECT rCBF reduction map that an rCBF reduction map is stationary and hence we have an impression that neuronal impairment is limited in these areas. As our mapping method has a higher time resolution, a dynamic behavior of neuronal impairment is observable. Fig.3 shows snap shots of neuronal abnormality maps at every 10 seconds. They look quite different one another. The time average of these snap shots shows a resemblance to the corresponding rCBF reduction map of SPECT.

5. Conclusions

MRI shows geometrical shapes, CT structure, SPECT blood flow reduction, and PET metabolism, and hence they do not display no direct information on neuronal activity in the brain. In this respect DIMENSION and L-DIMENSION give us direct information on neuronal activity.

Fig.2a

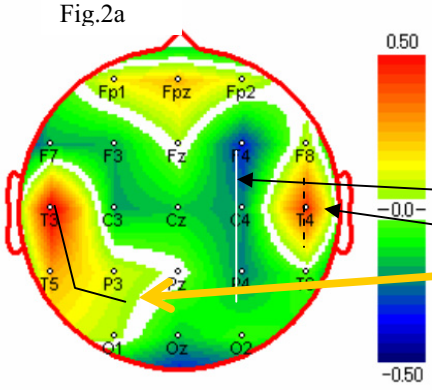


Fig.2b

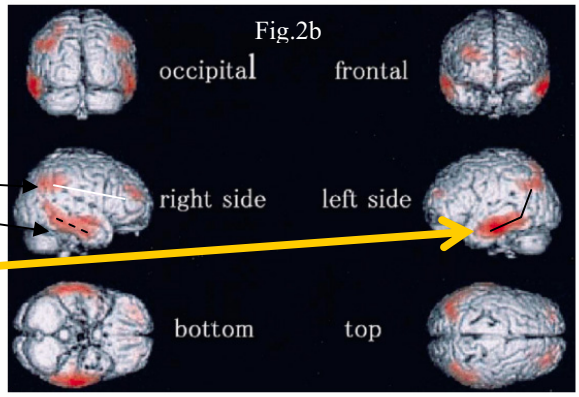
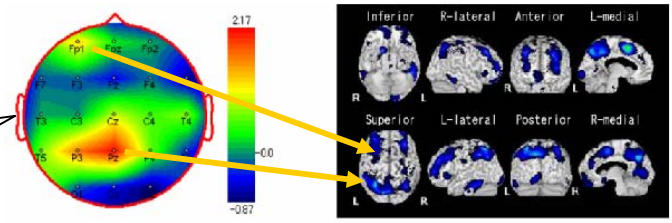
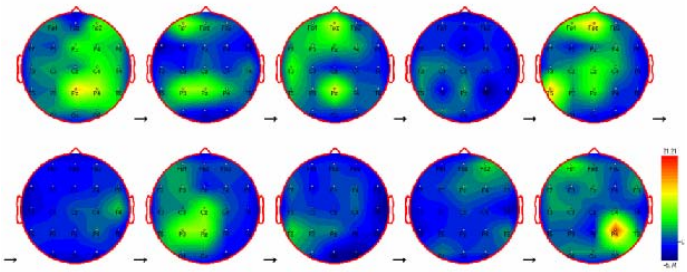


Fig.3

The averaged z-score map of an AD patient resembling regional cerebral blood flow reduction of SPECT.



Snap shots of neuronal abnormality at every 10 seconds. Neuronal impairment is not stationary. Neuronal activities in yellow and blue areas are more unstable or more inactive than in normal controls.



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