Correlation of EEG power ratio and severity of Alzheimer's disease

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Abstract

Objectives: *To test the hypothesis that the electroencephalography (EEG) power ratio are closely related with the staging of Alzheimer's disease (AD).*
Methods: *Segments of resting, artifact-free, 16-electrode scalp EEG signals were obtained from 47 patients of different severity of probable Alzheimer's disease. Using fast Fourier transform (FFT), EEG spectral profile was obtained for each candidate and averaged spectrum was demonstrated. The ratio of slow waves (theta and delta bands) to fast waves (alpha and beta bands) power, defined as power ratio, was calculated. The severity of Alzheimer's disease was classified into 4 stages - very mild, mild, moderate and severe, according to Clinical Dementia Rating (CDR) and Global Deterioration Scale (GDS). Each candidate was classified into one of the four groups. The correlation of power ratio and groups was observed.*
Results: *Characteristic spectral profiles of each group were demonstrated. Group mean power ratios (± Standard deviation) were 0.68 ± 0.32 (N=19) in very mild group, 1.12 ± 0.57 (N=12) in mild group, 1.84 ± 0.85 (N=9) in moderate group and 3.32 ± 1.54 (N=7) in severe group. Very mild group can be differentiated from moderate group (P=0.019) or severe group (P=0.023) and mild group can be differentiated from severe group (P=0.049). When comparing very mild plus mild and moderate plus severe groups, the discrimination was evident (P<0.01). However, There's no statistically significant difference between any two adjacent groups.*
Conclusions: *EEG power ratios can reflect spectral profiles in AD patients and is a useful EEG parameter to represent the severity of the disease. Although the trend of increasing ratio in more advanced stage is evident, discriminating any two adjacent groups are still not applicable.*

1. I. Introduction

Dementia is a common disorder among the elderly population. Major subtypes include Alzheimer's disease (AD), vascular dementia (VaD), Frontotemporal dementia (FTD), dementia of Lewy body (DLB)... etc. Among these, AD warrants special attention because of the popularity of victims and the new advance of effective drug treatment. AD is a progressive neurodegenerative of cerebrum, characterized by progressive cognitive decline, memory impairment, disability in daily activities and behavioral abnormalities. The incidence increases with age. The percentage of persons doubles with approximately every five years of age. However, the onset of the disease is insidious and the initial presentation is usually subtle. With application of the new drugs, cholinesterase inhibitor, the natural course of reluctantly progressive mental deterioration can be modified.

Two criteria are commonly used to diagnose AD, one from DSM-IV and another from National Institute of Neurologic and Communicative Disorders and Stroke Alzheimer's Disease and Related Disorders Association (NINCDS–ADRDA). To fulfill the criteria, typical history and presentations must be met and other alternative diagnosis must be excluded. Brain computerized tomography (CT) or magnetic resonance image (MRI) are commonly applied to evaluate the extent of cortical atrophy and to exclude other brain pathology. Traditional clinical assessments of severity of AD rely on psychometric scales, such as Mini-Mental Status Examination (MMSE), ADAS-cog, CASI, CIBIC-plus...etc. Clinical Dementia Rating (CDR) and Global Deteriorating Score (GDS) can be used to stage the illness course.

Electroencephalography (EEG) records electric activities from cerebral cortex and can reflect pathologic conditions in cortical and subcortical regions of cerebrum. Unlike CT or MRI, it is a simple, cheap, widely available and non-invasive procedure which may be a potential tool to monitor this disorder. However, it is not routinely applied during clinical practice either to diagnose or to monitor the illness course of AD. Typical EEG findings in Alzheimer's disease are decrease in fast (alpha and beta) activities and increase in slow (theta and delta) activities. Although these features have long been identified and described in the literatures, they are regarded as lack of sensitivity and specificity for AD. Textbooks and most clinicians believe that the EEG features won't appear until the late stage of the disease[21]. Recent studies[1-5] reveal that EEG can be helpful in many aspects to evaluate AD.

EEG can differentiate AD from depression[6,14], VaD[7-9,15], normal aging[10-12,15] and frontotemporal dementia[13]. EEG can also reveal abnormality at the very early stage of AD[16-19], as known as mild cognitive impairment (MCI). In addition, EEG may predict the progress and outcome of individual patient[13-18]. EEG is also valuable

In evaluating response to drug treatment. Several cholinesterase inhibitors have been shown to have positive effects on EEG. Among subjects receiving treatment, individuals with prominent EEG response may have better drug effect[25,26].

Rodriguez et al[28] described typical EEG spectral profile of AD of different GDS and tried to differentiate them by means of relative band power at 1.5 Hz interval. However, the 7 quantitative EEG bands were far from the experience of conventional 4 frequency bands by most clinical electroencephalographers. Bennys K et al[29] used power ratio between slow activities and fast activities to differentiate AD from normal control. The discrimination was striking throughout different scalp regions (except frontal region) and cutoff values was proposed. The ratios were also found to be correlated with severity of the disease, but the cutoff values were not mentioned.

To verify the supposition that cutoff value of power ratios are useful in clinical practice to stage the disease, we conducted this study.

II. Materials and methods

ub!ects

Candidates for this study are psychotropics-free probable AD and mild cognitive impairment (MCI). Two medical institutes in Taipei (Bojen General Hospital and Municipal JenAi Hospital) participated in this study. From separate registry system of the EEG laboratories, patients received EEG study from 2000 to 2005 with the impression of Alzheimer's disease, MCI, dementia or poor memory (ICD-9 332 and 290) were included. The medical chart of each patient were carefully reviewed by neurologists to confirm the diagnosis of probable Alzheimer's disease (NINCDS-ADRDA criteria[24]) and mild cognitive impairment (Peterson's criteria[25]). Brain CT or MRI, serum vitamin B_{12} and folic acid level, thyroid function, VDRL and anti-HIV antibody were routinely performed to exclude vascular dementia, hydrocephalus, nutritional deficiency, hypothyroidism, neurosyphilis and AIDS dementia complex. Alternative diagnosis, such as frontotemporal dementia, dementia with Lewy body, depression, or other unclassified dementia were excluded from this study. AD patients whose EEG recordings were in the acute delirium state, receiving potent antipsychotics and sedatives or in the presence of major systemic disease were also excluded. Clinical informations of MMSE, CDR and GDS of the candidates within 2 weeks before or after EEG recording were collected. Candidates were further grouped as very mild (CDR 0.5, GDS 3), mild (CDR 1, GDS 4), moderate (CDR 2, GDS 5) and severe (CDR 3, GDS 6) according to illness severity.

EEG recordin"

EEG studies were performed in quiet rooms. Sixteen scalp electrodes (Fp1, Fp2, F3, F4, F7, F8, C3, C4, T3, T4, T5, T6, P3, P4, O1, O2) were referenced to electronically linked earlobes (A1 and A2) according to international 10/20 system. All electrode impedances were kept below 5 kΩ. Concurrent surface EMG and EKG were also recorded for reference, but were not included in the EEG analysis. EEG settings were identical in 2 laboratories with sampling rate at 200 Hz, bandpass at 1-70 Hz and a notch filter at 60 Hz. During recording sessions, subjects sat on a comfortable chair with eyes closed. Activation maneuvers, including eyes opening, hyperventilation or photic stimulation were performed under instruction by technicians and the events were marked on the EEG recordings. Average recording duration was 10 to 15 minutes.

#uantitative EEG

All EEG data were reviewed by an experienced electroencephalographer by direct visual inspection. Artifact-free (free from muscle contraction, electro-oculographic deviations and body movements) epochs of 1-s duration were collected. The data were exported to Matlab for spectral power analysis. Power spectral profiles of 16 scalp electrodes as well as averaged spectrum were demonstrated for descriptive purposes. For averaged spectrum, absolute and relative power in four standard frequency band – delta (2-4 Hz), theta (4-8 Hz), alpha (8-13 Hz) and beta (13-32 Hz) – were calculated. We defined the "EEG power ratio" as the power ratio of slow to fast activities.

EEG power ratio=(theta band power+delta band power)/ (alpha band power+beta bad power) (1)

tatistics

Statistical analyses were performed using SPSS package. For each group, EEG power ratios were analyzed for the mean value, standard deviation, standard error and 90% CI. One-way ANOVA with Post Hoc multiple comparisons (Tamhane) was used to compared the power ratio between groups. Further analysis reclassified the candidates as early (very mild and mild groups) and advanced (moderate and severe groups) groups. Student's t test was used to compared these two groups. Statistical significance was defined as $p < 0.05$.

III. $esults

Clinical characteristics of sub!ects

Forty-seven patients, 25 male and 22 female, were included in this study. Mean age is 77.9 (range 59-90). Nineteen patients were in the very mild group (MCI) with mean MMSE score at 22.5. Twelve were in the mild group with mean MMSE score at 19.3. Nine were in the moderate group with mean MMSE score at 12.0. Seven were in the severe group with mean MMSE score at 9.4. (Table 1).