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ORIGINAL PAPER

Evaluations of dementia by EEG frequency analysis and psychological examination

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Abstract In order to evaluate the stage of dementia, we focused attention on EEG rhythms and Hasegawa-dementia-rating scale (HDS-R). Frontal EEGs were recorded from dementia patients and normal controls during music and photo-image stimulations, and frequency analysis was performed. In the controls, profiles of rhythm pattern during music stimulation seemed to be markedly different from those during photo-image stimulation. In contrast, in dementia patients, it was difficult to find those differences. Interestingly, as HDS-R decreases, the variability of rhythm patterns also decreases. These results suggest that a decrease in cognitive function might be related to a decrease in the ability to generate various cortical rhythm patterns.

Keywords EEG · Frequency analysis · Dementia · HDS-R · Music · Photo image · Theta frequency band · Alpha frequency band

Introduction

Dementia is considered to be a disease of cognitive dysfunction, but not to be an exaggerated condition of normal aging [9, 10]. Dementia has several stages of cognitive dysfunction, and has the feature of gradual exacerbation. Mild cognitive impairment (MCI) tends to convert into dementia, and once suffering from the dementia, it is difficult to improve cognitive function [11, 14]. Therefore, it is important to diagnose the early stage of cognitive dysfunction for prevention and treatment of dementia.

In order to evaluate dementia, Hasegawa-dementia-rating scale (HDS-R) and mini-mental state examination (MMSE) have been developed, and are generally used, as in psychometric assessment. Recently, for morphological and metabolic assessments, diagnostic criteria have been under development by using brain-imaging techniques, such as functional MRI and FDG-PET [7, 10]. These methods enable us to investigate from the surface to deep areas of the brain, and to provide information about regional atrophy and homodynamic changes. However, these medical examinations may to some extent impose stress on the patients. Among electrophysiological methods, evaluations of cognitive dysfunction by using event-related potential (ERPs) or electroencephalographic (EEG) frequency analysis have been developed [1, 6]. Although electrophysiological activities reflect neuron activities in the brain, it is presently difficult to evaluate precise stages of dementia.

For screening cognitive dysfunction, less invasive and less stressful examinations that reflect brain function are preferred. In this respect, we have focused attention on EEG frequency analysis, and psychological assessment, HDS-R, in the present study.

Methods

Sixteen outpatients, whose ages were 73.7 ± 4.8 years (mean ± SD), from Kanazawa Medical University

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Hospital, diagnosed as having dementia were included in this study. All patients underwent the psychological test of HDS-R. A medical doctor of geriatrics performed the psychological test. Ten healthy controls whose ages were 58.0 ± 13.8 years (mean ± SD) were recruited, and also underwent the neuropsychological test of HDS-R. All experiments were undertaken with the understanding of the subjects.

EEGs were recorded from frontal region of the scalp, by using EEG recorder, FM-515A (Futek, Tokyo, Japan). Frequency analyses of EEGs were performed with PRLUXII (Futek). Frequency bands were divided into theta (4–7 Hz), alpha1 (7–9 Hz), alpha2 (9–11 Hz), alpha3 (11–13 Hz) and beta (13–30 Hz). Data were collected for every 1 s. Occupancy rate of each frequency band was calculated as follows. Power of each frequency band was divided by the sum of the powers of all frequency bands, and the ratio was defined as a unit occupancy rate (%). Activities of each frequency band were firstly assessed by the unit occupancy rate per second. Then the unit occupancy rates through one course of session (180 s) were averaged, and we adopted the data of "occupancy rate" (%). Hereafter in this study, we refer to the averaged rate as occupancy rate.

Participants sit in the body sonic chair (Refresh 1 Excellent, Tokyo, Japan), and listen to the music in comfort. In front of the chair, a 150 cm × 100 cm screen was located at 2 m distance on which patients were able to see images of photographs. Images were projected on the screen through a PC Projector, EMP-1705 (Epson, Tokyo, Japan) connected to a PC. Famous Japanese standard songs in the category of country music, "Furusato" and "Nanatsuno-ko", were selected from Japanese music CDs, and presented as an auditory stimulation. Photographs of scenic Japanese spots were presented as visual stimulation. The auditory and visual stimulation were applied for 180 s each.

During one session (180 s), EEG epochs with artifacts were identified (threshold: 5 μV), and artifact-free EEG epochs were adopted for analysis. Thus, the "unit occupancy rate" through one session was not 180 but 154.3 ± 21.5 (mean ± SD, $n = 16$) in the case of the auditory stimulation for dementia patients, 133.8 ± 31.7 (mean ± SD, $n = 16$) in the case of visual stimulation for dementia patients, 163.8 ± 14.6 (mean ± SD, $n = 10$) in case of auditory stimulation for healthy controls, and 156.9 ± 26.8 (mean ± SD, $n = 10$) in case of visual stimulation for healthy controls.

Local institutional ethics committees of Kanazawa Medical University approved the present study, and all experiments were performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and the Guiding Principles for the Care and Use of Animals in the Field of Physiological Sciences. All persons gave their informed consent prior to their inclusion in the study.

Results

EEGs were recorded from a healthy control during both music and photo-image stimulations, and frequency analysis was performed. The occupancy rate of each frequency band is shown in Fig. 1a. In the case of the music stimulation, the occupancy rate of the alpha2 band was dominant compared with those of other frequency bands, whereas in the case of the photo-image stimulation, the occupancy rates of the theta and beta bands were relatively dominant compared with those of other frequency bands. The profiles of the rhythm pattern during music stimulation and during photo-image stimulation seemed to be markedly different.

In the same way, EEGs were recorded from a dementia patient during both music and photo-image stimulation, and frequency analysis was performed. The occupancy rate of each frequency band is shown in Fig. 1b. On comparing the occupancy rates of the five frequency bands obtained from a dementia patient with those obtained from a healthy control, it is difficult to find marked differences of rhythm pattern in the dementia patient (Fig. 1b). These results show that different patterns of frontal EEG rhythm seem to be generated in a normal control when different sensory stimulations are applied, whereas, in a dementia patient, it might be difficult to generate diverse patterns of frontal EEG rhythm.

Occupancy rates of theta frequency bands obtained from 10 normal controls are plotted together in Fig. 2a (Theta), and those obtained from 16 dementia patients are plotted together in Fig. 2b (Theta). In the same way, occupancy rates of other frequency bands are plotted in Fig. 2a, b. By comparing the occupancy rates obtained from normal with those obtained from dementia patents, occupancy rates elicited by music stimulation in normal controls tended to be different from those elicited by photo-image stimulation in a few frequency bands, whereas, in dementia patients, it is difficult to find differences of occupancy rates between the music and photo-image stimulations. These findings are statistically evaluated as follows.

In order to quantify the variability of rhythm patterns, the variation score of each frequency band was obtained by subtracting the occupancy rate in the case of photo-image stimulations from the occupancy rate in the case of music stimulations, which was executed for the five frequency bands. The data obtained from individual subjects were averaged, and are plotted in Fig. 3. In this figure, the variation score near zero indicates that there is a small difference between the occupancy rate during music stimulation and that during photo-image stimulation. Analysis of variance (ANOVA) was used to evaluate the statistical significance of the variation scores in all five frequency-bands. In the dementia group, there is no statistical difference ($F = 2.67$, $P = 0.038$), whereas in the normal group, there

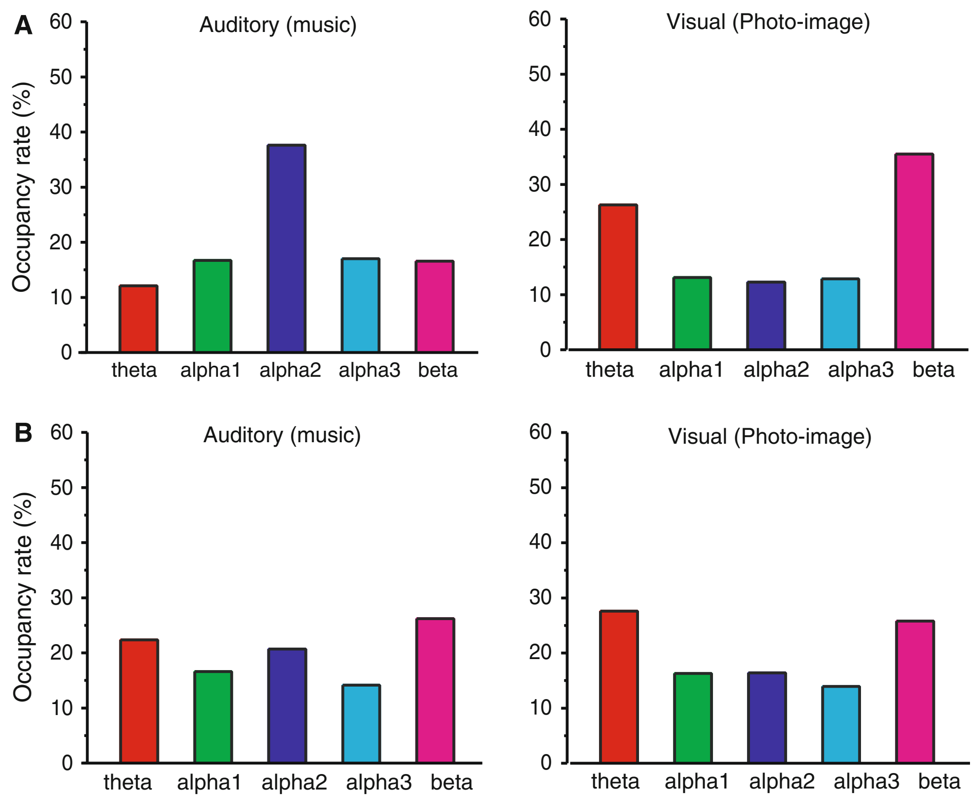

Fig. 1 Occupancy rates of the five frequency bands during music stimulation compared with those during photo-image stimulation. The frequency bands of interests are theta, alpha 1, 2, 3 and beta. Data were obtained from **a** a normal control and **b** a dementia patient

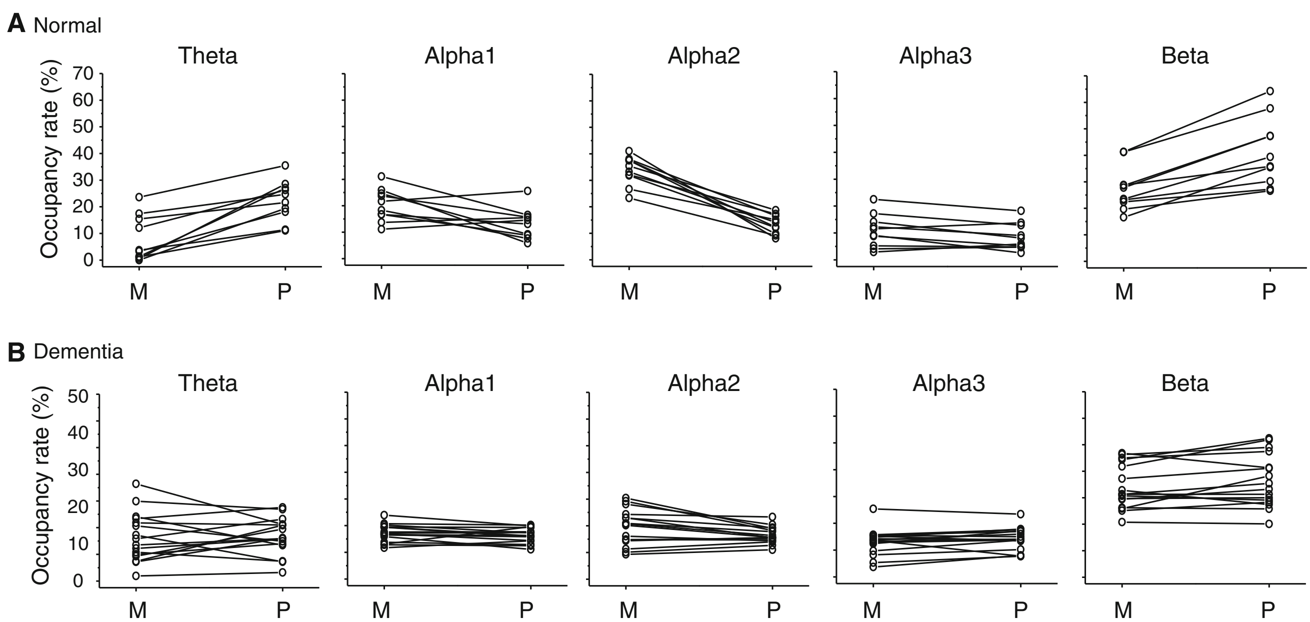

Fig. 2 Comparing the differences between occupancy rates of the five frequency bands during music and those during photo-image stimulation. Data were obtained from **a** 10 normal controls and **b** 16 dementia patients. Individual sets of occupancy rate between music and photo-image stimulations are plotted for 5 frequency bands of interest. *M* Music stimulation, *P* photo-image stimulation

is a large statistical difference ($F = 53.6$, $P = 1.1 \times 10^{-16}$), when the level of significance is 0.01. The data show that variability of rhythm patterns was much larger in normal controls than in dementia patients.

In the next analysis, correlations between the variability of rhythm patterns and HDS-R were investigated. In order to evaluate the variability of rhythm patterns, the variation score was used as described above. Variation scores in the theta frequency band were plotted against HDS-R in Fig. 4 (Theta). In the same way, variation scores about other frequency bands were plotted against HDS-R in Fig. 4 (Alpha1, Alpha2, Alpha3, and Beta). These analyses indicate that there is a negative correlation between variation score and HDS-R in the theta frequency band ($R = -0.77$, $P < 0.0001$) and in the beta frequency band ($R = -0.56$, $P = 0.0027$), and a positive correlation in the alpha2 frequency band ($R = 0.88$, $P < 0.0001$), when the level of significance is 0.01. Thus, in the theta and beta frequency bands, as HDR-S decreases, the variation score also decreases, and in the alpha2 frequency band, as HDR-S decreases, the variation score increases. These results also show that, as HDR-S decreases, the variation scores of the theta, alpha2 and beta frequency bands deviates from zero. This finding suggests that, as cognitive function decreases, the variability of rhythm patterns also decreases.

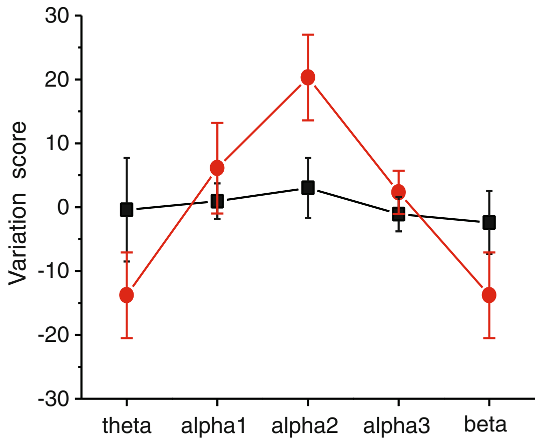

Fig. 3 Evaluation of EEG rhythm variations by calculating the variation score, where the occupancy rates during photo-image stimulations were subtracted from occupancy rates during music stimulations. The variation scores obtained from normal controls ($n = 10$) and dementia patients ($n = 16$) were averaged and are plotted (mean ± SD). *Circles* indicate data from normal controls, and *squares* indicate data from dementia patients. Note that variation scores distant from zero indicate that there is a large difference between the two occupancy rates

In the next analysis, correlations between the variability of rhythm patterns and age were investigated by using data from both healthy controls and the dementia group. The same data of variation scores plotted in Fig. 4 were used. Variation scores in the theta frequency band were plotted against age in Fig. 5 (Theta). In the same way, variation scores about other frequency bands were plotted against HDS-R in Fig. 5 (Alpha1, Alpha2, Alpha3, and Beta). These analyses indicate that there is a negative correlation between variation score and age in the alpha3 frequency band ($R = -0.56$, $P = 0.003$), but not in the other frequency bands, when the level of significance is 0.01.

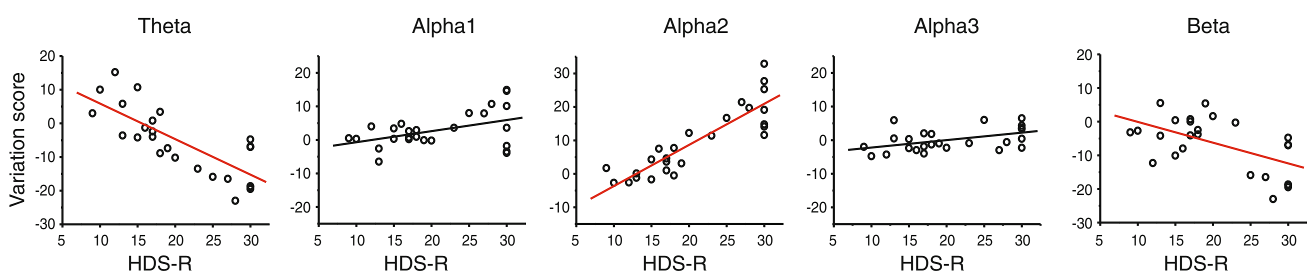

Fig. 4 Relationships between the variation score and HDS-R. The variation scores of the five frequency bands of interests obtained from normal controls ($n = 10$) and dementia patients ($n = 16$) are plotted against HDS-Rs, and linear fittings performed. Note that there are correlations between variation scores and HDS-R in the theta ($R = -0.77$, $P < 0.0001$), alpha2 ($R = 0.88$, $P < 0.0001$) and beta frequency bands ($R = -0.56$, $P = 0.0027$), when the level of significance is 0.01

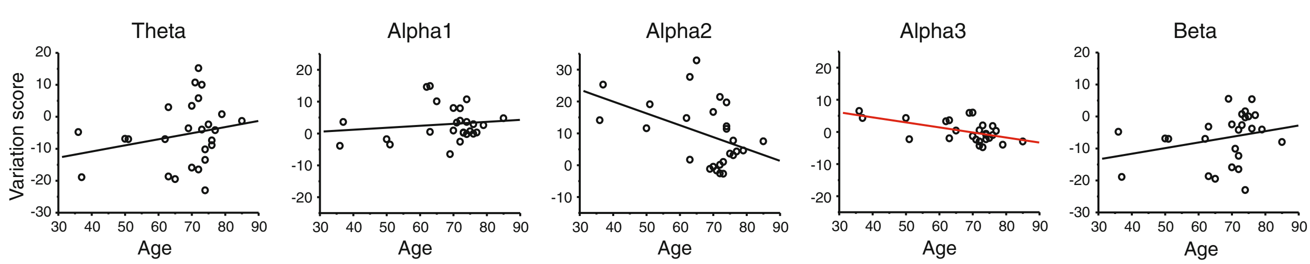

Fig. 5 Relationships between the variation score and age. The variation scores of the five frequency bands of interests obtained from normal controls ($N = 10$) and dementia patients ($N = 16$) were plotted against age, and linear fittings were performed. Note that there are correlations between variation score and age in alpha3 frequency bands ($R = -0.56$; $P = 0.003$), when level of significance is 0.01

Discussion

EEG recording from the scalp is widely used as a non-invasive electrophysiological recording method. In order to assess cognitive dysfunction, investigation of event-related potential (ERP), P300, could be a first choice [5]. Aging is one of the major risk factors that lead to cognitive dysfunction, and, indeed, the latency of ERP P300 tends to prolong as aging advances [2, 4]. In the case of Alzheimer disease (AD) patients, the peak latency of ERP P300 tends to be further prolonged compared to normal aging [12]. Thus, the P300 recording method has been developed as a diagnostic method.

Another method under development for assessment of cognitive dysfunctions is source analysis of EEG frequency. Previous studies reported that theta activities are increased and beta activities are decreased in AD patients when compared to controls [3, 8, 13]. Recently, it has been reported that sources of delta and alpha frequency bands differ in MCI and AD [1]. In those studies, EEG recordings were performed in the awake condition with the eyes closed. It was based on source analysis by dipole-fitting from multiple point data on the scalp.

In the present study, our attention is focused on less invasive and less stressful methods by EEG recording from the frontal area of the scalp. By comparing EEG rhythms evoked by different sensory stimulation, we successfully demonstrated that variations of rhythm patterns decrease in dementia patients as compared with healthy controls, and that a decrease in cognitive function might be related to a decrease in the ability to generate various cortical rhythm patterns. However, we must consider influences of aging on the decrease in variations of rhythm patterns, since normal healthy controls were recruited from a younger age group as well as older age group. In the case of alpha2 frequency bands, there is a negative correlation between variation score and age ($R = -0.44$, $P = 0.025$), when the level of significance is 0.05. Indeed, this suggests that aging also influences a decrease in variations of rhythm patterns in the alpha2 frequency band. But the influence of age seems mild, since there is no correlation when the level of significance is 0.01, and the P value between variation score and age ($R = -0.44$, $P = 0.025$) is much higher compared with that between the variation score and HDS-R ($R = -0.88$, $P < 0.0001$). In the cases of the theta and beta frequency bands, there is no correlation between variation score and age ($R = 0.23$, $P = 0.26$ and $R = 0.27$, $P = 0.19$, respectively). In the case of the alpha3 frequency band, there is a negative correlation between variation score and age ($R = -0.56$, $P = 0.003$), but there is no correlation between variation score and HDR-S ($R = 0.48$, $P = 0.13$), when the level of significance is 0.01. Thus, these findings suggest that influences of aging on a decrease in variations of rhythm patterns are relatively small.

Since EEGs were recorded from the frontal cortex only, the present data did not reflect whole brain activities, but the significance was that differences of electrophysiological activities between dementia patients and healthy controls were detected. Moreover, the present results suggest that a decrease in cognitive function might be correlated with a decrease in variations of cortical rhythm patterns between the different tasks. Combining the electrophysiological and psychometric examination, as we have shown in this study, might enable us to assess cognitive dysfunction comprehensively, and might be useful as diagnostic criteria of early-stage dementia.

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