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Abnormal information processing in dementia of Alzheimer type. A study using the event-related potential's field

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Abstract Electrical field changes of event-related potentials (ERPs) were investigated in 26 patients with dementia of Alzheimer's type (DAT) and 12 age-matched normal subjects. The patients were assessed with the Clinical Dementia Rating and Mini-Mental State. Each patient selected had only mild to moderate mental disability. Auditory oddball stimulation was presented at 1.5 s intervals and 1000 Hz for the nontarget and 2000 Hz for the target tones, both at 85 dB. The target tones were 20 % of all the tones. The reference-independent data (latency, global field power: GFP, dissimilarity index: DISS and location of centroids) were obtained and analyzed for each ERP component. The momentary electric strength or 'hilliness' of the ERPs landscape was indicated by GFP. The patients showed prolonged latencies and decreased P300 GFP amplitudes and of N100 GFP. These findings suggest that the abnormal electrical field of ERP may reflect abnormal information processing following the attentional process for target stimuli in DAT patients.

Key words Event-related potentials (ERPs) · Dementia of Alzheimer type (DAT) · Attention

Introduction

Because of reports that P300 latency in patients with cognitive impairment is significantly prolonged as compared with that for normal subjects, testing of intellectual performance with event-related potentials (ERPs) has been introduced to evaluate mental function. These P300 abnormalities were observed regardless of etiology (Polich et al. 1986). However, few reports on the role of N100 component of ERPs have been made. Processing negativity (Nd), which is evoked based on subject's attention, overlaps on the N100 component (Coull 1998). Dementia of the Alzheimer type (DAT) is characterized by progressive decline in memory, language, and other cognitive functions. Moreover, deficits in attentional processes have been suggested (Simone and Baylis 1997). However, it is reported that N100 in DAT is normal using usual analysis method. The aim of this study is to objectively prove disturbances of the early part of information processing in DAT using new electrophysiological method. It is difficult to detect minor change using the latency or amplitude of ERPs from a few electrodes. On the other hand, the EEG map seems to reflect the intracranial distribution of neural activity (Michel et al. 1992). Analysis of the ERP map should, therefore, be useful for evaluating minor abnormalities. However, the functional interpretation of ERP's topography seems to be difficult using the conventional analysis. In order to investigate the different map landscapes during ERP, we used the novel method described by Lehmann and Skrandies (1980). The electrical field change of ERP can be analyzed in terms of time and space by this method, so very small abnormal electrophysiological change as with N100 potentials can be detected.

We investigated the ERP electrical field change in DAT patients in order to detect minor abnormal change of N100 components.

Subjects

Twenty-six DAT patients (72.2±7.5yrs) and 12 age-matched normal subjects (69.0±3.3yrs) were studied. DAT patients were diagnosed by NINCDS-ADRDA (National Institute of Neurological and Communicative Disorders and Stroke-Alzheimer's disease and Related Disorders Association) criteria. The patients selected showed only mild

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to moderate mental disability because severely demented patients were not capable of performing the ERP test paradigm. Moreover, none of the participants were administered any drugs. The severity of dementia in the patients was assessed with the Clinical Dementia Rating (CDR; Hughes) and Mini-Mental State (MMS). The average CDR and MMS scores for the patients were 1.52±0.59 and 18.6±4.3 respectively and the MMS score for the normal subjects was 29.0±1.3. DAT patients and normal subjects were informed about the procedures and goals of the study and gave their informed consent.

Method

Brain electric recordings

After a verbal explanation of the procedures, an auditory oddball paradigm stimulation was presented at 1.5 s intervals. The frequent tones had a pitch of 2000 Hz, the rare tones of 1000 Hz, both at 80 db SPL. Twenty percent of all the tones were rare ones. The subjects were instructed to close their eyes and silently count the target tones; at the end of the session they were asked to report the count ("counting performance value").

Multichannel ERPs were averaged with 18 channels using the international 10/20 system for electrode placement (Fp1, Fp2, F3, Fz, F4, F7, F8, C3, Cz, C4, P3, Pz, P4, T5, T6, O1, Oz, O2) and a topography mapping system (Bio-Logic Brain Atlas, 0.53–30 Hz band pass) was used for recording and averaging. The averaged reference was used as a reference. On line artifact rejection was based on any electrode exceeding when136μV amplitude threshold.

ERP analysis

To evaluate the different map landscapes during the ERPs, we used the reference-independent measures of latency, global field power (GFP) and location of centroids as described by Lehmann et al. (Lehmann and Skrandies 1980; Brandeis and Lehmann 1986). The momentary electric strength or 'hilliness' of the ERPs landscape was indicated by GFP. GFP conventionally is computed as the square root of the mean of the squared voltages vs. the average reference.

There are different peak latencies between DAT patients and normal subjects. To evaluate the electrical field of ERPs, segments of ERPs were defined as follows. Changes in the map landscape can be assessed from the measure of global dissimilarity (dissimilarity index: DISS) between successive maps (Fig. 1) (Michel et al. 1992). The location of centroid (+C, -C) means gravity center of the ERPs potential (Lehmann and Skrandies 1980; Brandeis and Lehmann 1986). The location is projected onto the right-left axis and anterior-posterior of the head and plotted as the function of time. The segments of each component were defined from the crossing points of the trajectories of centroid's location and the increased DISS (Kochi et al. 1996) (Fig. 1). This evaluation was done for the normal control and DAT patient groups. The N100, P200-N200 and P300 segments for the normal controls (DAT patients) covered 58–132 (58–142), 136–268 (142–280), and 272–588 (280–678) ms.

Statistical evaluation

Statistical analysis was performed by student t-test (df=36). Correlations were tested for using Spearman's correlation test. (StatView-J 4.11).

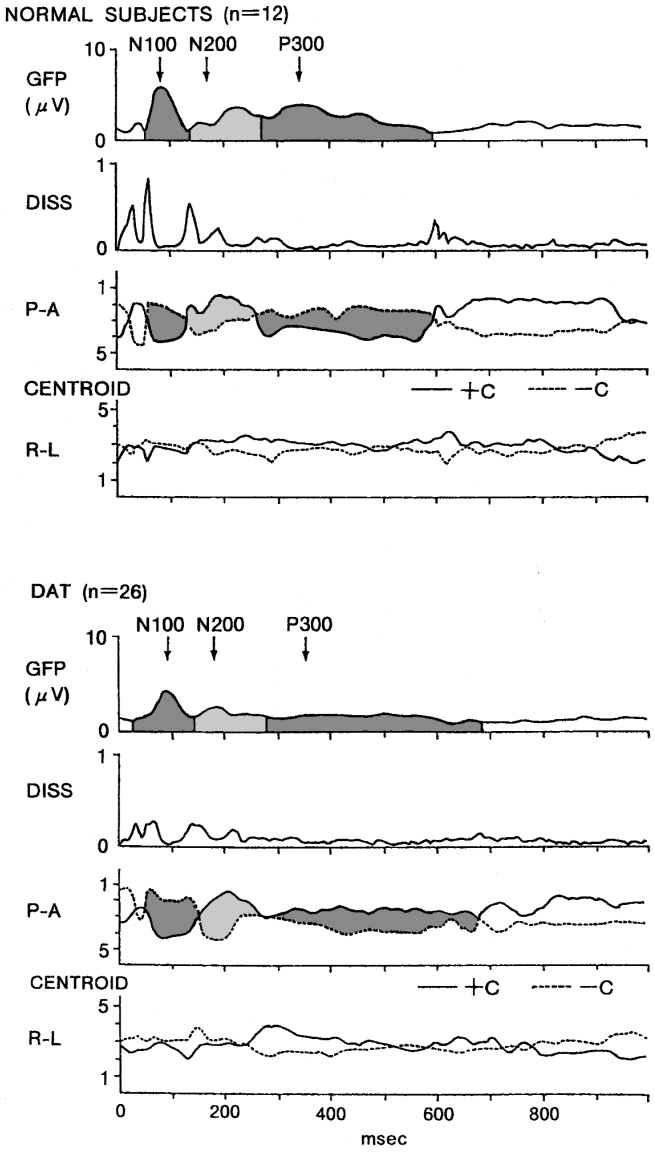

Fig. 1 Grand mean trajectories for global field power (GFP), the dissimilarity index (DISS) and the location of centroids for the respective target tones. Using the international 10/20 system, electrode positions were numbered in order from anterior to posterior (P-A) and from left to right (R-L), 3 indicating the electrode on the midline, and 1 the electrode most anterior on the A-P axis and most left on the R-L axis. DAT patients had prolonged latencies and decreased amplitudes for N100 and P300, and decreased DISS for N100, N200 and P300.

Results

"Counting performance value" of all subjects for the target tones was >99.5 %. The patients showed prolonged latencies (92.4±10.3ms vs. 85.9±9.4ms: $p<0.05$) and decreased GFP amplitude for N100 (5.94±1.77μV vs. 7.67±2.64μV: $p<0.05$). The latency for P300 GFP prolonged significantly (422.3±76.1ms vs. 357.5±69.2ms:$p<0.01$), and the P300 GFP amplitude also decreased (6.46±2.10μV vs. 8.86± 1.32μV: $p<0.05$).In contrast, GFP latency for N200 short-

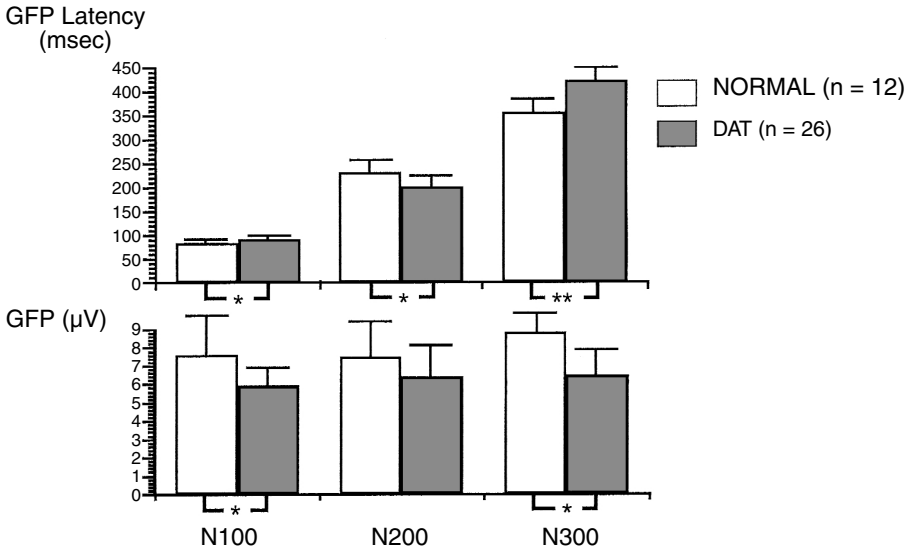

Fig. 2 Latencies and amplitudes for N100, N200, and P300 GFP. Vertical bars represent the standard deviation of the mean; *p<0.05, **p<0.01.

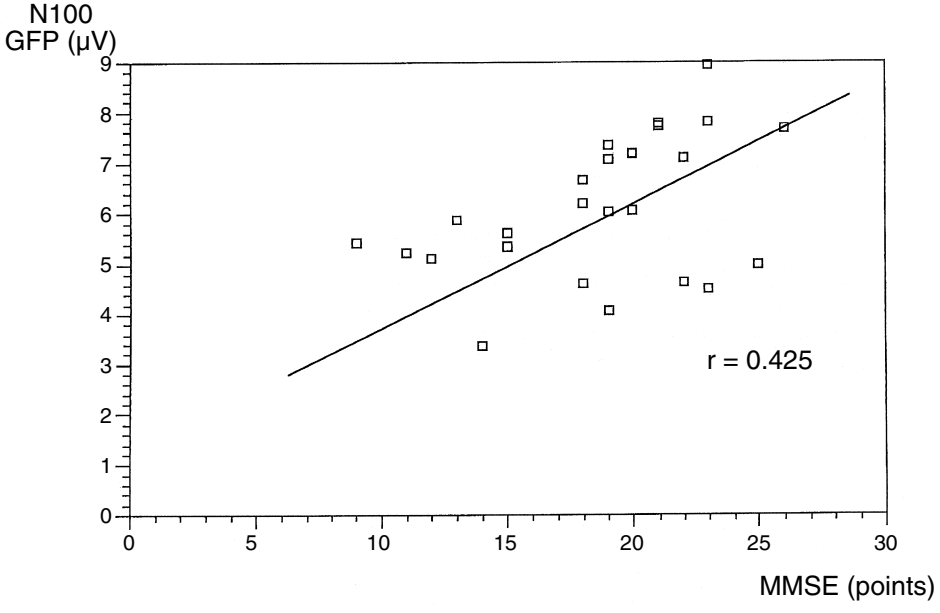

Fig. 3 The relationship between N100 GFP amplitudes and scores of MMS. There is a correlation between N100 GFP amplitudes and MMS scores (r=0.425, p<0.034).

ened in the DAT patients (203.4±27.7ms vs. 231.9±32ms: p<0.02), whereas amplitude did not change (6.46±2.45μV vs. 7.53±2.34μV)(Fig. 1, Fig. 2).

Decreased DISS of the segmental ends for N100, N200 and P300 was seen in DAT patients.

There was a relationship between ERP data and clinical data. There were mild negative correlation between P300 GFP latencies (r=–0.326, p<0.046), positive correlation N100 (r=0.425, p<0.034), and scores of MMS (Fig. 3).

Discussion

ERP electrical fields were recorded from the 26 DAT patients and 12 age-matched normal subjects. In agreement with previous studies, the P300 latencies were prolonged and amplitudes decreased, but not in N100 in DAT patients (Verleger R et al. 1992). Goodin and Aminoff (1986) reported that only subcortical dementia tends to affect the earlier N100 and P200 components, whereas subcortical and cortical dementia affect the later N200 and P300 components. They concluded that these differences may have major implications for distinguishing different types of dementia.

Memory and attention are interrelated cognitive processes that probably influence each other's functioning, but they often are difficult to distinguish in psychological experiments (Simone and Baylis 1997). DAT is characterized by progressive decline in memory, language, and other cognitive functions, and deficits in attentional processes have also been suggested. Overall reaction time was slower in the DAT group than in the control group (Sano et al. 1995).

Processing negativity (Nd) which is evoked based on the subject's attention overlapped the N100 component (i. e., the selective attentional process adds an extra degree

of negativity to the N100 component) (Hillyard SA et al. 1973). Therefore, the reduced power of N100 component reflects disturbance of the early information process. Bahramali H et al. (1998) used a conventional auditory oddball paradigm and demonstrated within-trial differences in ERP brain function associated with relatively fast and slow reaction times in normal subjects. Increased N100 was found in the fast but not the slow ERP subaverages. Their results also suggest that amplitude increases of N100 are elicited by attention.

N200 complex is composed of mismatch negativity (MMN) and N2b. Both components can best be seen in the difference curve formed by subtracting the non-target potentials from the target potentials. MMN seems to reflect (unconscious) automatic stimulus change detection in the human auditory system. N2b is believed to reflect consciously controlled stages of information processing (Naatanen R, Picton TW 1986). In our study, N200 peak of GFP compose MMN, N2b and P2 potentials so that we cannot achieve direct explanation for the N200 latency reduction. However, we think N200 change in our study is mainly due to reduction of N2b which indicates disturbance of consciously controlled stages of information processing in DAT (see Fig. 1).

It is difficult to detect minor abnormalities using latency or amplitude of ERP from a few electrodes, but the topography of the ERP map seems to reflect the intracranial distribution of neural activity. We, therefore, investigated different topography maps during ERPs using the novel method (Michel et al. 1992; Lehmann and Skrandies 1980; Brandeis and Lehmann 1986; Kochi et al. 1996).

The patients showed prolonged latencies and decreased amplitude not only of P300 GFP but also of N100 GFP which suggests that an abnormal ERP map, especially for N100, may reflect abnormal information processing following attentional process for target stimuli in DAT patients.

In summary, our findings indicate that electrophysiologically there is not only late but also early information processing disturbance in DAT patients.

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