P300 LATENCY AND AMPLITUDE IN THE DIAGNOSIS OF DEMENTIA

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P300 latency and amplitude were investigated in 10 normal elderly individuals, 10 institutionalized elderly persons with dementia not of the Alzheimer's types, and 10 elderly people with Alzheimer's disease. Significant differences between control and dementia groups (but not between dementia groups) were noted in the P300 latency, but not amplitude. Such differential latencies were observed in the anterior and in the left temporal and parietal areas of the brain.

Advances in electroencephalographic technology have allowed for more comprehensive analyses of the diagnosis of dementia (Kurlychek, 1989). For example, event-related potentials (ERPs) are believed to reflect patterns of neural activity associated with specific mental tasks. ERPs appear to provide information about memory, cognitive, and language functions in both normal and abnormal subjects (Hillyard & Kutas, 1983; Prichard, 1981). Of the ERPs variables, the P300 appears to be one of the most robust. For example, numerous published reports demonstrate the relations between P300 and different neuropsychological functions (Blackwood & Muir, 1990; Gevins & Cutillo, 1986; McCarthy & Donchin, 1983; Michalewski, Prasher, & Starr, 1986).

These data have led different investigators to suggest that the P300 is an excellent index of specific aspects of mental function and clearly more sensitive than conventional EEGs in evaluating patients with dementia (Blackwood, St. Clair, Blackburn, & Tyrer, 1987; Goodin & Aminoff, 1986; Thompson, Patterson, & Michalewski, 1986). Numerous studies have associated Alzheimer's disease and dementia with an increase in the latency and a reduction in the amplitude of P300 when subjects perform discrimination tasks (St. Clair, Blackwood, & Christie, 1985). The present study extends these previous findings by measuring both the latency and amplitude of the P300 in normal and demented individuals with and without a diagnosis of Alzheimer's.

METHOD

Subjects

Ten normal volunteers (6 males, 4 females; *M* age = 66.4) comprised the control group. For these subjects, no evidence of neurological or psychiatric disorders was found in medical records or by physical examination by a physician. Subjects for the experimental group were volunteers recruited from a nursing home. Ten individuals (7 males, 4 females; *M* age = 68.1) with dementia not of Alzheimer's type (e.g., Parkinson's; DNA group) and 10 persons with Alzheimer's disease (7 males, 3 females, *M* age = 66.8) (DA group) comprised the experimental groups. The DNA and DA groups were evaluated

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with the diagnostic criteria described by Kane, Ouslander, and Abras (1984) by a certified neurologist who employed standard neurological tests, with further information from neurologists, psychiatrists, and neuropsychologists. Neuropsychological tests used included a Spanish adaptation of the Mini-mental test (MMT) and the Wechsler Memory Scale. The control group obtained a mean Memory Quotient (MQ) of 93 (SD = 4.3; range = 88 to 105), while the dementia groups obtained an MQ of 69 (SD = 2.3; range = 58 to 82). In the MMS, the control group contained a mean of 27.8 (SD = 1.7), while the dementia groups obtained a mean score of 17.5 (SD = 2.8).

Procedure

The oddball paradigm of auditory stimulation was applied. In this paradigm, 20% of the 200 administered stimuli were "target," while the remaining stimuli were "non-target." The target tones were of 200 Hz, while the non-target tones were of 1000 Hz. All of the tests were performed in a light- and sound-attenuated room with the subjects seated in a comfortable armchair.

Apparatus

The electronencephalographic recordings were made with Ag/AgCl disk electrodes, with an impedance always less that 5 K Ohms and with a 16 channel EEG montage displayed in the following manner: 01, 02, P3, P4, T5, T6, C3, C4, Pz, Fz, F3, F4, F7, F8, Fp1, Fp2. The international 10/20 system with ear lobe reference was used. The signal was recorded and amplified by a NIC EEG 1A/97 system (Nicholet Biomedical Instruments) with a band pass filter of .5-120 Hz. An infraorbital electrode was used to control eye blinking in order to ignore changes associated with eye movements.

Data Analysis

The auditory ERPs elecited by infrequent (target) stimuli were analyzed. The P300 latency was measured at each electrode, the higher positive peak determined by a cursor. The P300 latency between 280 and 750 milliseconds (msc) was measured. The amplitude from baseline to positive peak was calculated and expressed in uV. Analyses were completed with a one-way analysis of variance (ANOVA; BMDP7M program). The small number of subjects per group was taken into account using Leven's test for equality of variance. Because no significance was found, it was deemed acceptable to use the ANOVA procedure. Additionally, discriminant analyses were completed (BMDP7M program) on the data from recordings of electrodes that suggested the possibility of between-group differences.

Results

Latency

Results show the existence of a considerable increase of latency in dementia groups when compared to the control group. This increase was greater in the DA than in the DNA group. In addition, there was a pattern of progressive increases in latency from the posterior to the anterior areas in both the dementia groups.

In Table 1 the differences between the control and DA groups are shown. The greatest differences are found in the anterior areas; in particular in the electrodes Fp1, Fp2, F7, F4, F3, although significant differences at electrodes Pz, P3, T5 also were found. These results demonstrate that the most robust group differences are essentially bilateral frontal, and temporal and parietal areas of the left hemisphere.

In Table 2 the differences between the control and DNA groups are illustrated. As can be noted, there are few significant differences between both groups. Differences were

observed in electrodes F3, F7, Fp1, and Fp2. Frontal, especially left fronto-temporal, areas appear to discriminate these two groups.

Table 1
Mean Differences of P300 Latency between Control and DA Groups

	Control		DA		
Electrode	*M*	*SD*	*M*	*SD*	*p*
Fp2	371.80	46.73	425.30	49.43	<.02
Fp1	371.30	39.63	422.40	53.32	<.02
F8	377.70	37.47	409.40	42.30	<.15
F7	357.00	29.25	421.40	51.19	<.00
F4	375.00	37.70	423.00	41.81	<.01
F3	356.20	32.32	429.60	51.48	<.00
Fz	372.80	34.08	425.60	46.26	<.10
Pz	358.10	35.54	415.70	58.64	<.02
C4	370.50	36.52	394.40	56.89	<.28
C3	369.10	33.64	400.80	65.99	<.20
T6	368.00	39.71	409.20	64.14	<.11
T5	363.20	34.34	403.00	50.30	<.05
P4	373.70	36.91	411.80	58.97	<.11
P3	363.20	28.93	402.30	51.61	<.05
02	372.90	34.67	405.70	46.42	<.09
01	373.00	37.85	402.70	37.74	<.10

With regard to DNA and DA groups comparisons, no statistically significant differences in the P300 latency between groups were found. However, as Figure 1 shows, an inversion tendency was noted in electrodes F4, Fz, and P4. This suggests that the greatest differences may be evident in the parietal-frontal areas of the right hemisphere.

In Figure 1 the P300 latency is plotted and shows increases in the anterior areas of all three groups. Quantitative differences among electrode locations do exist between the groups. For example, the greatest increase of latency in the DA group is present in the following electrodes: Fz, F3, F4, F7, F8, Fp1, and Fp2, while in the DNA group such increase can be seen only in F4, F7, F8, Fp1, and Fp2. In comparison, the control group showed shifts in latency only on electrodes F4 and F8. This evidence implies that there is an increase of latency in the P300 in elderly people that is seen mostly in the anterior areas. Differences among the three groups do exist, however; the DA group involves brain areas associated with higher cortical impairment. In Table 3, the classification matrix obtained from the discriminant analysis is shown. The data analysis is shown. The data analyzed included electrodes P4, C4, P_z, f_z, F_3, and F7. The two discriminant functions obtained represent more than 99% of the variance; the first represents 61.24% and the second 38.75% of the variance.

Amplitude

In Tables 4 and 5 the differences in P300 amplitude found among the control and DNA and DA groups are shown. Results show the lack of differences among groups

Table 2
Mean Differences of P300 Latency between Control and DNA Groups

Electrode	Control		DNA		
	M	*SD*	*M*	*SD*	*p*
Fp2	371.80	46.73	416.90	53.55	<.06
Fp1	371.30	39.63	416.70	63.83	<.08
F8	377.70	37.47	399.60	38.39	<.21
F7	357.00	29.45	408.69	56.42	<.02
F4	375.00	37.70	396.20	44.28	<.26
F3	356.20	32.32	406.70	61.26	<.04
Fz	372.80	34.08	391.00	38.81	<.28
Pz	358.10	35.54	393.60	62.10	<.14
C4	370.50	36.52	388.90	55.86	<.40
C3	369.10	33.64	385.00	47.52	<.40
T6	368.00	39.71	386.80	56.82	<.41
T5	363.20	34.34	398.00	65.02	<.16
P4	373.70	36.91	378.30	50.70	<.82
P3	363.20	28.93	342.80	62.74	<.20
02	372.40	34.67	394.70	50.61	<.28
01	373.00	37.85	392.60	68.03	<.44

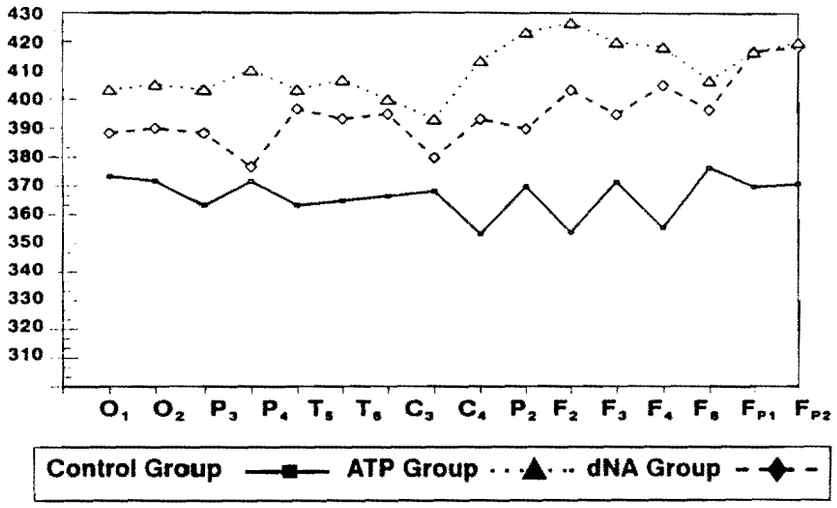

FIG. 1. Mean values of P300 latency by groups across electrodes.

Table 3
Mean Differences of P300 Amplitude between Control and DA Groups

Electrode	Control		DA		
	M	*SD*	*M*	*SD*	*p*
Fp2	7.94	7.55	8.39	7.30	<.89
Fp1	7.99	7.71	7.98	7.60	<.10
F8	4.40	3.23	4.74	3.07	<.81
F7	6.04	5.70	6.10	2.69	<.98
F4	5.13	5.05	5.39	3.26	<.89
F3	5.90	6.30	5.99	3.52	<.99
Fz	5.51	5.18	5.40	3.02	<.995
Pz	4.75	2.26	7.69	2.56	<.01
C4	4.90	2.97	6.24	2.86	<.32
C3	4.63	3.21	5.69	2.44	<.42
T6	5.16	1.77	6.03	2.60	<.40
T5	4.97	2.36	6.54	1.97	<.13
P4	4.97	2.49	7.24	3.53	<.12
P3	4.97	2.49	7.13	3.50	<.10
02	4.48	1.54	5.94	2.68	<.16
01	4.38	1.67	6.41	2.72	<.06

Table 4
Mean Differences of P300 Amplitude between Control and DNA Groups

Electrode	Control		DNA		
	M	*SD*	*M*	*SD*	*p*
Fp2	8.39	7.30	5.06	3.81	<.22
Fp1	7.98	7.60	4.84	3.47	<.26
F8	4.74	3.07	5.18	3.84	<.78
F7	6.10	2.69	3.74	2.84	<.08
F4	5.39	3.26	5.47	3.24	<.96
F3	5.99	3.52	5.22	4.63	<.68
Fz	5.40	3.02	5.51	3.16	<.94
Pz	7.69	2.56	5.29	3.48	<.10
C4	6.24	2.86	5.52	3.61	<.63
C3	5.69	2.44	6.20	3.25	<.69
T6	6.03	2.60	4.75	2.10	<.24
T5	6.54	1.97	5.20	3.01	<.26
P4	7.24	3.53	5.51	2.86	<.24
P3	7.13	3.00	6.04	3.65	<.48
02	5.94	2.68	2.34	2.11	<.16
01	6.41	2.72	4.90	2.44	<.21

with regard to the P300 amplitude in any of the scalp electrodes except between the control and DA group in the Pz electrode. (See Table 3.) In Figure 2, the amplitude of the P300 wave shows considerable increase in Fp1 and Fp2 in the DA group; of Fp1, Fp2, and Pa in the control group; and a decrease in 02 in the DNA group. Conversely, the greatest differences between the control and DA group were found in Pz, P4, P3, and 01, while between the control and DNA groups differences were found in F7, Pz, and 02. No significant differences were found between the dementia groups. Figure 2 plots the mean values of the P300 amplitude for the three groups.

Table 5
Classification Matrix

Group[a]	Percent correct	Number of cases classified into group		
		1	2	3
1	50.00	5	4	1
2	90.00	1	9	0
3	80.00	0	2	8
Total	73.00	6	15	9

[a]1 - Elderly control.
2 - Dementia, no Alzheimer's.
3 - Dementia, Alzheimer's.

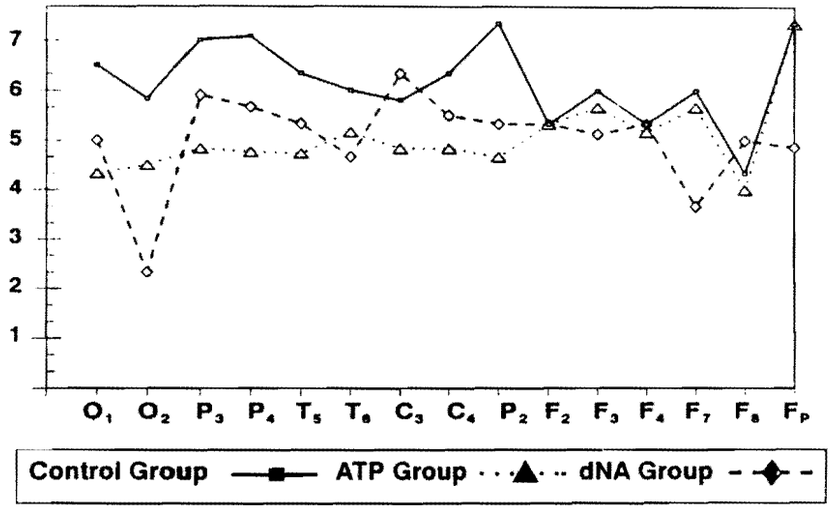

FIG. 2. Mean values of P300 amplitude by groups across electrodes.

DISCUSSION

The present results suggest the existence of significant differences between elderly control and dementia groups within anterior areas of the brain, especially in the left hemisphere. This observation is related to cognitive deficits characteristic of dementia (Moscovitch, Winocur, & McLachlan, 1986). Another important observation is that of the robust differences of P300 latency between the control and DA group not only in frontal areas, but also in temporal and parietal areas. This finding supports previously reported neuropsychological deficits as well as underlying cortical and subcortical neuronal degeneration specific to this disease (Ball et al., 1985; Hyman, Vanhoesen, Damasio, & Barnes, 1984; Moscovitch et al., 1986).

Analysis of the different cortical areas of the P300 latency in the entire scalp appears to be a robust indicator for such a differential assessment when one is considering neurological problems in older adults. The present results suggest that the P300 latency, especially in frontal, central-parietal and fronto-temporal areas, may be an excellent assessment and diagnostic tool for dementia. These findings are in contradiction to Patterson, Michalewski, and Starr (1988). However, in the present study 16 electrodes placed throughout the scalp were used, while in the Patterson study only three midline electrodes were recorded. Thus, the present study may reflect a more valid assessment of global cortical activity.

With regard to the amplitude of P300, two important questions arise. First, there are few significant differences among the three groups that could be related to interest, motivation, and attentional variables (Sutton & Ruchkin, 1984). In the present study, the "oddball" paradigm directed the subject to attend to both target and non-target stimuli. Further, subjects in this study appeared to be highly interested in the test paradigm (as based on behavioral observations and anecdotal reports). It is important to note that the auditory P300 amplitude is reduced in dementia (Brown, Marsh, & LaRue, 1983). In the present study, a decrease was noted in the dementia groups relative to the control group in most of the scalp electrodes, especially in posterior areas. Thus, these findings are probably not due to motivational or general attentional ability. Also, there is a significant difference in the Pz electrode between the control and DA groups that may be considered as indicative of Alzheimer's disease. However, such a discrimination cannot simply be attributed to the P300 latency.

The data suggest that the P300 may be a robust neurophysiological marker or index in dementia, but not between Alzheimer's and other forms of dementia. Increase in the latency of the P300 in frontal, bilateral anterior temporal and central parietal areas appears to differentiate significantly between experimental and groups. Additional research should consider alternatives to the "oddball" paradigm, such as mnemonic tasks (e.g., Gordon, Kraighim, Harris, & Monroe, 1986) and should compare different types of dementia, not just Alzheimer's and non-Alzheimer's types. Further studies that link the P300 to other measures of brain function and imaging should also provide greater understanding of brain function in demented individuals.

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