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Latency variability of the components of auditory event-related potentials to infrequent stimuli in aging, Alzheimer-type dementia, and depression [1]

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Summary Auditory event-related potentials (ERPs) were investigated in 15 demented (12 presumed Alzheimer's, 3 cerebrovascular), 8 depressed, and 15 normal older, and 12 normal young, subjects. Both latencies from conventional averages and latency variability measures from single trials were derived for the N100, P200, N200, and P300 components of the ERP recorded from Fz, Cz and Pz scalp placements in a task requiring detection of an infrequent target tone among a series of frequent non-target tones.

The P300 component most consistently separated the groups. Demented subjects had longer P300 latencies and greater P300 latency variability than both control groups and the depressed group. Age differences were observed for P300 latency, but not for P300 latency variability. Amplitudes were not significantly different among the groups. Reaction times (RTs) to the targets were longest for the demented subjects and shortest for the young controls, with the depressed and normal older control groups falling in between. Correlations between RT and P300 latency from single trials did not differentiate the groups. Using regression analysis to evaluate the deviation of P300 latency and latency variability for the patients from the predicted values for normal controls, no misclassifications of depressed patients occurred, but only 27% of the demented individuals were correctly classified using P300 variability, and 13% using P300 latency. These findings indicate that ERP measures using the 'oddball' target detection paradigm were useful in describing group differences, but were not sufficiently sensitive to be used in differentiating demented persons on an individual basis for clinical diagnosis.

Key words: Latency variability; Auditory event-related potential; Aging; Dementia; Depression

Some of the components of the event-related potential (ERP) appear to be correlated with cognitive processes such as stimulus registration, attention, stimulus evaluation, and memory (Picton and Hillyard 1974; Donchin et al. 1978; Donchin 1979; Hillyard and Picton 1979; Sutton 1979). A positive component appearing at approximately 300 msec reflects speed of stimulus evaluation and categorization independently of response selection and execution (Hillyard and Kutas 1983; Magliero et al. 1984). The data implicating P300 as a correlate of the speed of information processing have made it a likely candidate for indexing slowed cognitive function in normal elderly, as well as altered mental functions in patients with neurological disorders.

Using a paradigm which requires the detection of an infrequent auditory stimulus, the so-called 'oddball' task, a number of studies have reported that measures of P300 latency can reliably differentiate groups of demented individuals from controls and individuals with psychiatric disorders (Squires et al. 1979, 1980; Brown et al. 1982; Syndulko et al. 1982; Patterson et al. 1983, 1984; Thompson et al. 1986). Squires et al. (1979, 1980), for example, found that 80% of a group of demented subjects were correctly classified as abnormal using P300 latency, while only 3% of the psychiatric and 4% of the non-demented neuro-

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logical patients were misclassified. In contrast, other investigators have observed that measures of P300 latency in the target detection paradigm yielded an inadequate number of correct classifications in demented subjects, and too large a number of misclassifications in the psychiatric groups (Pfefferbaum et al. 1984b). The differences among these studies in reports of the sensitivity of P300 latency as a marker for dementia may be related to factors such as the etiology of patient groups (Squires et al. 1980), the severity of cognitive impairment (Patterson et al. 1984; Syndulko et al. 1984; Thompson et al. 1986), and task difficulty. A comparison of different patient etiologies, for example, shows that patients with metabolic encephalopathy have greater P300 latency deviations from normal (4.1 S.D.) than patients with presumed Alzheimer's disease (2.8 S.D.) (Squires et al. 1980).

Measures of the variability of component latency over single trials may be a possible method for increasing the sensitivity of P300 and ERPs as indices of altered cognitive status, especially in patients with Alzheimer's disease. In this procedure, a correlation-template procedure (e.g., Woody 1967) is used to estimate the latencies of the peaks of the ERP on a trial-by-trial basis and to derive measures of component variability. Pfefferbaum et al. (1984b) found evidence of larger P300 latency variability in a group of demented patients (with mixed etiologies including alcohol-related disease, presumed Alzheimer's disease, and cerebrovascular disease) compared to normal subjects, but these measures did not adequately differentiate the demented individuals from those patients with functional disorders. In the present study, we have made a systematic study of latency variability in demented patients (primarily with presumed Alzheimer's disease), in depressed individuals, and in both young and older control groups. Component variability was evaluated for both P300, and for the earlier components of the ERP wave form (N100, P200, and N200). The purpose of the study was to determine whether measures of ERP component latency variability can add to the sensitivity of traditional latency measures derived from conventional averaging procedures in differentiating the groups.

Method

Subjects

Fifteen demented individuals (age range 60–86 years, mean = 71.1), 8 depressed subjects (56–77 years, mean = 65.9), 15 age-equivalent normal older controls (57–81 years, mean = 70.3), and 12 normal younger controls (28–42 years, mean = 34.7) participated in the study. The patients were selected from those attending the Memory Disorders Clinic of the University of California, Irvine (UCI). Referral was based on a chief complaint of impaired memory. The diagnosis of dementia or depression was established by a neurologist and a psychiatrist on the basis of clinical history, clinical test results (MRI, EEG), and quantified tests for neuropsychological and memory functions. The etiology of the dementia in 12 of the cognitively impaired individuals was presumed Alzheimer's disease, while multi-infarct dementia was the suspected diagnosis in 3 other patients. Many of the older controls were spouses of the patients. The young controls were students or employees at UCI. Fourteen of the demented individuals, 5 of the depressed subjects, and 8 controls were given the Mini-Mental State examination (MMS; Folstein et al. 1975) prior to ERP testing. The mean MMS score (and S.D.) for the demented group was 18.3 (4.8), with a range of 11–25. Based on clinical impression and MMS score, 5 of these demented individuals were mildly demented (mean MMS = 23.6, S.D. = 1.9), and 10 were moderately to severely demented (mean MMS = 15.3, S.D. = 2.8). The mean MMS score (and S.D.) for the depressed group was 25.6 (2.7) with a range of 23–30, and for the older controls, 28.1 (1.4) with a range of 26–30. The MMS was not given to the young controls.

Procedure

Scalp electrical potentials were recorded from midline electrode sites Fz, Cz, and Pz referenced to linked earlobes. Eye movements were monitored from electrodes above and below the right eye; a forehead electrode served as a ground. Skin impedance for each electrode site measured below 3.0 kΩ. The EEG was amplified (2×10^5) with a

bandpass of 0.1–100 Hz (3 dB down, 6 dB/octave slopes).

ERPs were recorded in a standard auditory 'oddball' paradigm. Subjects were asked to press a reaction time (RT) key whenever rare (20%) 'high' pitched target tones (640 Hz, 50 msec duration) occurred among a series of frequent (80%) 'low' pitched non-target tones (440 Hz, 50 msec duration). A total of 300 tones was presented. The interstimulus interval between tones varied between 2 and 3 sec. Tones were presented binaurally at an intensity of 72 dB SPL. The order of target tones within the series of frequent tones was determined on a pseudorandom basis with the restriction that no more than 3 target tones occurred together in succession. A series of practice trials was first given to acquaint subjects with the stimulus tones and to verify target detection and appropriate response. Four channels of data (Fz, Cz, Pz, eye channel) were digitized (256 points/channel) for a total sweep period of 1000 msec beginning 200 msec (baseline period) before tone onset. Single trials were stored on disk for later analysis. Subjects were tested in a sound-attenuating chamber in a seated position with their eyes open and directed toward a fixation point. The EEG was monitored continuously during the recording period on a standard polygraph.

Conventional averaging

For each subject averages to target tones were computed from stored single trials free of eye movement artifacts. Peak latencies for N100, P200, N200, and P300 were measured from stimulus onset to the point of maximum voltage, or extrapolated from the intersection of ascending and descending limbs when a component was broadly contoured. (The extrapolation technique was used for only 2 demented individuals and 2 older controls.) Component amplitudes were measured as the difference between the maximum voltage of a peak and the average voltage of the 200 msec baseline period.

Single-trial analysis

The single-trial analysis of the ERPs to the targets used a modified version of the Woody correlational-template procedure (Woody 1967) to identify the N100, P200, N200, and P300 peaks of the ERP and to estimate the latencies of each component (Michalewski et al. 1986). The individual peak shapes for each component of the average wave form (N100, P200, N200, P300) were used as templates in the single-trial procedure. The source of the templates was provided by each individual's average ERP. The number of points in each component template was sufficient to include the descending and ascending limbs for negative peaks, and ascending and descending limbs for the positive peaks. Single trials were first examined to determine whether the eye movement channel fell within acceptable voltage ranges. Each trial was then digitally smoothed to attenuate high frequency activity (bandpass was equivalent to 0–37.5 Hz, 3 dB down at 37.5). Pearson product-moment correlations between the template and successive regions of the single trial were performed and the point of maximum correlation was used to define the latency for a given peak. These correlations were obtained by positioning the template before the expected component and 'moving' it along the single trial so that the pattern of correlations increased, reached a maximum, and then decreased as the template approached, reached, and passed the component. Peak latency was calculated by determining how far the template had been moved to the point of maximum correlation. Each component window was set to minimize the possible misidentification of a preceding (or succeeding) peak of the same polarity, and large enough to accommodate the expected peaks. The correlation computations were applied to each of the 3 midline electrode sites for 1 iteration or pass of the template along the single trial. The temporal resolution of peak latencies determined in this manner was 3.9 msec.

Measures of component variability were calculated for each individual as the standard deviation of the single-trial peak latencies. The average number of target trials used to determine ERP component latency variability did not differ significantly among the groups. Latency adjusted averages for each component were formed by summing the points in the single trials that corresponded to the maximum correlation between the template and the points comprising the detected

peak and dividing by the number of trials. Corrected peak amplitudes were measured as the difference between the maximum average peak voltage and the average voltage of the 200 msec baseline period.

Data analysis

Group differences in N100, P200, N200, and P300 latency from conventional averages and latency variability from single trials were analyzed using analysis of variance (ANOVA) procedures (group × electrode) with repeated measures (electrode). Group differences in RT also were analyzed using ANOVA (group). Post hoc comparisons of the means were carried out using the Newman-Keuls procedure (Winer 1971). Additionally, using regression procedures, separate regression equations relating age and P300 latency from the conventional averages, and age and P300 latency variability were determined. A criterion of 2.0 standard errors of the estimate (SEEs) around the normal regression line at the appropriate age was then used to evaluate the normality/abnormality of these measures for each individual in the demented and depressed groups. (When n is large and the deviation of x (age) around the mean x is large, the SEE may be used to approximate the confidence interval for a predicted y (Afifi and Azen 1979). Calculation of actual confidence intervals would slightly increase the level at which an individual would be labeled abnormal.) Correlation and regression procedures were used to examine the relationships between ERP component latencies and RT and between MMS score and P300 latency and latency variability. Significance levels were set at $P < 0.05$.

Results

Conventional averages

Mean latencies (and S.D.) derived from conventional ERP averages averaged over subjects for each group, component, and electrode site are given in Table I. Since no interactions of group and electrode were found, the reported differences among the groups represent main effects over all electrodes. Significant differences among the groups in P300 latency were found (F (3, 46) = 5.66, $P = 0.002$). The young controls had shorter P300 latencies than each of the other groups, including the older controls. The demented individuals had longer P300 latencies than both the depressed group and the older controls. P300 latency differences between the depressed group and the older controls were not significant.

Significant latency differences among the groups were also found for N100 (F (3, 46) = 3.10, $P = 0.035$), P200 (F (3, 46) = 3.85, $P = 0.015$),

TABLE I

Mean latency (msec) and standard deviations (parentheses) from conventional averages.

		Component			
		N100	P200	N200	P300
Young	Fz	97.9 (13.8)	180.0 (11.5)	238.4 (25.6)	335.9 (21.6)
	Cz	96.7 (10.3)	172.3 (9.7)	231.3 (26.6)	336.2 (25.1)
	Pz	92.3 (8.2)	170.7 (14.4)	227.1 (25.7)	337.2 (24.5)
Older	Fz	112.6 (10.7)	201.3 (14.8)	261.2 (22.4)	366.9 (32.1)
	Cz	109.1 (9.9)	193.9 (15.0)	260.1 (21.7)	372.9 (36.3)
	Pz	107.2 (12.4)	191.5 (19.2)	256.8 (22.7)	377.9 (34.4)
Demented	Fz	103.5 (15.5)	201.7 (21.5)	291.7 (38.2)	389.8 (45.4)
	Cz	107.7 (15.0)	188.3 (19.6)	281.0 (37.8)	392.2 (50.3)
	Pz	106.6 (14.5)	181.5 (22.2)	271.7 (39.8)	403.7 (53.5)
Depressed	Fz	105.9 (18.6)	190.6 (15.6)	247.8 (37.0)	357.2 (27.0)
	Cz	104.8 (11.2)	183.4 (19.6)	246.5 (34.7)	356.8 (24.3)
	Pz	101.9 (10.0)	182.5 (22.0)	238.5 (24.1)	364.0 (28.5)

TABLE II

Mean latency variability (msec) and standard deviations (parentheses) from single trials.

		Component			
		N100	P200	N200	P300
Young	Fz	19.4 (5.4)	25.5 (7.0)	52.8 (7.8)	53.5 (12.6)
	Cz	17.4 (4.9)	25.4 (6.6)	52.6 (11.7)	58.7 (13.5)
	Pz	21.2 (4.4)	27.9 (6.8)	49.6 (8.8)	54.7 (15.9)
Older	Fz	21.1 (4.8)	26.3 (6.7)	48.8 (8.6)	57.7 (10.5)
	Cz	18.7 (5.6)	24.7 (7.0)	51.2 (9.8)	61.4 (11.4)
	Pz	22.4 (4.8)	29.3 (5.9)	47.8 (6.2)	59.4 (9.9)
Demented	Fz	23.0 (5.3)	28.7 (6.2)	57.1 (6.4)	74.0 (7.9)
	Cz	20.5 (4.6)	26.4 (5.9)	56.0 (9.8)	72.1 (10.0)
	Pz	24.7 (4.1)	30.6 (4.7)	56.1 (7.6)	73.4 (11.6)
Depressed	Fz	22.1 (3.3)	27.8 (6.3)	53.4 (14.3)	65.8 (12.9)
	Cz	19.6 (3.9)	24.4 (4.9)	48.0 (11.5)	67.3 (11.9)
	Fz	24.3 (2.7)	29.6 (3.9)	47.0 (10.4)	64.9 (14.1)

and N200 (F (3, 46) = 6.57, $P = 0.001$). For both N100 and P200, individuals in the young group had shorter latencies than the other groups. N200 latency differences among the groups paralleled those for P300. Component amplitudes from the conventional averages (N100, P200, N200, P300) did not significantly differentiate the groups.

Latency variability measures

Table II shows the mean latency variability for each group and ERP component at each electrode site. These values represent the standard deviation of the single-trial peak latencies for each subject, averaged over subjects (with the standard deviation over subjects in parentheses). Significant differences among the groups were obtained only for P300 (F (3, 46) = 8.64, $P < 0.001$). Since no interactions of group and electrode were found, the differences among the groups represent main effects over all electrodes. Demented individuals had significantly greater variation in P300 latency over trials than both younger and older controls. Depressed patients also had greater P300 latency variability than both control groups. The demented group had greater P300 latency variability than the depressed group. In the demented group, P300 variability ranged between 56.4 and 85.9 msec, and P300 variability in the depressed group ranged between 42.1 and 78.0 msec. In the younger

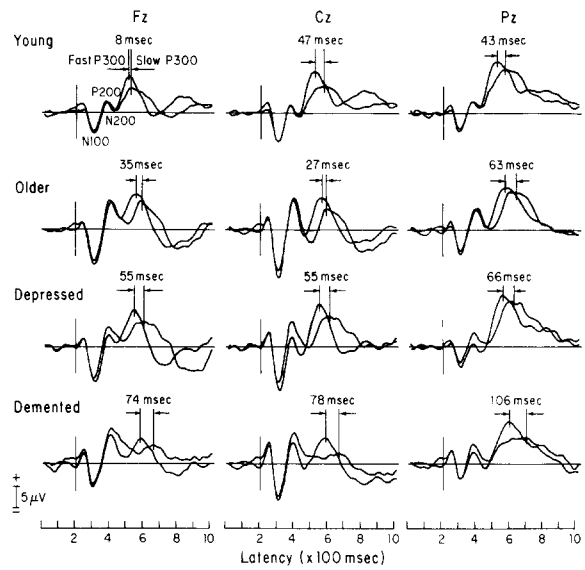

Fig. 1. Grand averages based on fast and slow P300 latencies for the young, older, depressed, and demented groups at the Fz, Cz, and Pz electrode sites. Fast and slow wave forms were derived for each individual by separately averaging single-trial P300 latencies that were below and above the mean, respectively. These wave forms were then grand averages over all subjects in each group. Stimulus onset and the end of the baseline period are indicated by the solid vertical line at 200 msec.

and older controls, the ranges were 26.9–65.6 and 39.5–75.9 msec, respectively. Differences in P300 latency variability between younger and older controls did not reach significant levels.

Measures of latency variability for the other components (N100, P200, and N200) did not differ significantly among the groups. Corrected component amplitudes derived from the single-trial procedure (N100, P200, N200, P300) also did not significantly differentiate the groups.

The differences in P300 latency variability among the groups can be illustrated by forming 'fast' and 'slow' P300 latencies. Fast and slow wave forms were derived for each individual by separately averaging single-trial P300 latencies that were below and above the mean P300 latency, respectively. Fig. 1 shows grand averages based on fast and slow P300 latencies at Fz, Cz, and Pz over subjects in the young, older, demented, and depressed groups. At Fz, note that the average difference between the fast and slow P300 latency (measured from the grand average) for the demented group is 74 msec, compared to 55, 35, and 8 msec for the depressed, older control, and young control groups, respectively. At Cz and Pz, these differences measure 78, 55, 27, and 47 msec, and 106, 66, 63, and 43 msec, respectively.

Regression analysis

Regression analysis allowed a comparison of the diagnostic sensitivity of P300 latency (conventional average) and P300 latency variability on an individual basis. In Fig. 2, the regression line relating age and P300 latency from the conventional averages for the normal controls is given, along with 1.0 and 2.0 SEEs around the mean. Individual P300 latencies for the young and older controls, demented individuals, and depressed subjects are also plotted. Fig. 3 provides the same regression information for P300 latency variability based on single trials. (Since heterogeneity of variance between the young and older groups could affect the accuracy of the regression analysis, for both P300 latency and P300 latency variability, the variances of the residuals as well as of the individual latencies and latency variabilities for the young and older groups were compared using the Bartlett test for homogeneity of variance

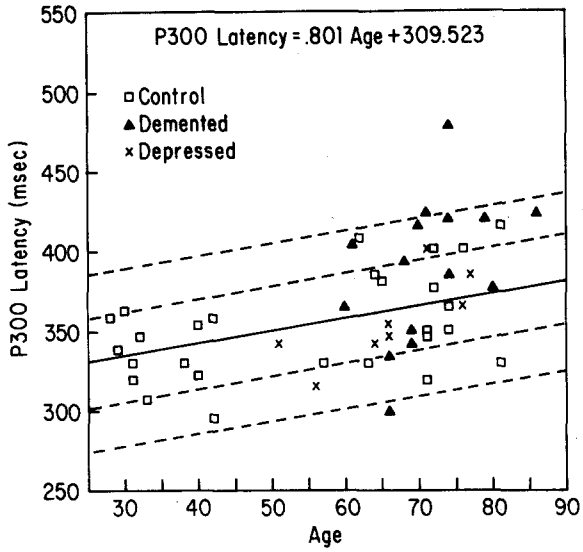

Fig. 2. Regression analysis relating age and P300 latency at Fz for the young and older controls. The regression line (solid line) and 1.0 and 2.0 standard errors of the estimate (SEEs, broken lines) are indicated. P300 latency for the depressed and demented individuals is also plotted.

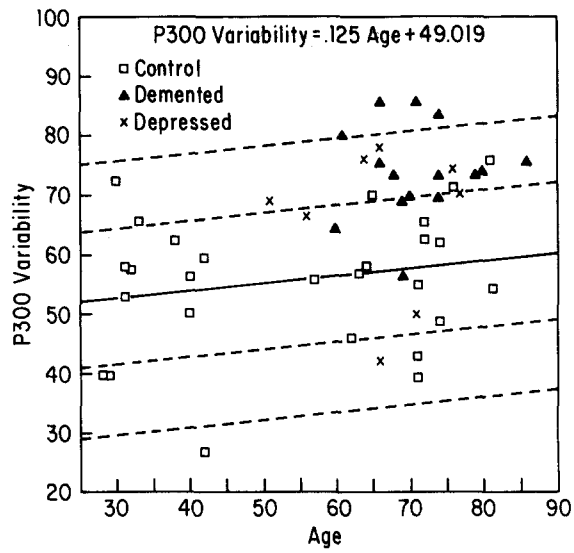

Fig. 3. Regression analysis relating age and P300 latency variability at Fz for the young and older controls. The regression line (solid line) and 1.0 and 2.0 standard errors of the estimate (SEEs, broken lines) are indicated. P300 variability for the depressed and demented individuals is also plotted.

(Walker and Lev 1953; Wall 1986). No significant differences between the variances of the 2 groups were found.)

The regression analyses are given for the Fz electrode site, where the differences in P300 latency variability among the groups were largest. For P300 latency (conventional average) at Fz, note that only 2 of the 15 demented individuals are beyond 2.0 SEEs of the regression line for normals at the appropriate age (Fig. 2). P300 latency variability for the same 2 demented individuals and 2 additional demented subjects is also beyond 2.0 SEEs (Fig. 3). For both P300 latency (conventional average) and P300 latency variability, the cognitively impaired individuals rated as abnormal using the 2.0 SEE criterion were classified clinically and by MMS score as moderately to severely demented. For the depressed group, in contrast, none of the 8 patients had P300 latency or P300 latency variability outside 2.0 SEEs. Also, none of the controls had P300 latency or P300 latency variability outside 2.0 SEEs. MMS score was significantly correlated with P300 latency at Fz ($r = -0.69$, $P < 0.01$) and Pz (-0.39, $P < 0.05$), and approached significance at Cz (-0.34, $P < 0.10$). Correlations between MMS score and P300 latency variability were significant at Fz ($r = -0.40$, $P < 0.05$), and approached significance at Cz (-0.34, $P < 0.10$) and Pz (-0.35, $P < 0.10$).

ERP component-RT associations

Mean RTs (and S.D.s) to the targets for the young, older, depressed, and demented groups are given in Table III. The RT differences among the groups were significant (F (3, 45) = 21.6, $P < 0.001$), and paralleled the results for P300 latency from the conventional averages. The young controls had shorter RTs than each of the other groups, including the older controls; demented subjects also had longer RTs than both depressed individuals and older controls. RT differences between depressed individuals and older controls were not significant.

Table III also shows the correlations between component latencies determined from single trials and the corresponding RT for each group at Fz, averaged over subjects. The multiple correlation between the combined latency for each ERP component and RT is also shown. These correlations were generally of low magnitude and did not reach significant levels. For example, P300 latency accounted for only 4% of the variance in RT in the young group, and 7% in the older controls. In the depressed and demented individuals, P300 latency accounted for only 12% and 3% of the variances, respectively. The correlations between component latencies and RT did not differentiate the groups.

Discussion

These results indicate that the ERP component latency (conventional average) and ERP component latency variability measures were useful in describing *group differences* among demented, depressed, and age-matched control groups, but were not sufficiently sensitive to distinguish *individual subjects* and thus serve as a clinical aid in differential diagnosis. Both the group (ANOVA) and the individual (regression) analyses revealed a lack of

TABLE III

Mean reaction time (S.D.) and correlations between reaction time and component latencies (Fz) from single trials.

	RT	(S.D.)	Component				
			N100	P200	N200	P300	N100 + P200 + N200 + P300
Young	300.9	(61.2)	0.19	0.25	0.21	0.19	0.45
Older	481.3	(92.8)	0.12	0.11	0.22	0.26	0.39
Demented	559.0	(71.8)	0.13	0.16	0.28	0.17	0.42
Depressed	470.3	(81.2)	0.13	0.08	0.34	0.34	0.52

sensitivity and specificity in the ERP measures. The addition of component latency variability did not significantly increase the diagnostic sensitivity of the ERP measures to dementing illness. Of the ERP components measured, the P300 peak provided the most consistent differences among the demented, depressed, and control groups. Using the ANOVA procedure, the demented group had longer P300 latencies (conventional average) and larger P300 latency variability than the older controls. Demented subjects also had longer P300 latencies and greater P300 variability than the depressed group. The depressed group had greater P300 variability, but not longer P300 latency, than older controls. In the regression analysis, no misclassifications of depressed patients occurred using the 2.0 SEE criterion, but only a small percentage of demented individuals were correctly classified as abnormal (13% for P300 latency from the conventional average; 27% for P300 variability).

The low percentage of correct classifications of demented subjects using both P300 latency and P300 latency variability is in agreement with Pfefferbaum et al. (1984b), but in conflict with previous reports of the relatively high sensitivity of P300 latency from conventional averages to dementing illness (Squires et al. 1980; Brown et al. 1982; Syndulko et al. 1982). Correct classification rates as high as 80–83% have been reported using P300 latency from conventional averages. There are several differences among studies which may account, in part, for the conflicting results, including task requirements and severity and etiology of the demented patients. As an indication that procedural factors may affect estimates of the sensitivity of P300, Gordon et al. (1986) replicated the counting task used by Squires et al. (1980) and obtained a similar percentage (80%) of correct classifications of demented subjects. Other studies which have used counting tasks have observed similar abnormality rates (Brown et al. 1982; Syndulko et al. 1982). Pfefferbaum et al. (1984b), however, required subjects to press an RT key to the target and, in addition, to detect 2 different infrequent events. Individuals in the present study were also instructed to press an RT key to the targets, but only 1 type of target stimulus was used. While it is unlikely that this task difference could account for the large discrepancies among some of these studies, it is possible that a counting task is more demanding than the RT task and leads to greater inaccuracies and fluctuations in task performance which are reflected in P300 latency, especially in a demented group. For example, the counting task may contain a larger memory component (continuously updating the count) than the RT task. Increased P300 latencies as well as greater P300 amplitudes have been observed in the count compared to the button press versions of the target detection task (Barrett et al. 1987; Polich 1987). However, Picton et al. (1984) found no difference in P300 latency when instructions to count and instructions to button press to targets were compared. Also, the rate of stimulus presentation used in the present study (every 2–3 sec) was slower than the presentation rate used in most previous studies (every second), which could be less demanding and lead to some differences in task performance.

Differences in the etiology and severity of the demented individuals tested are more likely to be major sources of discrepancies among studies in differentiating demented individuals using P300 latency. Different patterns of P300 latency deviations from normal are apparent in demented individuals as a function of the etiology of the illness. Squires et al. (1980), for example, showed that the average P300 latency deviation from normal of patients with presumed Alzheimer's disease was 2.8 S.D., compared to a deviation of 4.1 S.D. in patients demented due to metabolic encephalopathy. Additionally, the available evidence suggests that ERP measures can separate more severely demented individuals from controls, but not those with mild dementia (Patterson et al. 1984; Syndulko et al. 1984; Thompson et al. 1986). Differences among studies in the severity of the groups tested may lead to different estimates of the sensitivity of P300 latency or P300 latency variability. The mean MMS score of the demented subjects tested by Pfefferbaum et al. (1984b), for example, was in the mildly demented range (22.4 and 21.4 for individuals participating in the auditory and visual paradigms, respectively), while other studies have tested quite severely demented groups (e.g., Brown et al. 1982). The negative correlations ob-

tained in this study between MMS scores and P300 latency and latency variability offer some support for the suggestion that severity of dementia can affect P300 latency and P300 latency variability. Variations in the level of cognitive impairment within the psychiatric groups may also affect estimates of the specificity of P300. The 'misclassification' of psychiatric groups by P300 latency may simply reflect the presence of a mild cognitive impairment in some members of the group. However, the degree of cognitive impairment defined by the MMS may not always be a useful predictor of P300 latency since in the present study some of the subjects rated as severely demented had normal P300 latency and variability. More definitive answers regarding the source of the differences among studies in estimates of the sensitivity of P300 in the differential diagnosis of dementia will require further study.

The addition of ERP component variability did not appear to significantly increase the sensitivity of ERP measures in distinguishing demented individuals. Instead, the P300 variability measure closely paralleled the findings for P300 latency from the conventional averages. It may be that P300 latency and P300 latency variability reflect similar processes within the information processing system and hence exhibit similar differences among the groups. It is important to note that estimates of ERP component latency variability over single trials using the template-correlational procedure are very sensitive to factors such as the number of trials used to estimate variability, and to signal-to-noise ratio. While a similar number of trials was used to estimate ERP component variability in each of the groups tested, possible group differences in signal-to-noise ratio, especially within the demented group, could influence estimates of latency variability in 1 group compared to another. Several studies have shown the effect of signal-to-noise ratio on the single-trial procedure (Ruchkin and Sutton 1979; McCarthy et al. 1984; Michalewski et al. 1986).

The slope of the function relating age and P300 latency (0.8 msec/year) was comparable to, but slightly less than, the age/P300 latency slopes given in some previous reports (Goodin et al. 1978; Syndulko et al. 1982; Pfefferbaum et al. 1984a; Picton et al. 1984). The lower limit of the age range in the present study (approximately 8–10 years older than in previous studies) could account for a slight reduction in slope. Also, the age/P300 latency function may reflect small variations according to recording site. In the present study, for example, the slope found at the frontal site (0.8 msec/year) was slightly less steep than the slope observed at the central (1.0 msec/year) and parietal (1.0 msec/year) sites, comparable to the results of Syndulko et al. (1982). Variations in the age/P300 latency slope may also be affected by procedural differences or task difficulty. Picton et al. (1984), for example, found a slightly steeper age/P300 latency slope when instructions to press an RT key to targets in a target detection task were given, compared to instructions to count targets. Compared to P300 latency from the conventional average, we found that the effect of age on P300 variability was small, with a slope of only 0.125 msec/year.

It is interesting to note that group differences in RT paralleled the results for P300 latency. Reaction times were longer in the older than in the younger controls. Demented subjects had longer RTs than both the depressed and older control groups, but the depressed and older control groups were not differentiated by RT. Correlations between single-trial ERP component latency and RT did not differentiate the groups. Pfefferbaum et al. (1984b), in contrast, found significantly reduced RT/P300 latency correlations in the demented group compared to control and psychiatric groups for their visual target detection task. The association between P300 latency and RT is affected by the degree to which both reflect overlapping components of the information processing system (Hillyard and Kutas 1983; Magliero et al. 1984). For example, a response associated with incomplete evaluation of the stimulus may lead to a lower P300 latency/RT correlation (Magliero et al. 1984). Additionally, speed vs. accuracy instructions (Kutas et al. 1977; McCarthy and Donchin 1983; Pfefferbaum et al. 1983) and factors of task difficulty (Ritter et al. 1979; Hillyard and Kutas 1983) can affect the observed association between ERP component latency and RT.

Regardless of the source of the discrepancies among studies in estimation of the sensitivity of ERP component latency or latency variability to dementing illness, the conflicting results suggest a conclusion that ERP measures using the 'oddball' target detection paradigm are not sufficiently sensitive or specific to be used in differentiating demented individuals. While memory is certainly implied in the target detection paradigm, the task is not designed to test specific areas of cognitive impairment in demented individuals. Rather, the target detection paradigm probably requires the identification of an environmental stimulus change, a cognitive task that is unlikely to be affected until late in the dementing process. The clinical utility of ERP measures in indexing changes in mental status will only be improved by designing test procedures to measure specific areas of cognitive function that may be involved in dementing illnesses, such as memory, language, and spatial relations. The application of a task requiring the classification of a probe item as a member of a previously presented memory set (Sternberg 1966, 1969; Roth et al. 1975; Adam and Collins 1978; Ford et al. 1979) to measure ERPs in individuals with auditory short-term memory deficits (Starr and Barrett 1987) is an example of the usefulness of such an approach.

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