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Disordered auditory short-term memory in man and event-related potentials.

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of this disturbance in the short-term memory system is unclear and proposals including disorders of either storage (Shallice and Warrington, 1970), a perceptual analysis system (Allport, 1984) or of response selection (Kinsbourne, 1972) have been postulated. Alterations of auditory processes are unlikely because these patients have normal memories for sequences of sounds such as barks, train whistles and thunder but not for sequences of words (Shallice and Warrington, 1974).

Event-related potentials may be relevant for helping to understand this clinical syndrome. These potentials can be recorded with relative ease from scalp electrodes using computer averaging techniques. Investigations in normal subjects have indicated that at least one of the components, a positive deflection occurring at a latency of approximately 300 ms and designated by the conventional potential nomenclature as 'P300', reflects some aspects of neural processes underlying memory. This is based on the finding that the amplitude of P300 evoked by the target in tasks in which the subject is engaged in the detection of a rare event is influenced by both its frequency of occurrence, that is, the global probability (Donchin *et al.*, 1978), as well as by subjective expectancies (Duncan-Johnson and Donchin, 1977). Moreover, there have been several studies of event-related potentials in normal subjects engaged in probe identification tasks that test short-term memory capacities in which P300 amplitude and latency change in an orderly manner as the number of items to be remembered increases (Marsh, 1975; Roth *et al.*, 1975; Gomer *et al.*, 1976; Adam and Collins, 1978; Ford *et al.*, 1979; Pfefferbaum *et al.*, 1980; Kramer *et al.*, 1986). Among the cognitive processes comprising memory, P300 seems to be associated with stimulus classification rather than response selection (Pritchard, 1981). Thus the combination of measures of P300, performance accuracy and reaction times might provide a means for attributing disorders of memory to particular stages of the memory process.

We have had the opportunity to study 4 patients fulfilling the criteria of conduction aphasia using measures of both behaviour (response accuracy and reaction time) and event-related potentials (latency and amplitude) as they engaged in a digit probe identification task presented in both auditory and visual modalities. The results provide quantitative measures that shed insights into some of the neural bases underlying the patients' disorder of auditory short-term memory.

CASE REPORTS

Four patients with disordered auditory short-term memory were tested together with 5 healthy age-matched controls. The patients' impairment was manifested by a reduced auditory digit span and word list repetitions that were out of proportion to their other neurological deficits. Cases 1 and 2 have been described previously in papers detailing their memory and language impairments. Cases 3 and 4 have not been reported previously. The results of their Wechsler Adult Intelligence Scores

TABLE 1. NEUROPSYCHOLOGICAL TEST SCORES: AGE ADJUSTED WITH 100 AS THE MEAN

Test	*Patients*				
	1	*2*	*3*		*4*
			Test a	*Test b***	
*WAIS**					
Verbal	61	87	61	93	65
Arithmetic	4	8	2	10	4
Similarities	7	11	6	8	4
Digit Span	1	3	0	6	2
Vocabulary	6	9	7	11	8
Performance	93	101	92	118	104
Picture Completion	9	9	7	11	9
Block Design	7	7	12	13	7
Picture Arrangement	10	12	3	14	14
Digit Repetition					
Auditory presentation	1	4	2	4	2
Visual presentation	5	5	3	5	3

* WAIS = Wechsler Adult Intelligence Scale. ** Tests a and b refer, respectively, to the initial and subsequent evaluations.

and digit repetition abilities are contained in Table 1. The patients have the common features of a reduction of their Verbal Scores compared to Performance Scores with the Digit Span being reduced out of proportion to the other tests. The number of digits they could repeat after auditory presentation was lower than after visual presentation.

Case 1

This patient, referred to as R.A.N. in McCarthy and Warrington (1984), is a 53-year-old right-handed man who had a sudden onset of right hemiplegia, right hemisensory loss and aphasia four years earlier due to a haemorrhage into the left parietal lobe. No specific cause for the haemorrhage was defined. The patient's deficits have gradually improved. At the time of this study he had slight right-sided weakness with marked sensory impairment involving position sense and two-point discrimination. Sharp-dull appreciation was only slightly impaired. There were no visual field deficits. His spontaneous speech was fluent with occasional phonemic and paraphasic errors. There were some naming difficulties and comprehension was good. His ability to repeat sets of digits or words was markedly impaired. The digit span to auditory presentation was between one and two items, whereas to visual presentation he could repeat correctly strings of five digits. He has had both generalized and right-sided focal sensory seizures since recovering from the acute phase of the illness that are being treated with phenytoin and phenobarbital. A CT scan at the time of this investigation showed a well-demarcated area of cerebral damage involving the left parietal lobe in the region of the angular gyrus.

Case 2

This patient, described as J.B., Case 2, in Warrington *et al.* (1971) is a 50-year-old right-handed woman who had a 'tennis ball sized' meningioma removed from the left temporoparietal region in

1970. Subsequently she had language difficulties which improved within a month of the operation leaving her only with an impaired ability to repeat spoken names or numbers that has also gradually improved over the intervening years. At present her auditory digit span is four items and the visual span is five items.

Case 3

This patient is a 46-year-old right-handed man who had an acute onset of language impairment three days before his being studied by us. His original deficits consisted of marked naming difficulties with only slightly impaired comprehension and spontaneous speech. There were no visual field deficits. His digit span to spoken digits was only two items and to visually presented digits three items when the first set of event-related potentials were recorded (test a). He rapidly improved and when event-related potentials were recorded again three weeks later (test b), the auditory digit span had improved to four items and the visual span to five items. Speech was fluent with only occasional naming difficulties. An MRI scan showed infarction between the posterior temporal and inferior parietal lobes.

Case 4

This patient is a 40-year-old right-handed man who had a subarachnoid haemorrhage from a left middle cerebral aneurysm two years previously. The aneurysm was clipped. On recovery from the acute phase of the illness he had a right hemiplegia and marked speech impairment. The visual fields were full. These disabilities improved so that at the time of testing there was only slight weakness of the right hand. Speech was slow with marked naming difficulties but comprehension was excellent. The auditory digit span was only two items and the visual span only three items. In all other respects he is independent in managing his life and finances. He has had generalized seizures and is currently receiving phenytoin and carbamazepine.

Controls

These were selected to be close in age to the patients and ranged from 40 to 57 years. There were 2 females and 3 males. One of the women was the wife of the first patient, one of the men was a laboratory technician in the hospital and the other 3 subjects were neurologists. Informed consent was obtained from both patients and controls participating in these experiments.

METHODS

Event-related Potential Recordings

Silver disc electrodes were fixed on the scalp at Fz, Cz, Pz, C3, C4, P3 and P4 and each referenced to linked electrodes on the ear lobes. Eye movements were monitored by recording between electrodes above and below the right eye. Those trials containing high amplitude potentials due to eye movements were not included in the averages. The amplifier band pass was 0.01 Hz to 5 kHz. Electrical activity was sampled by the computer over a time base of 960 ms (dwell time 3.75 ms) or 1280 ms (dwell time 5.0 ms) and, in one instance in Case 1, at 1920 ms (dwell time 7.5 ms). All of the analysis times included a prestimulus baseline period of 120 ms.

Experimental Paradigms

Detection of infrequent stimuli, the 'oddball' tasks (test a). Event-related potentials in all the patients were recorded during the detection of an infrequent signal in both auditory and visual modalities. In the normal group of 5 subjects, 4 were tested with the auditory task and 2 with the visual task

and only the results from the auditory task were analysed. In the auditory task a sequence of two tones, 1.5 and 2.0 kHz in frequency, 50 ms in duration with rise and fall times of 10 ms, an intensity of between 50 and 70 dB nHL and an interstimulus interval of 1.2 s, were presented through earphones. The intensity level used was selected by the subject as being comfortable. The probability of the tone being higher pitched was 0.15. The subject was to press a response button when the higher pitched tone occurred. Separate averages to the rare and frequent auditory signals were made. Twenty-five trials to the higher pitched tone uncontaminated by eye movements were collected and a duplicate set of trials run again. In the visual task the two stimuli were an infrequent 'X' (probability 0.15) and a frequent 'T'. The subject was to press the response button every time the 'X' appeared. The visual stimuli were presented on a display placed 1.5 m in front of the subject with each letter subtending a visual angle of 12 min horizontally and 15 min vertically. The number of trials collected and their separation into rare and frequent categories was the same as in the auditory protocol. Reaction times for both modalities could be identified for up to 840 ms after stimulus presentation. A response to a stimulus occurring after that period could not be distinguished from the absence of response.

Detection of a probe digit, the 'Sternberg' tasks (test b). The experimental paradigm employed closely paralleled that described by Sternberg (1966) to evaluate short-term memory. Digits (1 to 9) were presented in strings of one or three items (in Case 1 a two-item string was also used). The time separation between each item in the string was 1.2 s. A 3 s pause followed the last item of the string before a test item, the probe, occurred (fig. 1). The probability that the probe was a member of the preceding string was 0.5. The subjects were instructed to press a response button if they identified the probe item as a member of the preceding string. If the probe was not in the preceding string the button was not to be pressed. The occurrence of a response (button press) was defined for each probe presentation along with its latency (reaction time). Event-related potentials were subsequently classified as being associated with a correct response (hit), a correct absence of response (correct rejection), a failure to respond (miss) or a response to a probe digit not occurring in the preceding set (false alarm). Five seconds elapsed after the presentation of the probe before the next trial commenced signalled by the word 'start' followed 0.85 s later by the items in the string. In contrast to the 'oddball' paradigm, the occurrence of a button press in this task could be defined for 4150 ms after the presentation of the probe, allowing event-related potentials to the probes to be accurately classified along with their associated reaction times. The digits contained in each trial were selected in a pseudorandom manner with the restriction that no probe digit could occur in two consecutive trials and no more than three consecutive correct or incorrect probes occurred in sequence. The proportion of correct probes relative to the position of the matching digit in the preceding string (i.e., first, second or third) was adjusted to be approximately equal.

The digits were presented in either of two ways in separate runs of the experiment. One was visually on a videoscreen located 2 m in front of the subject with each digit subtending a visual angle of 12 min horizontally by 15 min vertically. The raster display of the videoscreen produced a variable delay of up to 20 ms between the signal to start the display and the actual appearance of the digit. No effort was made to correct for this variability in the subsequent analysis of the event-related potentials. The second presentation mode was acoustic. The phonemic sequences comprising each digit and the word 'start' were generated by a personal computer (BBC model B fitted with a speech synthesizer) and presented by earphones at an intensity between 40 and 60 dB nHL, depending on each subject's assessment of what was 'comfortable and clear'. The onset of the earphone voltages occurred within 20 ms of the signal to initiate speech production. Both the test items and the probe were presented in the same modality except on one testing session for Case 1 when the modality of the test string and the probe could differ.

Procedure

The subjects were presented with a series of practice trials using the digit probe identification task in the visual modality to acquaint them with the procedures and to instruct them how to relax their

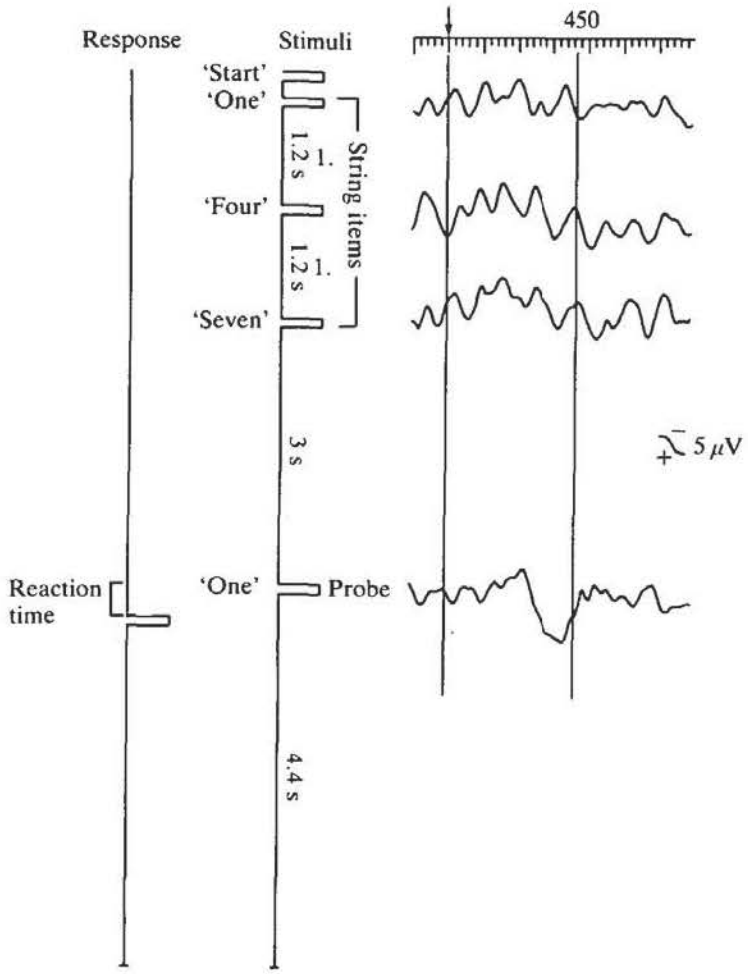


FIG. 1. Stimulus sequence employed in the probe identification tasks. The 'Stimuli' line contains pulses indicating the initiation of the trial ('Start') followed by the string items to be remembered and the probe to be identified. The temporal relationship between the items is noted in seconds (s) between the pulses. The stimuli could be presented acoustically or as arabic symbols in the visual modality. The occurrence of the button press to the probe is indicated in the line labelled 'Response' and its latency as 'Reaction time.' Examples of the EEG of individual trials (recorded between Pz and linked earlobes) accompanying both the string items and the probe are to the right of the figure. The time difference between the large vertical marks on the time base is 120 ms. The arrow at the initial vertical line marks the stimulus onset and the second vertical line marks the 450 ms poststimulus time. Note the appearance of a large positive deflection in the potential evoked by the probe at approximately 400 ms.

facial muscles and reduce the frequency of blinking. Data collection began with the digit sequences being presented in blocks of 20 trials beginning with the one-item test string in the visual modality and alternating in a balanced design with the auditory mode. The three-item sequences followed after four blocks of the single item string had been presented and then the one and three-item test sequences alternated until at least 20 trials containing a correctly identified in-set probe (hits) for the single item sequences and 40 trials for the three-item sequences in each modality had been collected. In one of the patients (Case 1) we also presented test strings containing two items. At the end of the probe detection tasks the subjects were tested with the infrequent stimulus detection tasks, i.e., the 'oddball' paradigms.

Data Analysis

The event-related potentials for each trial were stored in digital form on magnetic tape. These single trials were sorted according to response type and then combined to make group averages for 'hits', 'misses', etc. Averages were filtered with a zero phase shift low band pass digital filter having a cut-off at 30 Hz for display and measurement. The amplitudes and latencies of the peaks of the components were measured at those electrode sites where they were most prominent (*see* figs 2 and 3 for examples of the wave forms). Amplitude was defined as the difference between the mean of the baseline voltage in the 120 ms preceding stimulus presentation and the voltage at the peak of the component. In the auditory 'oddball' tasks there was a sequence of components designated as N100 (largest at Fz or Cz), P200, N250 and P300 (all largest at Cz or Pz). In the visual tasks the sequence was similar except that the N100 could not be identified consistently. In the digit identification tasks in the auditory modality the earliest consistent peak occurred at about 150 ms, was of negative polarity (N150) and was of largest amplitude frontally. In the visual modality the earliest consistent peak also occurred at approximately 150 ms but was of positive polarity (P150) and most prominent frontally or centrally. In both modalities a negativity occurred in response to the probe at approximately 200 to 300 ms that was largest centrally and parietally. This component (N250) was occasionally separated from the N150 component by a brief positive-going deflection. However, in many averages to the auditory probe the trace remained negative after the N150 with several smaller negative deflections superimposed until it turned positive to form the next component. This turning point was selected as the latency of N250. Its amplitude was often slightly positive relative to the prestimulus baseline. The subsequent large positive deflection (P450) was long-lasting and did not return to baseline before the end of the analysis window (960 or 1280 ms). We chose to measure amplitude at the peak of this deflection at the midline parietal electrode (Pz). This was done by drawing lines paralleling the positive-going slope and the sustained positive shift and choosing the latency at their point of intersection. An earlier deflection (P350) was most prominent frontally (Fz) but this component was not measured because it could not be identified consistently in every subject in the control population.

Latency and amplitude measures were made on the averages evoked by the probes classified as hits, correct rejections, misses or false alarms. A second set of analyses was performed separating the single trials comprising the correctly identified probes (hits) into new averages formed as a function of the associated reaction times, i.e., the fastest third, the middle third and the slowest third. A third set of analyses was performed on the event-related potentials associated with correctly identified probes (hits) as a function of the position of the matching digit in the preceding string, that is, first, second or third item.

Reaction times and P450 latencies and amplitudes were analysed using repeated measures analysis of variance (ANOVA) with program BMDP2V of the Biomedical Computing Package (Dixon, 1983). Although an unweighted means solution may be more appropriate for comparing groups of unequal size in repeated measures designs, the least squares ANOVA provided by program BMDP2V produces a similar result when the group sizes are not markedly different, as is the case here (Winer, 1971). Probability values for significant within group factors reported in this paper are those obtained using the Greenhouse-Geisser correction available in program BMDP2V.

RESULTS

Performance

Performance was relatively free of errors on digit probe identification for normal subjects with the exception of an occasional response to a probe not contained in the preceding test string (false alarm). In contrast, the patients had varying degrees of difficulty on these tasks (Table 2). Case 1, tested on three occasions over three

TABLE 2. PERFORMANCE ON THE DIGIT IDENTIFICATION TASKS

Modality	*Auditory*				*Visual*			
String length	*1*		*3*		*1*		*3*	
Probe response	*%Hits*	*%FA*	*%Hits*	*%FA*	*%Hits*	*%FA*	*%Hits*	*%FA*
Patients								
1, a	100	0	62	11	100	0	96	4
b	100	0*	81	15	100	0*	100	0
2	100	0	84	4	100	0	85	1
3, a	100	0	77	0	100	0	92	0
b	100	0	100	0	100	0	96	0
4	77	7	63	8	87	2	60	0
Normals	100	<1	100	1	100	<1	100	3

Hits = correct responses to in-set probes. FA = false alarms; incorrect responses to out-of-set probes. The number of trials contributing to these measures ranged from 29 to 81. * String length of 2 in the auditory modality: Hits = 90%, FA = 10%; String length of 2 in the visual modality: Hits = 98%, FA = 0%. a and b refer respectively, to the initial and subsequent evaluations.

weeks (two of which are in Table 2 and the other is in Table 4) had a stable and substantial deficit on the three-item auditory task. With a two-item auditory string the deficit was much less. Case 2 showed a slight impairment in performance in both modalities to strings containing three items. Case 3 had a greater impairment on the three-item string during auditory (77% accuracy) compared to visual presentation (92% accuracy) on the initial testing session (test a). The improvement in performance to 100% for the auditory modality and to 96% for the visual modality on the second test (test b) coincided with the improvement in his clinical condition. Case 4 did not perform much above chance in either modality when the number of items in the string was three and even missed a number of matching probes when only one item was presented. This latter patient was the only subject whose performance on detecting the rare stimulus in the 'oddball' task was impaired as judged by the absence of a button press within 840 ms of the presentation of the target on one-third of the trials and by a false alarm rate of approximately 10%.

Further data analysis is described first in terms of overall performance using reaction times and event-related potential wave forms obtained from all accepted trials and secondly, in terms of data obtained by selectively averaging potentials according to reaction time or to the position of the matching stimulus in the presentation set.

Reaction Times

Mean reaction times and SDs are given in Table 3 and significant comparisons from the repeated measures ANOVA for the digit identification task appear in Table 6. These analyses include only the initial testing session for the first 3 cases and exclude Case 4 whose performance on the three-item string was at chance and both impaired and slowed on the one-item string. The patients' reaction times were

TABLE 3. REACTION TIMES IN MS TO THE PROBES ON THE DIGIT IDENTIFICATION AND TO THE TARGETS ON THE RARE SIGNAL DETECTION TASKS (MEAN (SD))

Modality	*Auditory*			*Visual*				
Test	*1-item*	*3-item*	*Rare*	*1-item*	*3-item*	*Rare*	*Aud 3–1*	*Vis 3–1*
Patients								
1, a*	609(129)	915(304)	578(118)	477(58)	607(123)	562(142)	306	130
b**	561(123)	811(223)	393(76)	477(78)	614(120)	NT	250	147
2*	629(108)	862(293)	426(120)	554(116)	710(277)	446(72)	233	156
3, a*	664(96)	1121(559)	414(93)	756(264)	779(311)	433(50)	457	23
b	740(80)	883(179)	NT	738(74)	770(136)	NT	143	32
4	1285(516)	1338(519)	?	1224(224)	1348(469)	?	53	124
$\bar{X}$ of*	634(28)	966(137)	473(91)	596(144)	699(87)	480(71)	332	103
$\bar{X}$ of SD*	111(17)	385(150)	110(15)	146(106)	237(10)	88(48)	274	71
Normals								
Male, 53 yrs	450(87)	488(95)	332(52)	403(72)	457(85)	371(56)	38	54
Male, 55 yrs	306(49)	437(75)	250(30)	323(49)	407(75)	386(62)	131	83
Male, 57 yrs	564(83)	564(70)	296(45)	520(90)	579(123)	NT	0	59
Female, 40 yrs	478(98)	582(80)	NT	529(68)	576(120)	NT	104	47
Female, 53 yrs	569(80)	672(88)	498(74)	517(90)	585(80)	NT	103	68
$\bar{X}$	473(107)	549(90)	344(108)	458(92)	521(83)		76	63
$\bar{X}$ of SD*	76(18)	82(10)	50(18)	77(18)	97(23)		6	20

* Indicates the first testing session for the patients included in the mean ($\bar{X}$ of *) and mean ($\bar{X}$ of SD*). ** String length of 2 in the auditory modality: 733(285). String length of 2 in the visual modality: 594(105). NT = not tested. ? = values could not be derived due to slowed or absent responses. a and b refer, respectively, to the initial and subsequent evaluations.

significantly longer than those of the normal controls (g term in Table 6), especially for the auditory modality (sg term) and the three-item presentation set (ig term). The difference between the auditory reaction times in the three and one-item conditions compared with the visual reaction times in the same conditions was significantly greater for patients than controls (332 vs 76 ms for auditory, 103 vs 63 ms for visual; sig term in Table 6). Note from Table 3 the similarity of the reaction times between the two tests (a and b) in Case 1, a patient with stable clinical deficits and the shortening of the reaction times in Case 3, a patient whose deficits of digit span and word repetition improved in the period between the two tests.

As well as differences in absolute reaction times between patients and normal controls, the patients also showed considerably more variability (*see* SD columns in Table 3). This heightened variability is particularly prominent both with auditory strings of three items (mean of 82 ms in normals vs 385 ms in patients) and with the increase in auditory string length from one to three items (3 − 1 difference of 6 ms in normals vs 274 ms for patients).

Case 1 was tested with two-item strings in both the auditory and visual modalities. There was a substantial increase in both the mean reaction times (172 and 117 ms,

respectively) and their SDs (162 and 27 ms, respectively) compared with these measures to the one-item strings. Thus in this patient, both accuracy and reaction time became impaired when the number of items to be remembered exceeded the patient's digit span as defined by repetition of orally presented items.

The reaction times to the detection of the rare event in the auditory 'oddball' task were approximately 150 ms faster than those to the identification of the correct probe (hits) on the one-item auditory string in the Sternberg paradigm for both the patient and normal groups (Table 3). The increased variability of reaction times in the patients compared with normals is evident even in the 'oddball' task.

Performance and Reaction Time on Crossed Modal Digit Probe Identification

In Case 1 we had the opportunity to assess whether the deficits in accuracy and reaction time on the identification of the probe in the Sternberg tasks of auditory short-term memory were affected by presenting the items to be remembered in one modality and using a probe of the opposite modality. For example, could the poor performance with auditory presentation of both items to be remembered and the probe be improved by changing the probe presentation to the visual modality? Presenting the three-item string in the auditory modality and testing with a visual probe barely affected accuracy or reaction time (aud/aud vs aud/vis for three-item string in Table 4). In contrast, the mean reaction time lengthened by approximately 300 ms and its SD increased three-fold when a visually presented string was probed in the auditory mode (vis/vis vs vis/aud for three-item string in Table 4). Introducing an auditory component even with a one-item string impaired accuracy and slowed reaction time.

All these results document the impairment of short-term memory in these patients particularly when the auditory modality is employed. The main deficit is in ident-

TABLE 4. PERFORMANCE AND REACTION TIMES IN MS ON CROSS-MODAL DIGIT IDENTIFICATION TASKS IN CASE 1 (STRING MODALITY/PROBE MODALITY)

	Performance		*Reaction time*
	%Hits	*%FA*	*Mean(SD)*
String length of 1 item			
Aud/aud*	100	0	561(129)
Aud/vis	100	10	706(331)
Vis/vis*	100	0	477(78)
Vis/aud	93	0	712(142)
String length of 3			
Aud/aud	73	12	887(279)
Aud/vis	73	27	859(277)
Vis/vis	95	5	630(90)
Vis/aud	90	3	975(290)

Aud and vis = auditory and visual, respectively. Hits = correct responses to in-set probes. FA = false alarms; incorrect responses to out-of-set probes. * Values derived from test b of Table 2.

ifying probes when the number of items to be remembered increases from one to three digits. Even when the patients were correct in identifying matching probes their reaction times increased excessively and were more variable than for the shorter string length. Evaluation of the event-related potentials accompanying the presentation of the probes and the patients' responses may clarify some of the neural processes underlying this deficit of auditory short-term memory.

Event-related Potentials: Scalp Distribution

The scalp distribution of the averaged potentials from 1 normal subject to the correctly identified matching digits in the three-item auditory and visual probe identification tasks is illustrated in fig. 2. The components are labelled with P or N reflecting their polarity and a number indicating their approximate latency in ms. Note the presence of an early frontal component that is negative for the auditory modality (N150) and positive for the visual mode (P150). For the auditory modality there is an extension of the N150 negativity to form an N250 component, whereas for the visual modality the P150 is succeeded by an N250 component. In both modalities there follows a sustained high amplitude positive deflection that is widespread but largest over the parietal region. The positivity could be subdivided into an earlier P350 component prominent frontally and a parietal P450 component. The potentials in the probe identification tasks differ from the event-related potentials recorded to the detection of the infrequent stimulus in the 'oddball' task (fig. 2) by the absence of a P200 component, the long duration of the late positive deflection (the P450 component compared to the P300 component in the 'oddball' task) and the longer latency of all components.

Event-related Potentials to the Probes in the Digit identification Tasks as a Function of the Number of Items in the Presentation Set

Event-related potentials recorded at Pz for hits and correct rejections obtained from all normal subjects and patients for the one and three-item strings are shown in fig. 3. The normal subjects' traces are shown for hits on the three-item task on the right side of the figure (Normal Hit_3) along with the grand average. There is a striking disparity between the amplitudes of the P450 component evoked during the auditory tasks in the normal and patient groups with the latter being quite small. In contrast, the potentials to the visual tasks are comparable in the two groups. Note that in both modalities the P450 components associated with correct rejections (CR in fig. 3) are of large amplitude and similar in morphology to the P450 component associated with hits. Thus probes evoked comparable P450 components regardless of their relation to the items in the preceding set, a feature which is in direct contrast to the small-to-absent P300 component evoked by the frequent stimulus in the 'oddball' tasks.

Measures of the amplitude and latency of the components evoked by the probe stimuli in the Sternberg task and by the infrequent stimuli in the 'oddball' task are contained in Table 5. The major differences between the patients and the normal

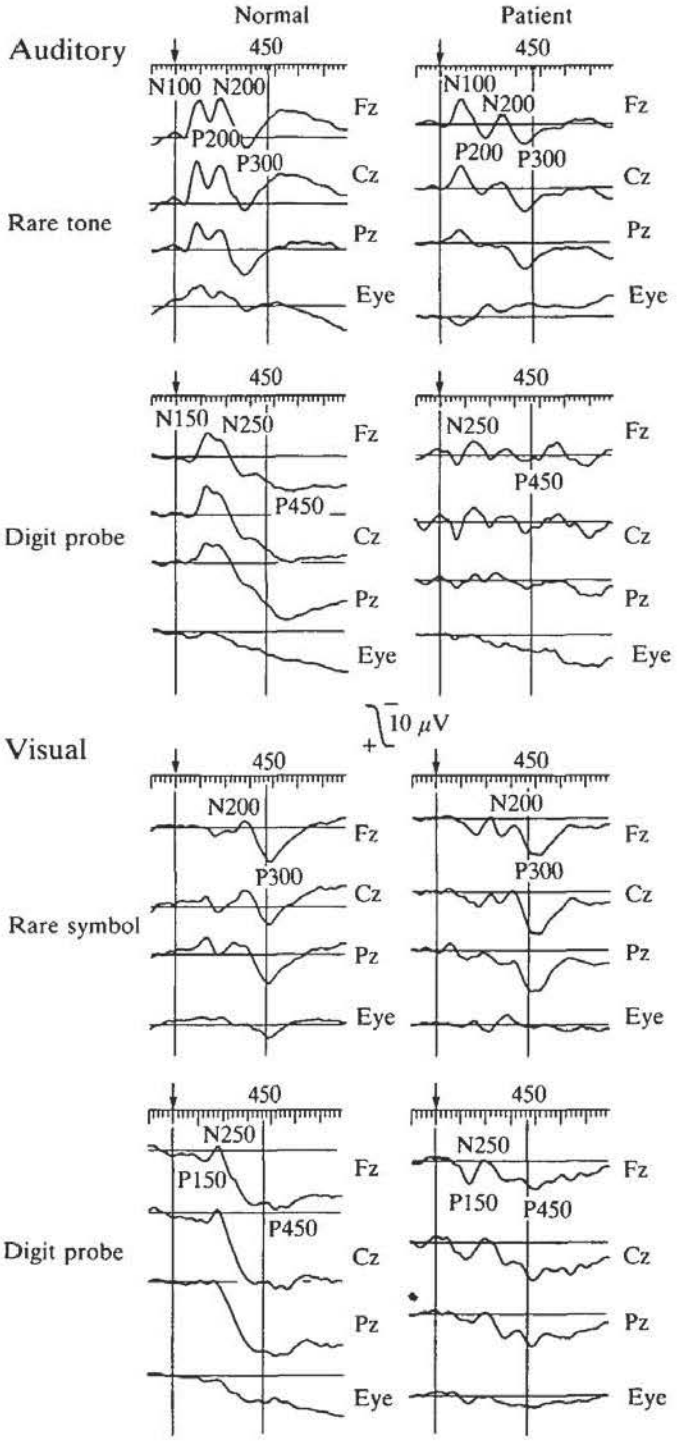


FIG. 2. Scalp distribution of the potentials at Fz, Cz and Pz referenced to linked earlobes along with the monitor of eye movements ('Eye') evoked by the stimuli in the two tasks used in this study that were accompanied by a correct response. The first task required the detection of a rare signal (a tone in the auditory modality and a symbol in the visual modality) occurring with a probability of 0.15 in a train of frequent stimuli and the second task required the identification of a probe as having been a member of a preceding set of items (*see* fig. 1 for a representation of this second task). The event-related potentials shown are from a normal subject (male, aged 55 yrs) and one of the patients with impaired auditory short-term memory (Case 1, test a). The components are labelled by their polarity (P or N for positive or negative) and their approximate latency in ms. Note that the event-related potentials to the rare stimuli are fairly similar in the normal subject and patient. In contrast, the event-related potentials to the digit probes show that the amplitude of a positive deflection at approximately 450 ms in the auditory digit probe task is difficult to define in the patient compared with the normal subject and is present but small relative to the normal subject for the visual digit probe. In this and all subsequent figures, the initial vertical line in the averages marked by an arrow indicates the occurrence of the stimulus. The distance between the large vertical deflections on the time base is 120 ms.

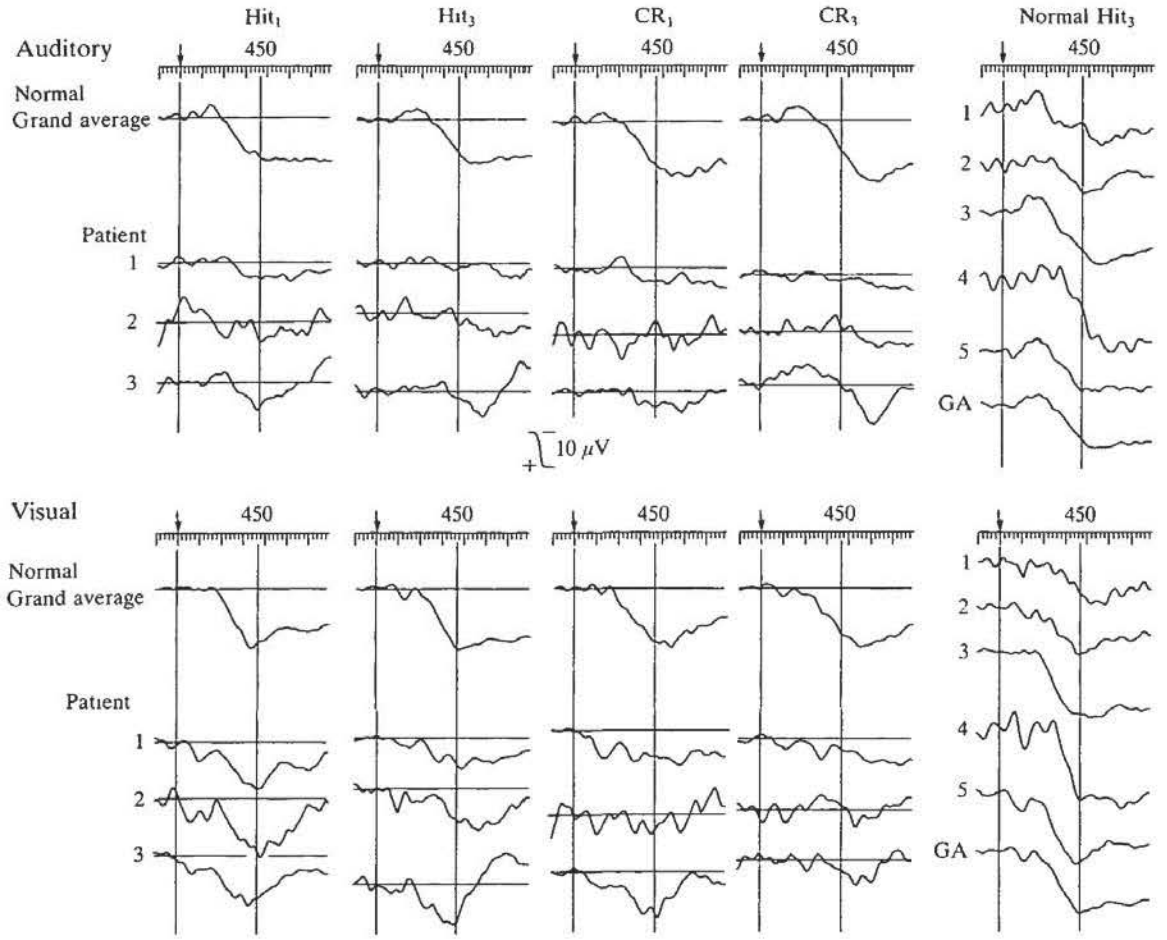


FIG. 3. Event-related potentials (Pz referenced to linked earlobes) accompanying the presentation of the probe following one or three-item strings with auditory and visual presentations. The panels on the right labelled 'Normal Hit_3' contain the event-related potentials from the 5 normal controls and their grand average (GA) to in-set probes that were associated with a correct button response following the presentation of three-item strings (Hit_3). The grand average of the normals as a function of the number of items in the string (1 or 3) and the response category (Hits, Correct Rejections labelled 'CR') is shown with the 3 patients' event-related potentials in the other portions of the figure.

subjects are in the P450 component. Significant comparisons from the repeated measures ANOVA of P450 latency and amplitude for hits and correct rejections in the digit probe identification task appear in Table 6. P450 amplitudes were significantly smaller for patients (g term in Table 6). They were also smaller for auditory stimuli (s term) with this effect being significantly more pronounced in the patient group (sg term). P450 latency was longer for auditory than visual stimuli (s term) as were the latencies to the three-item set compared with the single item set (i term). This latter effect was significantly more pronounced for auditory than visual stimuli (si term). P450 latency for correct rejections was significantly longer than for hits (c term).

TABLE 5. LATENCY IN MS AND AMPLITUDE IN μV OF EVENT-RELATED POTENTIALS

Task		Digit probe								'Oddball' Rare	
Category		Hit_1		Hit_3		CR_1		CR_3			
		Lat	*Amp*	*Lat*	*Amp*	*Lat*	*Amp*	*Lat*	*Amp*	*Lat*	*Amp*
Auditory											
N150											
Patient	$\bar{X}$	164	3.8	175	3.8	170	2.5	169	4.2	108	4.4
	SD	33	1.3	31	3.0	37	1.0	22	1.0	10	3.2
Normal	$\bar{X}$	155	5.3	171	4.9	154	5.2	160	5.3	93	7.2
	SD	13	1.7	18	1.6	20	2.7	15	1.7	11	1.7
P200											
Patient	$\bar{X}$	- - - - - - - - - - - - - - - -				ND		- - - - - - - - - - - - - - - -		191	3.8
	SD									21	2.4
Normal	$\bar{X}$	- - - - - - - - - - - - - - - -				ND		- - - - - - - - - - - - - - - -		170	5.6
	SD									12	3.3
N250*											
Patient	$\bar{X}$	295	2.0	348	2.2	324	3.2	383	3.9	268	+1.3
	SD	83	1.0	66	0.5	97	0.2	125	3.0	37	2.0
Normal	$\bar{X}$	233	1.3	235	4.2	247	1.1	225	2.4	221	0.6
	SD	25	1.3	56	1.2	34	1.7	80	3.1	16	2.9
P450											
Patient	$\bar{X}$	441	5.7	642	5.6	438	4.3	646	6.6	387	9.9
	SD	19	1.9	62	1.6	95	0.9	46	3.9	34	4.1
Normal	$\bar{X}$	455	14.6	519	13.6	488	14.9	602	16.9	343	13.1
	SD	91	2.2	66	5.2	83	5.3	35	7.0	18	7.8
Visual											
P150											
Patient	$\bar{X}$	147	5.2	143	4.0	158	4.8	134	3.3	ND	
	SD	23	2.2	21	1.6	26	2.3	20	1.7		
Normal	$\bar{X}$	141	2.8	150	3.5	127	3.2	152	4.4	**	
	SD	14	1.3	34	0.7	59	2.4	33	2.0		
N250											
Patient	$\bar{X}$	219	+2.3	250	0.0	255	+0.4	294	1.7	301	+1.5
	SD	22	1.2	72	1.5	16	3.8	51	1.8	66	3.2
Normal	$\bar{X}$	213	0.9	231	1.7	224	0.3	278	0.2	**	
	SD	36	2.4	38	4.4	65	2.5	56	3.4		
P450											
Patient	$\bar{X}$	436	14.8	476	10.2	545	10.1	558	6.5	441	16.6
	SD	31	1.8	71	1.5	74	3.1	53	1.1	25	7.0
Normal	$\bar{X}$	424	18.0	450	17.2	469	15.6	535	16.8	**	
	SD	51	3.5	31	3.7	68	6.4	38	4.2		

* 4 of the 5 normals were tested. ** 2 of the 5 normals were tested but data not included. CR = correct rejections. ND = not detected. Lat = latency. Amp = amplitude.

TABLE 6. SIGNIFICANT COMPARISONS FROM REPEATED MEASURES ANOVA OF OVERALL REACTION TIMES AND GRAND AVERAGE P450 LATENCIES AND AMPLITUDES IN THE DIGIT PROBE IDENTIFICATION TASK

	ANOVA term	*P*
Reaction time	g	*
	s	**
	sg	**
	i	***
	ig	***
	si	*
	sig	*
P450 latency	s	*
	i	***
	si	*
	c	**
P450 amplitude	g	*
	s	***
	sg	**
	ig	*
	sc	*

ANOVA terms: g = subject group (control or patient); s = stimulus modality (auditory or visual); i = number of items in presentation set (1 or 3); c = response category (hit or correct rejection). *** $P<0.001$, ** $P<0.01$, * $P<0.05$.

Event-related Potentials to the Probes in the Digit Identification Tasks as a Function of Reaction Time

The finding from the analysis of the overall data that P450 amplitudes are reduced on those tasks of auditory short-term memory for which the patients' performance was also impaired (percentage accuracy and reaction times) are congruent. However, the observation that P450 amplitudes were similar in both the one-item task of auditory short-term memory, when the patients performed almost like normals, and the three-item task, when their performance was grossly impaired, was unexpected and merited further inspection. We therefore examined the potentials associated with hits as a function of reaction time for each subject (fastest third, middle third, slowest third) as well as with the serial position of the matching stimulus in the three-item task (first, second or third).

Fig. 4 contains the event-related potentials from both a normal subject and a patient for hit trials analysed according to reaction time. In the patient, there is a remarkable increase in P450 amplitude in the one-item auditory task for those probes associated with the fastest reaction times, whereas the changes are minimal for the three-item auditory task and for both visual tasks. It is particularly apparent in the one-item auditory task that the P450 component, which is difficult to define

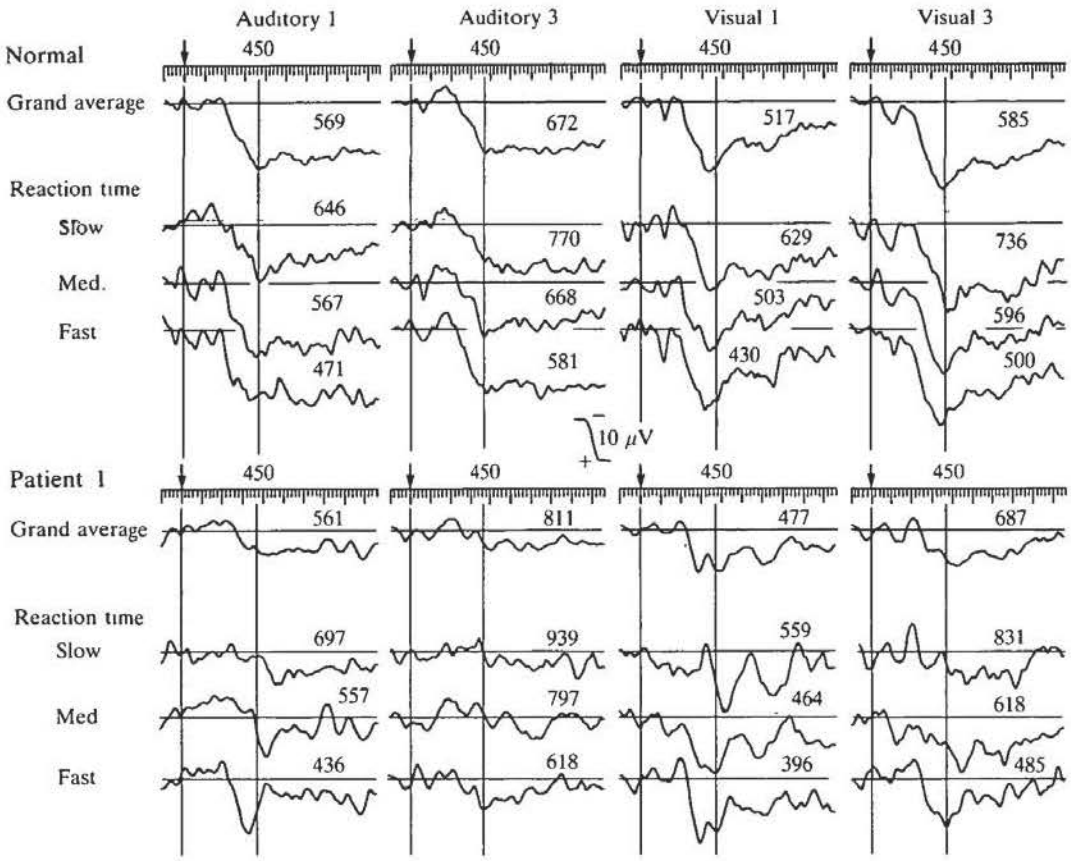


FIG. 4. Effect of averaging event-related potentials to correctly identified in-set probes as a function of reaction times. The trials comprising the grand average were subdivided approximately into thirds according to reaction time: fastest third ('Fast'), medium third ('Med.'), and slowest third ('Slow'). The event-related potentials from a control subject (female, aged 53 yrs, the wife of Case 1) and from Case 1 on the second testing session (test b) are presented in both the visual and auditory modalities. The numbers above each average represent the mean reaction time for the trials comprising that particular average. Note the profound effect that reaction time speeds have on the latency of the initial portion of the positive component occurring at about 450 ms in the patient in both modalities compared with the normal subject. The amplitude of this positive deflection in the patient is enhanced as a function of reaction time only following the one-item string in the auditory modality. The time base in this figure is 1280 ms compared with the 960 ms employed in the other figures.

in the grand average, becomes clear as the average is subdivided according to reaction time. This increase in amplitude of the P450 component is transient, principally involving the earliest portion of the component without affecting the sustained portion of the deflection. There are only slight changes in amplitude of the normal subject's P450 components as a function of reaction time.

Fig. 5 compares mean values of reaction times and P450 latencies and amplitudes for the patients and normal control groups according to stimulus modality (auditory and visual) to the correctly identified probes (hits). Table 7 contains the significant comparisons from the repeated measures ANOVA of the data summarized in fig. 5. The mean data for the auditory P450 amplitude associated with fast reaction times confirm the observation from the single patient depicted in fig. 4 that for the single-item set this amplitude is equivalent to that for normal controls.

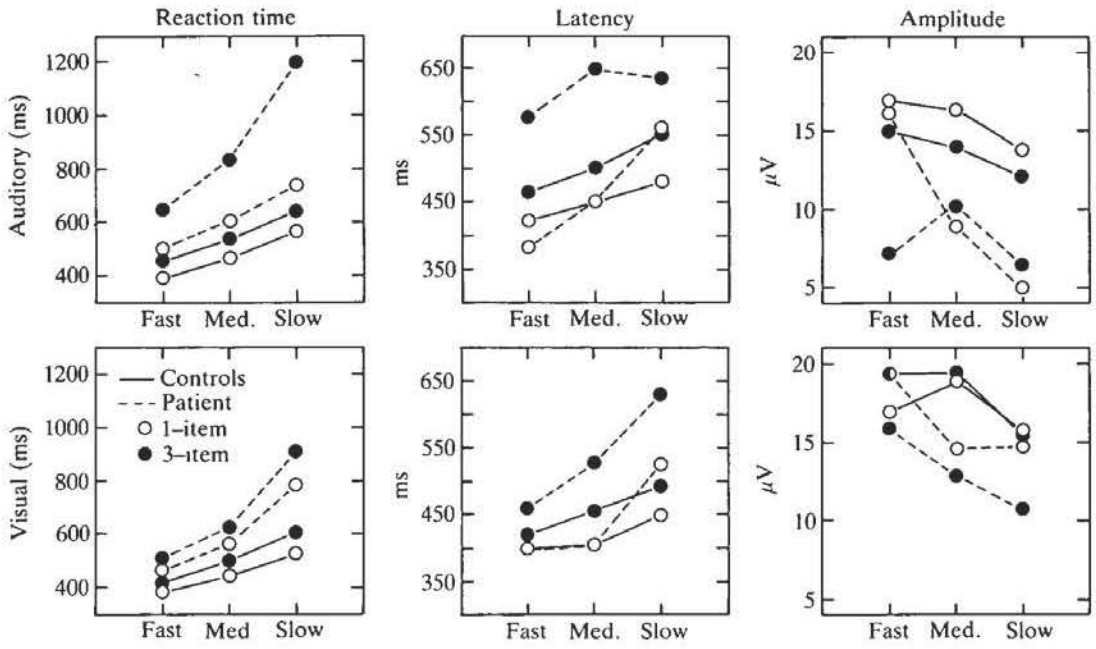


FIG 5 Comparison of mean reaction times and P450 latencies and amplitudes for hit trials in the digit probe identification task averaged according to fast, medium or slow reaction time in the auditory and visual modalities. The ANOVA analyses of these data are given in Table 7. Open circles are from the one-item presentation set and filled circles from the three-item presentation set Data from controls are indicated by solid lines, and those from patients by interrupted lines.

This observation contrasts sharply with that for the grand average data in which there is a difference of 8.9 μV between controls and patients for the P450 component accompanying the probe in the single-item task. The increase in P450 latency from the one to three-item presentation sets was significantly greater for patients than controls (ig term in Table 7), paralleling a similar increase in reaction time. P450 latency increased and P450 amplitude decreased with increasing reaction time (r term). The general conclusion to be drawn from fig. 5 and Table 7 is that the patients' performance and event-related potential measures are comparatively similar to those for controls for fast reaction times in the one-item task but that these parameters deteriorate dramatically for the three-item presentation set, particularly in the auditory modality.

With regard to individual patients, Case 1, whose neurological deficits were stationary, had similar enhancements of P450 amplitude for fast reaction time trials in the one-item auditory condition on both testing sessions. However, Case 3, who recovered between tests, showed a substantial enhancement of P450 amplitude at the first recording session and comparatively little change at the second test.

In contrast to the influence of reaction time on both the latency and amplitude of P450, the analysis of the event-related potentials to probes as a function of the position of the matching digit in the preceding set showed no apparent effects.

These results may provide an explanation for the finding in patients of a reduced

TABLE 7. SIGNIFICANT COMPARISONS FROM REPEATED MEASURES ANOVA OF REACTION TIMES AND P450 LATENCIES AND AMPLITUDES FOR DATA DIVIDED ACCORDING TO FAST, MEDIUM OR SLOW REACTION TIMES IN THE DIGIT PROBE IDENTIFICATION TASK

	ANOVA term	*P*
Reaction time	g	*
	s	**
	sg	*
	i	***
	ig	**
	si	*
	sig	*
	r	***
	rg	**
	ir	***
	irg	***
P450 latency	i	***
	ig	*
	r	***
P450 amplitude	g	*
	s	***
	r	*

ANOVA terms are: g = subject group (control or patient); s = stimulus modality (auditory or visual); i = number of items in presentation set (1 or 3); r = reaction time division (fast, medium, slow). *** $P<0.001$, ** $P<0.01$, * $P<0.05$.

amplitude of P450 to hits in the one-item auditory memory task. The patients had an increase in the peak latency of P450 of 180 ms between the fastest and slowest reaction time divisions, whereas in the normal group the peak latency increased by only 60 ms. Thus in the process of averaging all of the single trials to form the grand average, the P450 component will show a loss of amplitude due to cancellation by overlapping of preceding N250 components from 'slow' reaction time trials with P450 components from 'fast' reaction time trials. This process of cancellation is prominent in the patients' averages and only slightly evident in the normals' averages. Superimposition of the single trials comprising the three reaction time divisions for a normal subject and a patient (fig. 6) shows how readily the average will be confounded in the latter but not the former. It is clear, therefore, that the patient group can form normal-sized P450 components in the one-item auditory task but their latency variability is an important factor accounting for the reduction of amplitude of the grand average of all single trials. The effect of selective averaging by latency of reaction time on the amplitude of P450 seems to enhance the earliest portions of the P450 component as the sustained portions of this deflection are barely affected. The reduction in amplitude of the P450 component evoked in the three-item auditory task could not be modified by selective averaging.

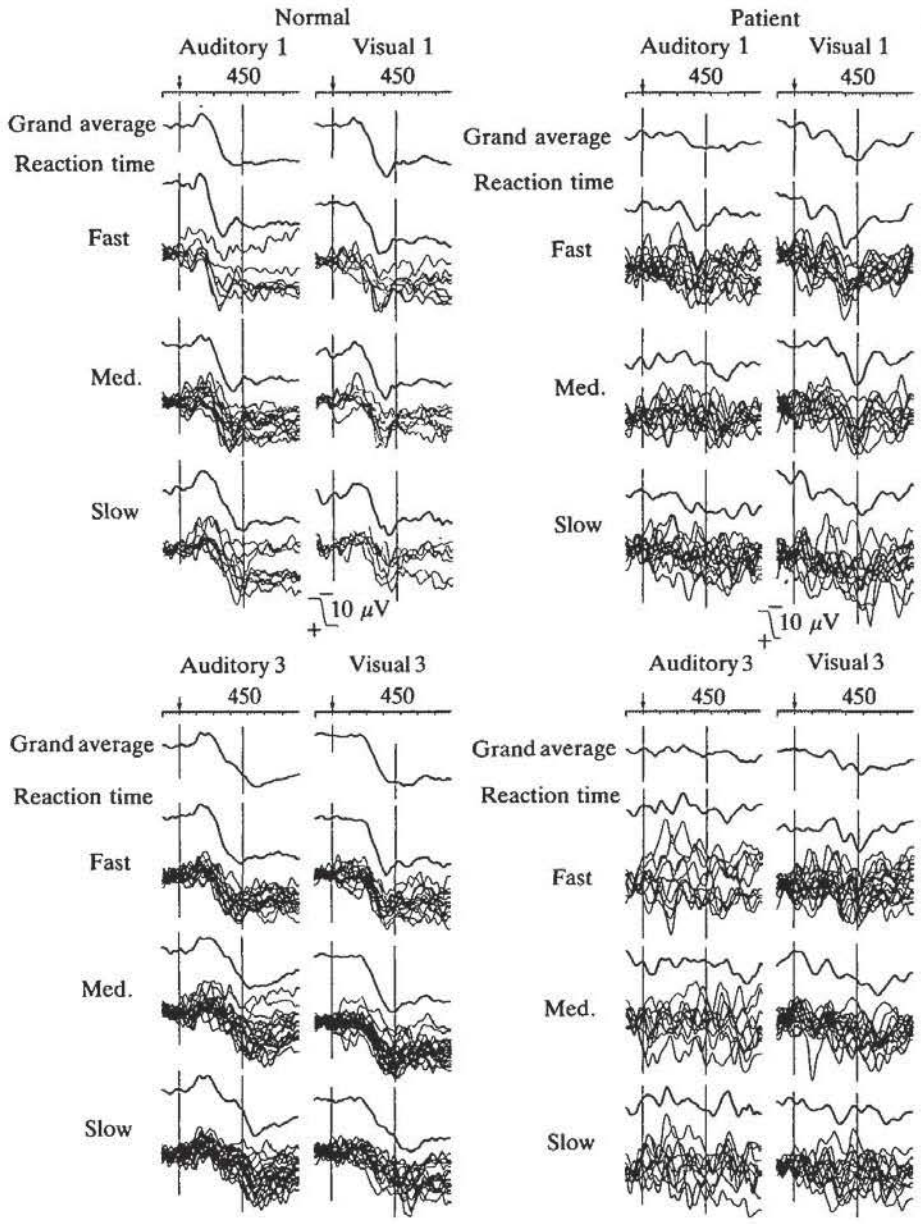


FIG. 6. This shows how the latency of individual event-related potentials in a patient can vary with reaction time and affect the grand average in comparison with a normal control subject. The individual trials evoked by the correctly identified in-set probe in the auditory and visual modalities were subdivided into three groups as a function of reaction time and then the average made of these subgroups. Note that the latency shift of the individual event-related potentials in the patient as a function of the reaction times (Fast, Med., Slow) results in major differences in amplitude and latency between the newly created averages and thus leads to attenuation of components in the grand average, particularly a reduction in amplitude of the P450 component. The latency shifts in a normal control (male, aged 57 yrs) are much less and therefore the grand average is little affected in amplitude.

DISCUSSION

Reaction Time Measures in the Digit Identification Tasks

The results of this study in patients with disordered short-term memory show that measures of reaction time in a probe identification task can provide quantitative indices of the deficit. When the number of items to be remembered during auditory presentation increased from one to three the mean reaction time of the patients to correctly identified probes increased four-fold compared with normal subjects (332 vs 76 ms). The latter value from our normal subjects compares well with previously published normative data showing an increment of reaction time of 25 to 50 ms per item in a probe identification task of short-term memory (Sternberg, 1969). In our patients there is also a sizeable increase in the SD of reaction time between the one and three-item sets when compared with normals (274 vs 6 ms). Thus even when the patients are performing correctly in identifying the matching probes, they become inordinately slowed and more variable with only a two item increase in the number of items to be remembered. These effects were seen in Case 1 with a lengthening of the string by only a single item, from just one to two. The data cannot distinguish where along the memory process the impairment occurs. It obviously is at a critical point because slowing of reaction time occurs after so few items have been presented. There is a suggestion from the SD measures in the one-item probe identification and rare target identification tasks that perhaps even the processing of single items employing auditory short-term memory may also be impaired. The deficits of memory are evident whenever the auditory system is used. For instance, in the visually presented one-item digit probe task, the reaction time for Case 1 slowed and became more variable when the probe was presented acoustically rather than visually even though the performance scores on the two tests were almost identical (Table 4). However, it may be that the deficits of short-term memory also involve visual processes as with visual presentation alone reaction times and their accompanying SD were also greater than normal (Table 3).

The reliability of reaction time measures in the digit probe identification tasks is evidenced in Case 1 who had a stationary clinical deficit of short-term memory. His reaction times were consistent on three separate assessments over a month. In contrast, Case 3 showed a normalization of the reaction time measures as the clinical manifestations of the short-term memory deficits improved. These results are certainly congruent with previously published studies of the performance of patients with conduction aphasia and deficits in auditory digit span (Shallice and Warrington, 1977). Moreover, the reaction time data from the present study complement our understanding of the behavioural consequences of impaired auditory short-term memory through the demonstration of an increase in both the absolute reaction times and their variability with increases in the number of items to be remembered.

Event-related Potentials

The event-related potentials accompanying correct identification of matching probes consisted of a high amplitude sustained positivity commencing at about 350 ms, reaching a plateau at 450 ms and, following auditory presentation, persisting with little decrement for more than 500 ms and for a slightly shorter duration following visual presentation. This component is comparable to the 'P300' of Ford *et al.* (1979) evoked in a similar digit probe identification task employing the visual modality. It is to be distinguished from the P300 component evoked by targets in the infrequent signal identification tasks by the shorter latency and brief duration of the latter. There is also a major difference in amplitude between the potentials evoked by stimuli not requiring an overt response by the subject; the P300 to the frequent signals in the 'oddball' task is of very small amplitude, whereas the P450 component associated with correct rejections in the digit probe identification tasks occurs with a similar high amplitude to that for hits and slightly longer latency. This difference in amplitude may be due, in part, to the different probabilities employed in the two tests. In the rare signal task the frequent stimulus occurred with a probability of 0.85, whereas in the probe identification tasks the out-of-set probes occurred with a probability of 0.5. Further differences between the potentials evoked by the two tasks occur in the early components preceding the major positivities. Event-related potentials to in-set probes consist of an initial negativity (auditory) or positivity (visual) at 150 ms followed by a negativity at about 250 ms. For auditory probes this second negativity cannot be easily distinguished from the N150 in contrast to the potentials evoked in the 'oddball' task in which a P200 component clearly demarcates the N100 from the N200.

In the probe identification tasks there are several differences between the patients' and normal controls' P450 components evoked by the matching probes. First, the mean amplitude of the patients' P450 to the probes following the presentation of the one-item string in the auditory modality is less than half of that of the control group but of equal value in the visual modality. Secondly, there is a greater mean increase in latency of the P450 component when the string length increased from one to three items in the auditory modality for the patients (201 ms) compared with the controls (64 ms). Previously published values of latency increment as a function of string length in normals using the visual modality are comparable to our normative data (Ford *et al.*, 1979).

In the patients, the latency, amplitude and even occurrence of the P450 component evoked by each presentation of the probe was quite variable. We therefore reanalysed the single trials to correctly identified in-set probes (hits) according to reaction times (fastest, middle and slowest thirds) and, where appropriate, by the position of the matching item in the preceding sequence (first, second or third) to determine the influence of these variables. For the one-item string presented in the auditory modality the patients' P450 was of larger amplitude and shorter latency in those trials associated with the fastest reaction times compared to the grand

average. These measures were substantial compared with the modest changes accompanying selective averaging by reaction times for the normal group (*see* figs 4, 5). Thus the patients can generate a normal amplitude P450 component to correctly identified auditory probes in the one-item task when the average is based on those trials having the fastest reaction time. However, the amplitude of this component was not comparably enhanced in the auditory three-item task, either by averaging according to reaction time or position of the matching item in the set preceding the probe.

The change in amplitude of the patients' P450 component with reaveraging according to the fastest reaction times particularly affected the earliest portion of this component, whereas the sustained portion of the positive shift was only slightly modified. This finding raises the possibility that P450 may consist of two subcomponents, similar to the segregation of the P300 component evoked in the rare signal detection task into an early P3a and late P3b component. The former has been associated with orienting (Näätänen *et al.*, 1980) and arousal, independent of an overt response to the rare signal (Squires *et al.*, 1975), whereas the latter P3b component is more intimately associated with the classification of the stimulus (Pritchard, 1981). The definition of an increase in amplitude of the early portion of P450 in the patients may reflect activity of normal arousal processes, whereas the absence of substantial growth of the sustained portion of this component may indicate a defect in the patients' ability to classify stimuli.

Averaging of individual event-related potential trials is most suitable when there is little temporal jitter of the components from trial to trial. The sensory evoked potentials of short latency, such as the auditory brainstem potentials, are an example of a sensory event-related potential having relatively constant latency for each component in each trial (Galbraith, 1984). In contrast, the late components evoked in the probe identification tasks are extremely variable in latency and this affects their amplitude in the conventional average. The use of latency-adjusted averages has been employed to compensate for the smudging effect of latency jitter in these circumstances. In the present study, some of the variability of latency of the P450 component in the patients was closely allied to reaction times. The finding in the patients of an increase in the variability of certain of the components of the event-related potentials may be an important indicator of their disorder. A similar observation of increased P300 variability has also been defined in some patients with Alzheimer's disease in the 'oddball' task (Patterson *et al.*, 1985).

The P300 component of event-related potentials has been well studied and classified as endogenous, reflecting cognitive processes and, more particularly, aspects of memory function involved in 'memory updating' (Donchin, 1981). This is based on the increment in amplitude accompanying the presentation of novel stimuli, either with regard to their global probability or to the pattern of stimuli in the immediately preceding sequence (Squires *et al.*, 1976). The finding of alteration in amplitude of a P300-like component, designated as P450 in this study, in patients with a disorder of auditory short-term memory provides support for the

concept that the component bears some relationship to the memory process. The amplitude decrement of P450 is particular to auditory rather than to visual probes and correlates well with the accompanying behavioural deficits in the auditory modality. These findings can be considered as additional evidence linking the P450 component to activity of neural circuits subserving memory. However, the present results cannot be taken as evidence of a causal link between P450 and short-term memory processes. Instead, the alteration of P450 found in these patients indicates that the disturbance in tests of short-term memory represents a disorder of memory rather than a disorder of response selection as has been suggested by Kinsbourne (1972) in this syndrome. A disorder of response selection could have been proposed to account for the poor performance had these patients demonstrated a normal P450 amplitude and latency.

It is clear that the adaptation of behavioural tasks that reflect particular cognitive functions, such as the probe identification task of short-term memory in this study, provides a more powerful analytic method than the standard infrequent target detection or 'oddball' tasks. Measures of P300 in the 'oddball' tasks were normal in our patient group (with the exception of Case 4 who could not perform the task and who did not have a P300 component) suggesting that this latter task probably puts little demand on short-term memory functions. Thus the observation of normal P300 in some patients with dementing illness using the 'oddball' paradigm should not be too surprising (Goodin *et al.*, 1978). It is not clear what cognitive function the oddball task measures, but the detection of novelty (i.e., stimulus change) would be a reasonable candidate. Such cognitive processes have not been clearly identified as being abnormal in demented patients. Certainly it would seem more appropriate to examine patients with electrophysiological measures that are relevant for their behavioural deficits. The benefits of such analyses may provide evidence for mechanisms of their cognitive disorders as well as providing objective parameters of the neural structures subserving cognition.

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