

Two- and three-stimuli auditory oddball ERP tasks and neuropsychological measures in aging

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Received 17 July 2001; accepted 2 August 2001

The purpose of this study was to decide whether the P300 from an auditory three-stimuli oddball task is more sensitive to aging than the P300 from a two-stimuli task, and to investigate the relationship between neuropsychological tests and the different ways of eliciting the P300. Thirty-one adults (21.8–94.7 years) completed five neuropsychological tests and two ERP tasks. The way P300 was elicited did not influence its

relationship to aging or neuropsychological scores, and the correlations between the two paradigms were strong for amplitude, but rather weak for latency. The main conclusion is that the P300 from an auditory three-stimulus paradigm is sensitive to aging and neuropsychologically valid. *NeuroReport* 12:3149–3153 © 2001 Lippincott Williams & Wilkins.

Key words: Aging; Cognition; ERP; Neuropsychology; P300

INTRODUCTION

Psychometric tests and the endogenous electrophysiological components elicited to repeated stimuli, event-related potentials (ERPs), have been applied in a wide range of studies to investigate cognitive changes with age [1–5]. In most ERP studies on aging, the traditional two-stimuli oddball paradigms have been employed. Two types of stimuli of unequal probability is presented, and attention is to be paid to the infrequent ones. The component elicited to the target in such paradigms has been termed the P3b [5,6]. The P3b is a positive-going potential with parietal maximum amplitude, and a peak latency of about 300–350 ms in young adults. With increasing age, the amplitude typically decreases while latency increases [5,7]. Another component, often coined the P3a, may be elicited with a three-stimuli paradigm. A third, infrequent type of deviant non-target stimuli, is inserted into the sequence of target and standard stimuli. The P300 elicited to these deviant stimuli has peak latency at about 250–350 ms after stimulus onset, and its maximum amplitude is over the fronto-central recording sites. The component reflects involuntary, transient allocation of attention to salient stimuli changes and novel stimuli [8]. Katayama and Polich [9] have demonstrated that the P300 from target stimuli in the single-, two- or three-stimuli paradigm is essentially the same. Studies further show that the P300 from the deviants in the three-stimuli paradigm is determined by probability and task demand variables in the same way as the P300 elicited from targets in both two- and three-stimuli paradigms [6,10]. However, the neural generators responsible

for producing the components may not be identical. The P3a has an anterior scalp distribution, shorter latency, habituates rapidly, and has been interpreted as reflecting frontal lobe function [11].

Three-stimuli paradigms have recently been employed in several studies of clinical groups, e.g. males at high risk for alcoholism [12], alcoholics [13], and patients suffering from closed head injuries [8,14] and dementia [15]. However, three-stimuli paradigms have not often been compared to the traditional two-stimuli task in groups of different cognitive and neuropsychological functioning. The comparison of the two and three-stimuli P300 is especially interesting in groups with variations in frontal lobe functioning, e.g. groups of different ages. There are theories of cognitive aging focusing on functioning of the frontal lobes: theories of disinhibition [16], and theories focusing on the prominent loss of neurons in frontal cortex associated with old age [17]. If increased age brings with it deficits of frontal lobe function, then the frontal and the parietal P3b may relate to aging in different ways. Polich [5], by meta-analysis, found that the simple two-stimuli paradigm yielded stronger relationships between P300 latency and aging than the three-stimuli paradigms.

While P300 from a two-stimuli ERP paradigm is moderately related to global measures of intellectual function [18], a more robust relationship may be observed with more complex paradigms [19]. Three-stimuli paradigms have been little studied in relation to age-sensitive neuropsychological measures. It is important to investigate this relationship to gain knowledge of how electrophysiological

activity and cognitive functioning are connected. Comparing the two- and three-stimuli paradigms in aging, the following predictions were made: (1) both measures should be sensitive to aging, and the frontal three-stimuli paradigm should be the most sensitive to age changes. (2) If the claim that the different P300s reflect different underlying processes is valid, then they should be only moderately related to each other. (3) Tests bearing on frontal function should be relatively more related to the distractor P300.

MATERIALS AND METHODS

Sample: The participants were 31 healthy volunteers, 18 females and 13 males, aged 21.8–92.0 years (mean 58.8) recruited on campus, through charity organizations, and activity centers for the elderly. All participants were community dwellers, and were given a moderate sum of money to refund possible costs. Criteria for exclusion were neurological conditions or hearing problems. Audiograms were obtained, and all participants could hear tones of 40 dB at one ear at 1000 Hz.

Cognitive tests: In order to screen for dementia and obtain a measure of cognitive functioning, the Norwegian version of Wechsler Abbreviated Scale of Intelligence, WASI [20], and digit span from the Wechsler Adult Intelligence Scale-Revised, WAIS-R [21], were administered. Due to fatigue, one of the subjects completed only 3 of 4 WASI test conditions. The digit span test was included in the study only after initial testing of six participants, and was thus administered to 25 of 31 subjects. WASI is the only known test of fluid and crystallized intelligence with norms up to 89 years of age. We used a cut-off IQ score of 85, and all participants satisfied this criterion.

ERP stimuli: First, we presented an auditory two-stimuli oddball task, with 0.20 target probability (80 dB, 80 ms duration, 1200 Hz) and 0.80 standard (80 dB, 80 ms, 750 Hz) probability. The participants silently counted the target tones. ANOVA showed no significant effects of age on number of incorrectly counted tones. An auditory three-stimuli paradigm, with 0.10 target tones (80 dB, 80 ms, 1200 Hz), 0.10 distractor tones (100 dB, 80 ms, 500 Hz) and 0.80 standard tones (80 dB, 80 ms, 1000 Hz) probability was presented next. All participants reported the correct number of tones. In both paradigms, inter-stimulus interval was 1.5 s, and a total of 240 tones were administered. The tones had a rise/fall time of 10 ms, and were presented through insert earphones calibrated to fit the stimulus presentation system. An example of the task with 25 stimuli in a mixed sequence was presented, to make sure all participants could easily discriminate the tones and to prime the subjects for each task.

ERP procedures: Subjects were seated in a chair within a sound attenuating recording chamber. The electrodes (Ag/AgCl) Fz, Cz, and Pz were used for recording, referred to the left mastoid, and placed in accordance with the international 10-20 system. A VEOG channel was obtained from the left eye, and ground was placed anteriorly. Inter-electrode impedance was generally <10 k Ω . For the recording of EEG activity, A/D rate was 500 Hz, and filter

setting was 0.10 Hz (high pass) and 70 Hz (low pass), in addition to a 50 Hz notch filter. The signals were amplified by a SynAmp DC amplifier (Neuroscan Inc.). Epochs were rejected if amplitude exceeded ± 110 mV, and eye blinks were corrected in accordance with Semlitsch *et al.* [22]. EEG was segmented in epochs of 900 ms (–100 ms to 800 ms relative to stimulus onset). Data average files were digitally filtered (30 Hz low pass) and subjected to linear detrend and baseline correction. Neuroscan software was used to present stimuli, record, and analyze EEG activity. In accordance with Pfefferbaum *et al.*'s [23] recommendations, peaks were determined algorithmically, defined as the most positive or negative point constituting a peak within 250 and 550 ms, using Readpeak software [24].

Statistical analyses: We employed regression analyses and/or correlation analyses to investigate the relationship between the different P300 components and age, between the different P300 components themselves, and between the P300 components and the neuropsychological measures. By regression analyses, we investigated whether hearing influenced the P300.

RESULTS

Correlations between P300 components and age: Correlations are presented in Table 1 and scatterplots in Fig. 1. Both for amplitude and latency, the correlations with age were strong at Pz and Cz, but not at Fz, and depended more on electrode site than paradigm. Hearing did not influence P300 amplitude as evidenced by regression analyses, but hearing and P300 latency to the target in the two- and three-stimuli tasks were significantly related.

Correlations between P300s: Correlations between P300 amplitude/latency from the two paradigms are shown in Table 2. The amplitude correlations are generally strong, especially at Cz and Pz. The latency correlations are substantially weaker.

P300s and neuropsychological measures: Correlations are presented in Table 1. As expected, the verbal tests showed no or very weak relationships with P300. For both amplitude and latency, the correlations with fluid measures were strongest at Pz and the distractor P300 did not show a stronger relationship than the other P300s.

DISCUSSION

P300 and aging: Our results show that the P300 is sensitive to aging, and the different ways of eliciting the component did not make much of a difference in this respect. While the distractor P300 is thought to reflect frontal lobe functioning, the relationship between Fz and age was generally weak for all paradigms. The relationship between decrease of frontal lobe functioning and P300 is, however, a complex one. At the frontal recording sites, amplitude is often non-correlated or even positively correlated with age [7]. The reason may be that increased age brings with it a need for stronger involvement of frontally based neural circuits, or that age may effect frontal and parietal generators of the P300 in different ways [25]. Our

Age and P300

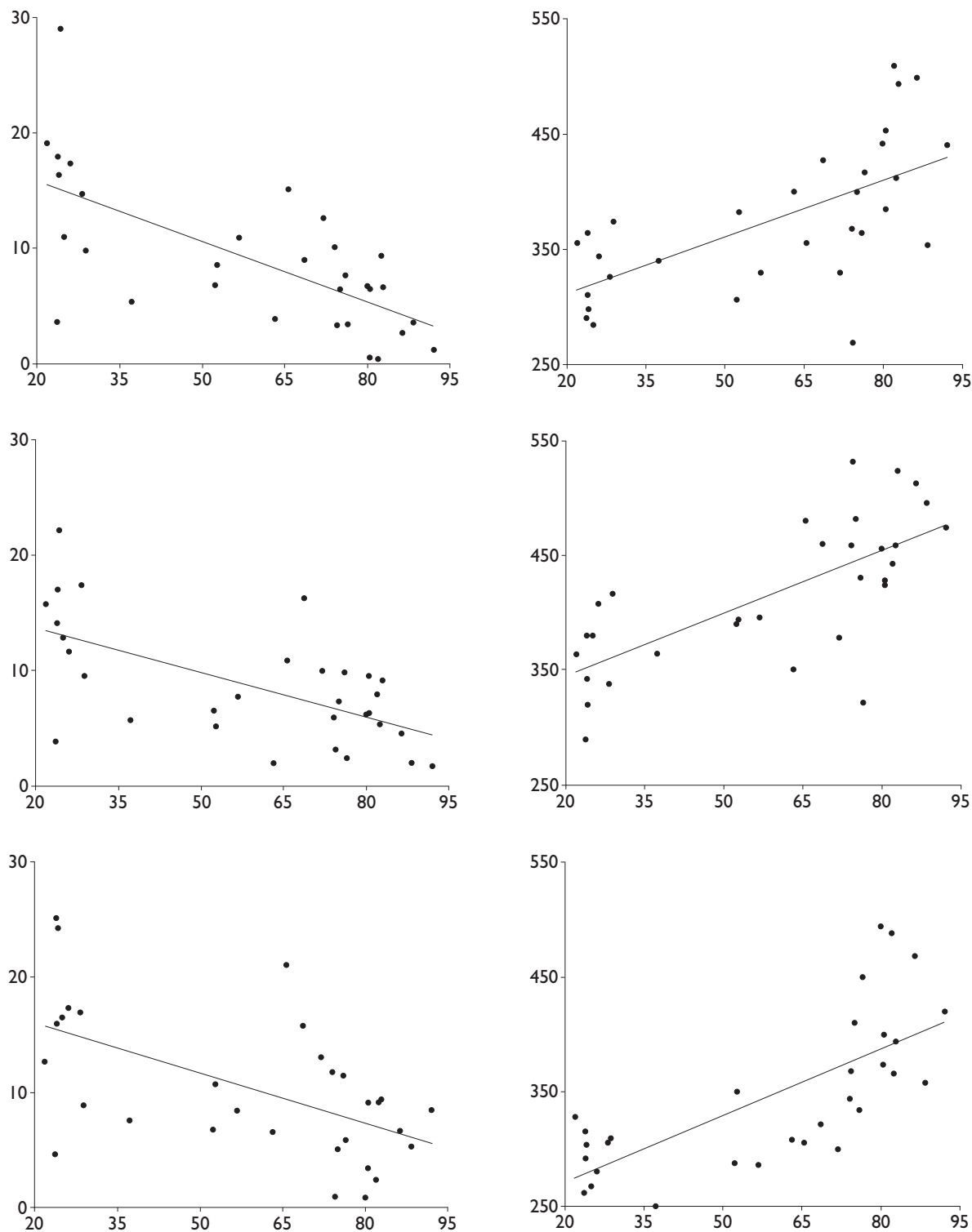


Fig. 1. Regression slopes for age and P300 at Pz. Left column: age and amplitude for P300 from target in the two-stimuli task ($y = 19.25 - 0.17x$, $p < 0.001$), target in the three-stimuli task ($y = 16.21 - 0.13x$, $p < 0.001$), and distractor from the three-stimuli task ($y = 18.90 - 0.14x$, $p < 0.001$), respectively. Right column: Latency and age for P300 from target in the two-stimuli task ($y = 278.12 + 1.65x$, $p < 0.001$), target in the three-stimuli task ($y = 308.34 + 1.83x$, $p < 0.001$), and distractor from the three-stimuli task ($y = 233.04 + 1.93x$, $p < .001$) respectively. Both for amplitude and latency, the regression slope is very similar for the three P300s.

Table 1. Correlations between P3a/ P3b amplitude/latency and neuropsychological measures and aging.

Paradigm/component	Matrices	Block design	Similarities	Vocabulary	Digit span	Age
Amplitude						
3-stim FzTarget	0.02	-0.07	-0.14	-0.07	0.03	-0.10
3-stim FzDistractor	0.11	-0.09	-0.11	-0.04	0.03	-0.05
2-stim FzTarget	0.05	0.06	-0.08	-0.02	0.25	0.10
3-stim CzTarget	0.32	0.21	0.07	0.04	0.36	-0.50**
3-stim CzDistractor	0.41*	0.25	0.05	0.02	0.35	-0.39*
2-stim CzTarget	0.40*	0.33	0.06	0.04	0.32	-0.56**
3-stim PzTarget	0.46*	0.33	0.18	0.06	0.43*	0.61
3-stim PzDistractor	0.51**	0.36*	0.02	-0.10	0.35	-0.56**
2-stim PzTarget	0.51**	0.47*	0.08	-0.06	0.31	-0.67**
Latency						
3-stim FzTarget	-0.08	-0.10	0.16	0.39*	0.04	0.31
3-stim FzDistractor	-0.19	-0.06	-0.01	0.12	-0.19	0.28
2-stim FzTarget	-0.04	-0.06	0.12	0.14	-0.23	0.22
3-stim CzTarget	-0.03	-0.18	0.17	0.32	-0.11	0.44*
3-stim CzDistractor	-0.45*	-0.38*	-0.23	-0.06	-0.39	0.65**
2-stim CzTarget	-0.52**	-0.43*	-0.27	-0.07	-0.39	0.57**
3-stim PzTarget	-0.62**	-0.60**	-0.48*	-0.21	-0.43*	0.71**
3-stim PzDistractor	-0.49**	-0.42*	-0.14	0.06	-0.40*	0.72**
2-stim PzTarget	-0.43*	-0.33	-0.25	-0.11	-0.40*	0.64**

* $p < 0.05$; ** $p < 0.01$ **Table 2.** Correlations between P300s amplitude/latency from two- and three-stimuli paradigms

Paradigm/component	3-stim FzDistractor	2-stim FzTarget	3-stim CzDistractor	2-stim CzTarget	3-stim PzDistractor	2-stim PzTarget
Amplitude						
3-stim FzTarget	0.80**	0.45*				
3-stim FzDistractor		0.61**				
3-stim CzTarget			0.71**	0.81**		
3-stim CzDistractor				0.79**		
3-stim PzTarget					0.78**	0.84**
3-stim PzDistractor						0.85**
Latency						
3-stim FzTarget	0.53**	0.33				
3-stim FzDistractor		0.37*				
3-stim CzTarget			0.38*	0.09		
3-stim CzDistractor				0.54**		
3-stim PzTarget					0.52**	0.47**
3-stim PzDistractor						0.79**

* $p < 0.05$; ** $p < 0.01$

study indicates that the distractor P300 is related to age in a way that mimics the target P300 of the two- and three-stimuli paradigm.

Distractor and target P300s: The correlations between P300 amplitudes from the different paradigms indicate that the same neurophysiological processes are measured, especially for Pz and Cz. At Fz, the correlations between the P300s were substantially weaker, so it is possible that the underlying neurophysiological processes generating the different P300s are less tightly coupled at this area. The latency correlations were lower, although seven of the nine were significant ($p < 0.05$). This may be interpreted in three ways: (1) the latency of the different components may

index different, though related, neurophysiological processes; (2) the reliability of the components may be lower. This is doubtful, because of the strong relationship at Pz between the two-stimuli target P300 and the three-stimuli distractor P300; or (3) since the different P300s are elicited by tones differing in intensity and frequency, differences in hearing may cause the variations in latency. Since age and hearing problems correlate, it is difficult to decide what independent influence hearing exerts on P300 latency. Amplitude is more independent of hearing problems.

P300s and neuropsychological measures: The strongest relationship between P300s and cognitive performance is found at Pz. Fz did not correlate with the neuropsychologi-

cal measures. This is due to the fact that Fz is not sensitive to aging, while the neuropsychological measures are. The digit span task can be said to be related to frontal lobe functioning. This test correlates slightly stronger with Fz than the others. However, it seems that the frontal lobe functioning measured by the ERP paradigms in our study hardly represents the same processes that underlie performance on the digit span test. Otherwise, we would expect the distractor P300 to show stronger correlations with this test.

CONCLUSION

The three ways of eliciting P300 in our study yield comparable results with regard to amplitude, as evidenced both by their correlations, and by their relationship to aging and neuropsychology. For latency, the results are harder to interpret. The distractor P300 is currently the subject of much clinical and theoretical research, and it is thus important to gain knowledge of its relationship to both normal aging and established neuropsychological instruments. Our results may be taken as an internal and external validation of the distractor P300. On the negative side, however, the results indicate that the component, especially with regard to amplitude, adds little to the already explained variance from the simpler classical two-stimuli oddball task.

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Acknowledgements: This research was supported by the Norwegian Research Council, grant 137228/300. We thank Ivar Reinvang for generous help and support during the initial phases of this research. The authors have contributed equally to the present paper, and the names are presented in random order.