THE EFFECT OF AGE ON CONVENTIONAL PARAMETERS OF EVENT-RELATED POTENTIALS

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SUMMARY: The aim of the study is to investigate the effect of age on conventional parameters of visual event-related potentials (ERPs). Forty two healthy subjects ranging in age from 20 to 73 were divided into three groups according to age; a young group (20-33 years), a middle-aged group (34-49 years) and older group (50-73 years). Event-related potentials (ERPs) of three groups were recorded in two different experimental conditions of which the infrequent stimulus was counted (Test 1) or uncounted (Test 2). ERPs were elicited using infrequent and frequent stimuli as red and green lights respectively. Significant amplitude and latency differences were found in comparisons between Test 1 and Test 2 for three groups. When the count stimulus condition was examined, significant latencies differences were observed between groups. The P_{3b} latency increased significantly with age at a rate of 1.75 ms/year ($r=0.65$, $p<0.0001$).

Key Words: Event-related potentials, P_3 , aging, decision making.

INTRODUCTION

Several components of event-related potentials (ERPs) observed within an interval ranging from 100 to 600 ms after task specific processing events, have been intensively studied over the past decade (1-7). The main component of interest has been a large positivity occurring at latencies of 250 to 600 ms (7-13). This potential, named P_3 or P_{300} is generated in response to infrequently attended, task relevant stimuli in the auditory, visual or somatic modalities (1,2, 5,14). It is also associated with various specific psychological constructs including stimulus discrimination, directed attention, sequential information processing, short term memory, a sign of decision and learning (1-3,14-17).

In the two decades growing attention has been focused on age-related differences of ERPs with respect to the clinical application of P_3 component for the assessment of cognitive disorders (14,18-21). Because it was shown that the P_3 progressively increases in latency but diminishes in amplitude in normal aging without some kinds of brain disease such as dementia, schizophrenia, epilepsy (7,12,22-30). So diagnostic utilization of P_3 ultimately depends on more precise knowledge of the normal age/P_3 latency (12,13,27-32).

In the literature, there have been many studies on the auditory ERPs, but there has been little research on visual ERPs. Therefore, we could not find enough data to compare with our results. On the other hand, the effect of age on ERPs of Turkish people has not been considered in the previous studies. Consequently, the aim of the study is to evaluate the conventional parameters of visual ERPs of Turkish people in normal aging.

MATERIALS AND METHODS

Forty two subjects (21 females, 21 males) ranging in age from 20 to 73 participated in the study. The subjects were divided into three groups according to age; a young group (20-

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30 years, mean 25.21 ± 4.87 years, n=14), a middle-aged group (34-49 years, mean 39.79 ± 4.68 years, n=14) and older group (50-73) years, (mean 58.43 ± 6.63 years, n=14). All subjects were healthy and intellectually active and had no history of neurological or psychological disability.

ERPs were recorded with disc electrodes from parietal region (Pz) referred to glabella. The grounding electrode was placed on the forehead.

ERPs were recorded using Medelec MS6 EMG equipment in two different experimental conditions that the infrequent stimulus was counted (Test 1) and uncounted (Test 2). In Test 1, all the subjects were instructed to count mentally the number of the infrequent stimuli interspersed in the frequent stimuli. The infrequent (red light) and frequent (green light) stimuli were produced by 4 mm diameter light-emitting diode (LED). Lights were presented in a random sequence with infrequent stimuli occurring with a 0.2 probability. Each stimulus was delivered at rate of .9/s and duration of stimulus was 0.5 s.

For Test 1 and Test 2, 64 artifact-free responses to infrequent stimuli were averaged separately. The frequency bandwidth of the amplifier was between 0.16-32 Hz and gains were selected between 10 and 50 μV/div. The analysis time was 1000 ms. Trials in which subjects became drowsy, or in which the count of infrequent stimuli was error by more than 3, were discarded. Averaging epochs contaminated by eye movement artifact were automatically rejected and at least two averages were obtained to ensure the response reproducibility.

Latency was defined as the time from stimulus onset to the peak of each wave. In instances of broad peaks or 'doublets', the point of intersection between lines from the positive and negative slopes of the waves was considered the peak. P_3 was identified by comparing Test 1 with Test 2. When P_3 had separate peaks, the former was labeled as P_{3a} component, the latter as P_{3b} component. When a single peak was identified, it was considered as corresponding to the P_{3b} component according to the previous descriptions (33). P_3 amplitude was measured as the amplitude of N_2-P_{3b} deflections.

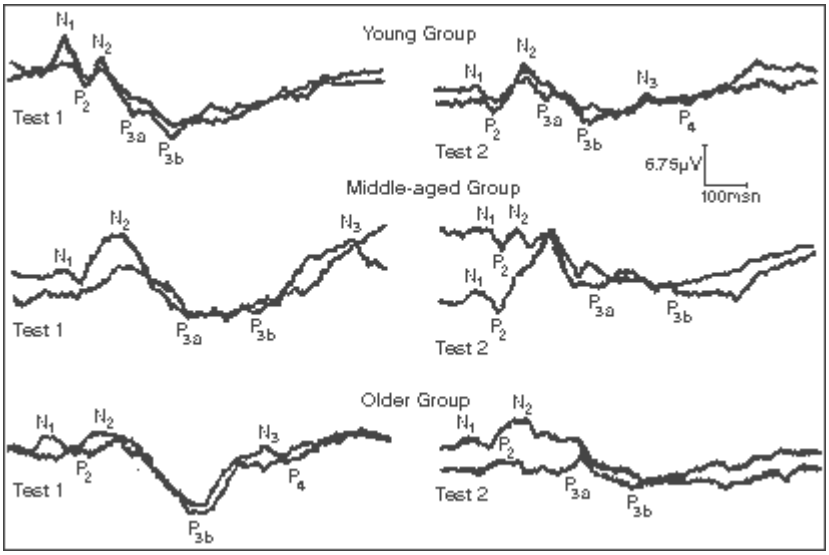
RESULTS AND DISCUSSION

ERPs recorded in two experimental conditions where the rare stimulus was counted (Test 1) or uncounted (Test 2). These potentials are presented in Figure 1. The P_3 peak was absent or much reduced in amplitude when the stimuli were uncounted (Figure 1). A statistically significant amplitude increment was also evidenced in comparisons between Test 1 and Test 2 for three groups (Table 1).

Table 1: Mean and standard deviation of peak latencies and peak-to-peak P_{3b} amplitudes for two cases (Tests 1 and 2) of three groups.

		Latency, ms							Amplitude N_2-P_{3b}, μV
Groups		N_1	P_2	N_2	P_{3a}	P_{3b}	N_3	P_4	
Young Group	Test 1	151.36 ±45.56	192.69 ±44.94	241.07 ±33.35	303.33 ±35.31	382.21 ±32.14	513.92 ±87.53	598.92 ±122.88	15.47 ±3.53
	Test 2	177.50 ±40.36	205.77 ±42.51	253.93 ±39.67	330.00 ±43.68	424.54 ±55.74	510.76 ±95.01	550.55 ±96.06	6.94 ±4.17
P		<0.02	n.s.	<0.04	<0.002	<0.002	n.s.	n.s.	<0.001
Middle aged Group	Test 1	196.54 ±28.96	236.07 ±31.87	281.43 ±27.63	325.83 ±35.53	432.14 ±24.24	593.24 ±97.44	641.82 ±70.54	13.07 ±5.05
	Test 2	196.15 ±25.17	243.21 ±23.90	297.86 ±23.92	353.21 ±38.56	452.15 ±31.50	612.69 ±98.16	703.33 ±113.90	3.79 ±3.89
P		n.s.	n.s.	<0.003	<0.001	<0.006	n.s.	n.s.	<0.001
Older Group	Test 1	211.25 ±31.99	253.33 ±27.24	295.71 ±20.92	349.39 ±8.21	464.64 ±45.46	654.61 67.81	716.50 ±54.67	13.59 ±4.76
	Test 2	191.50 ±32.29	259.61 ±17.49	316.43 ±26.41	385.35 ±42.31	505.91 ±66.14	613.46 ±70.92	728.89 ±60.09	6.90 ±4.31
P		n.s.	n.s.	<0.04	n.s.	<0.001	n.s.	n.s.	<0.001

Figure 1: Representative waveforms from one subject of three groups in two experimental conditions in which infrequent stimuli were counted (Test 1) or uncounted (Test 2). As seen in the figure, ERP peaks were absent or much reduced in amplitude when the stimuli were uncounted. When P_3 had two peaks, the former was labeled as P_{3a}, the latter as P_{3b} component. When a single peak was identified, it was considered as corresponding to the P_{3b} component.



Mean latencies and deviations for N_1, P_2, N_2, P_{3a}, P_{3b}, N_3, and P_4 across all subjects in Test 1 and Test 2 are summarized in Table 1. Paired t test indicated that latencies of N_2 and P_{3b} were prolonged in the Test 2 case compared to Test 1 case for three groups. Additionally, the latency of N_1 and P_{3a} in young group whereas P_{3a} in middle-aged group was longer in Test 2 than Test 1 (Table 1).

The results of one-way ANOVAs were given in Table 2. One-way ANOVA proved that significant differences were found between groups. The results of regression analysis were shown in Table 3. The P_{3b} latency increased significantly with age at a rate of 1.75 ms/year (r=0.65). The mean intercept value was approximately 353.15 ms (SE= ±0.39 ms). The P_{3b} latency data for subjects are plotted as a function of age in Figure 2. On the other hand, any significant correlation was not observed between P_3 amplitudes and ages.

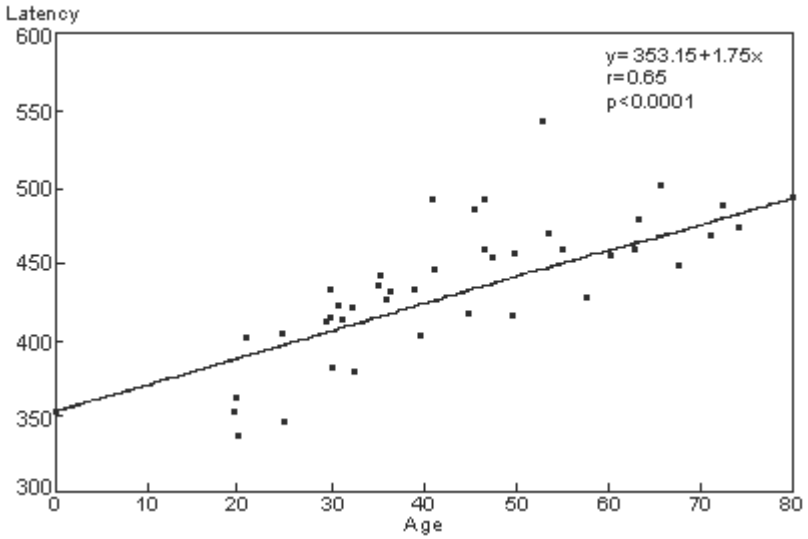
Table 2: Analysis of variance results for Test 1 case.

ERP Componnents	Groups		
	Young-Middle aged	Young-Older	Middle-Older aged
N_1	F=8.68, p<0.01	F=13.5, p<0.002	n.s.
P_2	F=8.47, p<0.01	F=16.29, p<0.001	n.s.
N_2	F=12.15, p<0.002	F=26.97, p<0.0001	n.s.
P_{3a}	n.s.	F=12.91, p<0.003	n.s.
P_{3b}	F=20.68, p<0.001	F=29.94, p<0.0001	F=5.57, p<0.03
N_3	F=5.13, p<0.04	F=21.55, p<0.0001	n.s.
P_4	n.s.	F=7.95, p<0.01	F=7.2, p<0.02

Our results indicated that there were substantial differences in latencies of ERP components across age groups. The latencies of ERP components (P_2, N_2, P_3) have all been shown to increase as a function of age (23,34). The findings in the present study agree with these studies.

Our data confirm the generally reported result that P_3 latency increases significantly with age. Visual P_3 latency prolongation (1.75 ms/year) was within the range of previously reported values (auditory: 1.8 ms/year (22,26), 1.3 ms/year (18,23), 1.1 ms/year (24), 1.12 ms/year (25), visual: 1.45 ms/year (29), 1.4-1.7 ms/year (35)).

Figure 2: P_{3b} latency plotted as a function of subject age.



In an agreement with previous studies (12,35,36), it was found that visual P_3 amplitudes were not affected by age. Our data were in controversy with those (12,23,25,34) who found that auditory and somatosensory target P_3 amplitudes were inversely correlated with age.

Our data in respect to latency prolongation of ERP components showed that cognitive processing was affected by aging. Our results are also in good accordance with many papers reported latency prolongation of P_3 in normal aging that is regarded as an evidence of cognitive decline (14,20,30,33). Decreased cognition as sometime recognized as being one of the most severe and consistent behavioral impairment related aging (37). Cognitive alterations observed in aging have been related to dopaminergic and cholinergic systems which, play important roles in the process of cognition (2,15,38-41). Because the number of muscarinic Ach receptors in the central nervous system and the activity of choline acetyltransferase in nerve terminals were shown to decrease with aging (37,42-44). On the other hand, nigrostriatal axons (45), nigrostriatal dopaminergic neurons (46), strial endogenous dopamine concentration in human brain (47) and D_2 dopamine receptor binding sites (48) were found to decrease with age. So cognitive decline have been caused by deterioration of dopaminergic and cholinergic systems.

Table 3: Regression equations of ERP components.

n_1	y=125.37±1.50x r=0.5	F= 11.32	p<0.002
P_2	y=161.39±1.62x r=0.53	F= 14.78	p<0.001
n_2	y=212.86±1.46x r=0.6	F= 22.46	p<0.0001
P_{3a}	y=261.66±1.62x r=0.62	F= 18.25	p<0.0002
P_{3b}	y=353.15±1.75x r=0.65	F= 30.1	p<0.0001
n_3	y=442.95±3.49x r=0.51	F= 13.71	p<0.001
P_4	y=532.09±2.86x r=0.42	F= 7.34	p<0.02

In conclusion, our study has clearly shown that conventional parameters are sensitive enough to serve as diagnostic tests in evaluating cognitive decline as age the increases.

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