THE EFFECT OF HYPERLIPIDEMIA ON EVEN-RELATED BRAIN POTENTIALS (P_3)

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SUMMARY: The purpose of the study is to investigate cognitive changes in hyperlipidemic patients by means of event-related potentials (ERPs). ERPs of twenty hyperlipidemic patients and age-matched healthy controls were measured by applying infrequent and frequent stimuli as red and green lights respectively. The infrequent stimulus had a 15% probability. ERPs were recorded in two different experimental conditions that the infrequent stimulus was counted (Test 1) or uncounted (Test 2). P_{3b} amplitudes of both groups were decreased significantly in Test 2 compared to Test 1. N_2, P_{3a} and P_{3b} latencies of the count stimulus condition (Test 1) were found to be prolonged in the hyperlipidemic group. In addition, peak-to-peak amplitudes of P_{3b} were observed to be decreased ($F=5.84$, $p<0.3$)

Key Words : Hyperlipidemia, decision making, P_3 (P_{300}).

INTRODUCTION

Several components of event-related potentials (ERPs) observed after task specific processing events, have been intensively studied over the past decade (1-9). The main component of interest has been a large positivity occurring at latencies of 250 to 600 ms (7,10,11). This potential P_3 or P_{300}, is related to the fundamental cognitive event such as stimulus discrimination, directed attention, sequential information processing, short term memory, decision making and learning (1,2,8,12-14).

The P3 component of event-related potentials (ERPs) is used to evaluate the cognitive function of human subjects. Prolongation of latency and/or decrease of the amplitude have been employed as an objective measurement for assessing the degree of cognitive disorders and reported in a variety of diseases (3,8,15-17). On the other hand, the effect of hyperlipidemia on ERPs has not been reported yet. According to our previous studies on EEG (18,19), somatosensory evoked potentials (20,21) and peripheral nerves (22), and to other reports (23-25), lipids are known to be important in the regulation of membrane fluidity and excitability, they can in turn influence the cellular behavior toward external ligands (24-28). Therefore the purpose of the present study was to investigate changes in event-related potentials, particularly P_3, in hyperlipidemic patients.

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MATERIALS AND METHODS

Twenty hyperlipidemic patients (10 females and 10 males) within the age range from 39 to 70 years (mean = 52.5 ± 9.28 years) and twenty control subjects were studied. The healthy control subjects were 12 females and 8 males, ranging in age from 38 to 73 with a mean of 51.65 ± 9.97 years. All patients included in this study had earlier undergone clinical and investigative evaluation of their disease at the Faculty of Medicine of Akdeniz University. None of the subjects reported neurolog-

ical or psychiatric problems.

Disc electrodes were attached with collodion to all the electrode sites. The event-related potentials (ERPs) were recorded from the parietal region (Pz) referenced to glabella, using MS6 EMG equipment. The ground electrode was placed on the forehead.

The ERPs were recorded in two different experimental conditions where the rare stimulus was counted (Test 1) or uncounted (Test 2). In Test 1, the subjects were asked to count silently the number of rare stimuli (red light) presented randomly in sequence of green lights. Fifteen per cent of the stimuli were at red light and the remainder at green light. Red and green lights were produced by 4 mm diameter light-emitting diode (LED). Each stimuli was delivered at rare of 0.9/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 100 ms. Trials in which subjects became drowsy, or in which the count of infrequent stimuli was error by more than 3, were discarded. The microprocessor was programmed to reject any sweeps contaminated with eye movement artifacts, 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 two 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 the previous descriptions (29). P_3 amplitude was measured as the amplitude of N_2-P_{3b} deflections.

Cholesterol and triglyceride in serum were determined in a Dacos auto-analyzer using enzymatic Dart reagents (Coulter Inc. Hialeah, Miami, USA). The statistical analyses were included for several comparisons. First, differences of parameters between Test 1 and Test 2 were analyzed by paired t-test. Second, one-way ANOVA was used to establish significant differences between patients and controls.

RESULTS

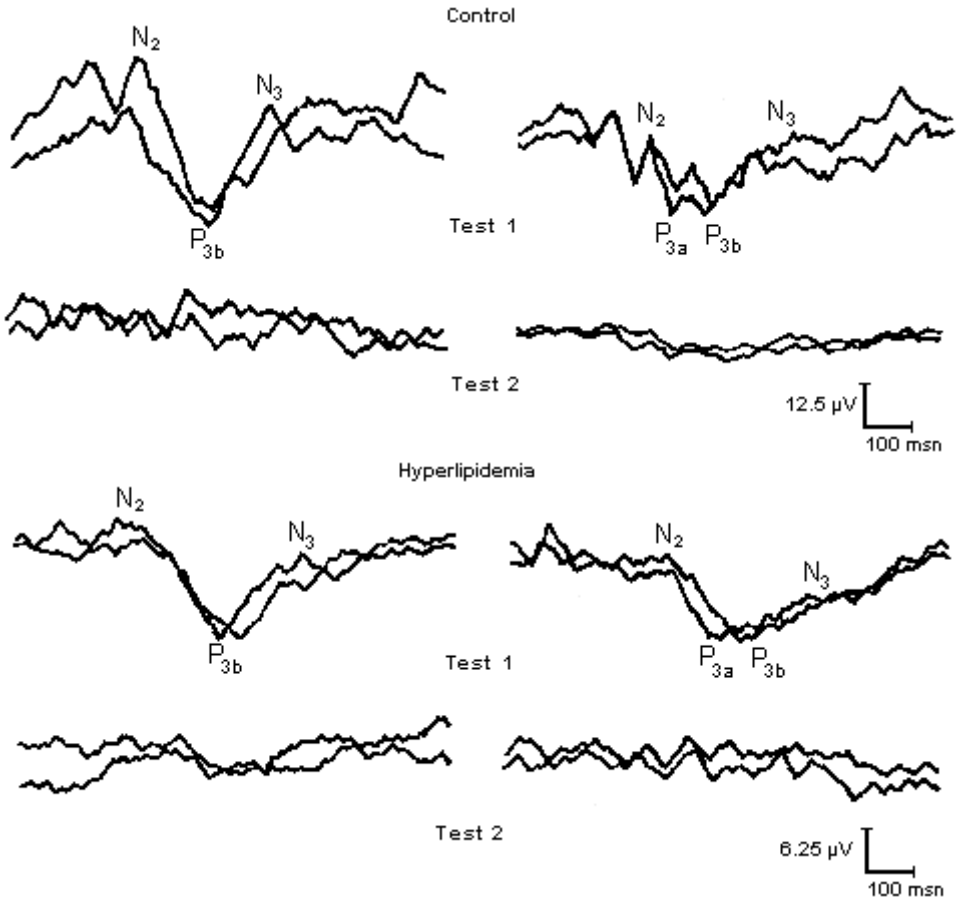
Triglyceride and total cholesterol values of control and patient groups are indicated in Table 1. Differences between control and patient groups were highly significant.

ERPs recorded from patients and normal subjects in the count (Test 1) and uncounted stimulus conditions (Test 2) are shown in Figure 1. When subjects counted the rare stimuli, a large P_3 was present in those recordings; this potential was absent or markedly attenuated

Table 1: Latencies (mean±SD) of ERP components recorded in the case Test 1 for hyperlipidemic and normal matched control subjects. The table reports also the amplitude of N_2-P_3 deflections and cholesterol, triglyceride values.

Latency, ms							
	N_1	P_2	N_2	P_{3a}	P_{3b}	N_3	P_4
Control Group	206.94 ±28.34	243.95 ±29.98	292.00 ±23.02	343.21 ±20.25	451.00 ±42.45	610.53 ±77.92	690.28 ±70.09
Hyperlipidemic Group	197.67 ±16.78	250.94 ±36.84	315.50 ±39.09	376.00 ±37.77	512.75 ±82.68	601.00 ±73.73	668.84 ±56.54
One-way ANOVA	n.s.	n.s.	F=5.36 p<0.03	F=7.59 p<0.02	F=8.83 p<0.006	n.s.	n.s.
	Amplitude N2-P3, μV		Cholesterol mg/dl			Triglyceride mg/dl	
Control Group	13.97 ±4.71		185.15 ±29.89			111.70 ±27.74	
Hyperlipidemic Group	10.51 ±4.42		324.95 ±40.14			327.40 ±60.26	
One-way ANOVA	F=5.84 p<0.03		F=156.09 p<0.0001			F=90.29 p<0.0001	

Figure 1: Representative waveforms of two subjects from each group in two different experimental conditions in which infrequent stimuli were counted (Test 1) or uncounted (Test 2). Notice variations in P_3 waveform morphology A. Single-peaked, B. Bifid-peaked.



in the recording of the uncounted stimuli (Figure 1). A statistically significant amplitude increment was also evidenced in comparisons between Test 1 and Test 2 for both groups (Table 2). Mean latencies and standard deviations of N_1, P_2, N_2, P_{3a}, P_{3b}, N_3 and P_4 in controls age-matched with patients are reported in Tale 2. Paired t-test indicated that the latencies of N_1, N_2, P_{3a}, P_{3b} in controls whereas P_4 in patient group was delayed in Test 2 compared to Test 1.

The mean and SD of the latencies for peaks N_1, P_2, N_2, P_{3a}, P_{3b}, N_3 and P_4 in count stimulus condition are shown in Table 1. One-way ANOVA proved that patients yielded significantly ?lorger? N_2, P_{3a}, P_{3b} latencies compared to the control subjects (Table 1). The latencies of N_2 and P_{3a} in 3 patients and P_{3b} in 7 patients were above the mean value of latency plus 2 SD of age-matched controls. The latencies of N_2 and P_{3a} in 2 patients and P_{3b} in 5 patients were above the mean value of latency plus 3 SD of controls.

The mean and standard deviation of P_{3b} amplitudes in Test 1 for both groups are reported in Table 1. The mean amplitude of P_{3b} was found to be decreased in the patient group compared to the control group ($F=5.84$, $p<0.03$) (Table 1).

DISCUSSION

Persons with the total cholesterol levels above 240 mg/dl and with triglyceride levels higher than 250 mg/dl are considered hyperlipidemic according to the crite-rion given by Peters (1991) (30) in this study.

Our latency and amplitude results of visual ERPs are consistent with previously reported data (4,31-33).

Table 2: Mean and standard deviation of peak latencies and peak - to -peak P3b amplitude for two cases Test 1 and Test 2.

Latency, ms									
		N_1	P_2	N_2	P_{3a}	P_{3b}	N_3	P_4	Amplitude N2-P3, μV
Control Group	Test 1	206.94 ±28.34	243.95 ±29.98	292.00 ±23.02	343.21 ±20.25	451.00 ±42.45	610.53 ±77.92	690.28 ±70.09	13.97 ±4.71
	Test 2	193.82 ±24.01	250.00 ±20.62	307.00 ±26.97	373.75 ±40.75	490.38 ±67.96	605.53 ±81.22	712.50 ±93.27	5.13 ±4.31
Paired t test		p<0.04	n.s.	p<0.03	p<0.008	p<0.002	n.s.	n.s.	p<0.0001
Hyperlipidemic Group	Test 1	197.67 ±16.78	250.94 ±36.84	315.50 ±39.09	376.00 ±37.77	512.75 ±82.68	601.00 ±73.73	668.84 ±56.54	10.51 ±4.42
	Test 2	207.50 ±8.80	237.78 ±34.92	303.82 ±38.79	379.12 ±41.39	513.33 ±64.19	589.64 ±64.43	700.77 ±73.34	4.64 ±3.65
Paired t test		n.s.	n.s.	n.s.	n.s.	n.s.	n.s.	p<0.05	p<0.0001

The ERPs latencies have been found to be longer in the visual stimuli than in the auditory stimuli in their studies.

Two types of P_3 event-related potential have been described in the visual (34,35), auditory (29,36,37) and somatosensory (10,11) modalities. These components, termed P_{3a} and P_{3b} have been shown to differ in their latency, scalp topography and psychological correlates (5,10,11,29,38,39). P_{3a} may provide a valuable index of orienting or automatic attention capacity in subjects (10,11,38,39). The patients' delayed P_{3a} is possibly the evidence of the interruption of orienting or automatic attention in hyperlipidemia.

The P_3 and N_2 components of ERPs have been related to various cognitive processes and studied in a variety of diseases (6-9,12,14,15,40). Prolongations of P_3 and N_2 latencies have been reported in cases with dementia (7,15,40), epilepsy (12), multiple sclerosis (8) and Parkinson's diseases (6). Our results in respect to latency prolongations of these components in patients reflect changes in cognitive functions associated with hyperlipidemia.

The changes in binding of transmitters agonists and antagonists and other processes involved in synaptic transmission such as release and uptake as well as in synaptic plasticity may be associated with modulation of membrane architecture caused by changes in membrane lipid fluidity. Thus it is expected that each receptor has an optimal lipid fluidity for maximal physiological response (41,42). The fundamental neurotransmitters such as acetylcholine, serotonin, opioids, noradrenalin related to cognitive functions (12,43-47) have been shown to be modulated by changes in membrane lipid fluidity (48). Therefore, decrease in the membrane fluidity may cause cognitive alterations in hyperlipidemia.

In conclusion, these data are also in line with the statement that the P3 waves appear to be a valuable tool for investigating the electrophysiological correlates of cognitive processes and is sensitive index of cognitive dysfunction in several diseases.

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