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Auditory Brainstem Potentials in Sons of Alcoholic Fathers

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With the use of event-related brain potentials we have observed sensory as well as cognitive deficits in abstinent alcoholics. By recording auditory brainstem potentials (BSP) from abstinent alcoholics we demonstrated significant delays in brainstem transmission time. We have also reported that P3 amplitudes are significantly reduced in abstinent alcoholics compared to control subjects.

Although the neurophysiological deficits observed in abstinent alcoholics are presumed to be alcohol-related effects, it is possible that some of these deficits may exist prior to alcohol exposure, and may be present in subjects at high risk for alcoholism. We have recently observed significantly reduced P3 components in young sons of alcoholics similar to those observed in abstinent alcoholics. In the present study, we examined auditory BSPs in young boys at high risk for alcoholism and matched controls. We found no statistically significant difference in brainstem transmission time between high risk individuals and matched control subjects. These findings suggest that while some brain deficits observed in abstinent alcoholics may antecede the development of alcoholism (P3) and may represent a predisposing factor, other deficits (BSP) appear to be the consequence of alcohol and/or nutritional-related effects.

IN RECENT YEARS a number of neurophysiological investigations have demonstrated several evoked brain potential (EP) deficits in abstinent alcoholics.[1-3] In various experiments conducted in our laboratory, we have examined the P3 component of the event-related brain potential (ERP) in abstinent alcoholics. A P3 component is a late (300–600 msec) endogenous component that is related to the subjective "significance" of a stimulus. We have repeatedly observed that P3 amplitudes to target stimuli were significantly decreased or absent in alcoholic patients.[4-9] This finding was most pronounced over parietal areas, where P3 amplitude is maximal at the scalp.[3,4] While normal control subjects manifested differentially enhanced late P3 components to significant stimuli, alcoholics manifested low amplitude P3 components regardless of whether a stimulus was significant or not. Thus the major event-related brain potential (ERP) aberrations manifested by abstinent alcoholics are the low voltages of their P3 components, and the lack of differentiation between their responses to relevant and irrelevant inputs.[4,5,7,8]

It has been suggested that the P3 component of the event-related brain potential indexes the motivational properties of stimuli and may be involved in the process of memory.[10,11] Intracranial recordings in humans have indicated that the hippocampus and frontal lobe may make substantial contributions to the scalp-recorded P3 potentials.[12-14] Magnetoencephalographic studies have also suggested the hippocampus as a possible neural generator of the P3 component.[15]

In addition to the P3 deficits which have been reported in abstinent alcoholics[1,2,3,16] we have also examined the Auditory Brainstem Potential (BSP) in alcoholic patients abstinent from alcohol for 1 month.[17] We observed that abstinent alcoholic patients manifested significant delays in latencies and central conduction velocities of peaks II–V.

It is generally assumed that the neurophysiological deficits observed in abstinent alcoholics, such as low P3 voltage and increased brainstem transmission time,[2] represent the sequelae of long term chronic alcohol abuse, nutritional deficits, or an interaction of alcohol neurotoxicity and nutritional factors. While the aforementioned neurophysiological deficits in alcoholic patients may be the result of long term alcohol abuse, it is possible that these electrophysiological anomalies antecede the development of the disease. Recent findings in population genetics suggest that sons of alcoholic fathers are at high risk for developing alcoholism.[18,19] A number of studies have indicated that genetic predisposing factors may be present in sons of alcoholic fathers.[20]

The possibility that brain function may be involved in the genetic predisposition for alcoholism has led us to study various event-related brain potentials in children at high risk for alcoholism. Event-related brain potentials appear ideally suited because they are known to be influenced by genetic factors[21-23] and are aberrant in abstinent alcoholics.[2]

In recent years we have undertaken a major program of research to study brain function in young sons of alcoholic fathers with the use of a number of evoked brain potential techniques. We have recently examined the P3 component of the event-related brain potential in high risk and matched control subjects.[24] Our data indicate a significantly lower P3 voltage in sons of alcoholic fathers as compared to a matched group of control children. These

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neurophysiological findings are rather striking as they were obtained without the use of alcohol in sons of alcoholics never exposed to alcohol or other drugs of abuse. Moreover, these neurophysiological deficits obtained in children at high risk are similar to our findings in abstinent alcoholics.

In light of the similarity in P3 findings obtained in abstinent alcoholics and boys at high risk for alcoholism, and the auditory brainstem anomalies observed in abstinent alcoholics, we undertook to examine auditory brainstem transmission time in boys at risk for alcoholism.

METHODS

Potential subjects were screened by obtaining careful alcohol intake and drug histories. This was accomplished by conducting separate interviews at the same time with two independent interviewers. Approximately 60% of the subjects interviewed were excluded from the study because of minimal exposure to alcohol.

Twenty-three sons of alcoholic fathers between the ages of 7 and 13 years with a mean age of 12.2 years (SD = 2.1) were tested in this study. In each case the father had received the exclusive diagnosis of alcoholism in accordance with DSM III criteria and had at one time or another been in treatment for alcoholism. We excluded boys whose mothers had ever been alcoholics or who drank excessively during or after pregnancy. This was established by interviewing the mothers about their daily alcohol intake during and after pregnancy. Only boys without medical problems and without exposure to alcohol or other substances of abuse were included in this study. In this study a new sample of young boys at risk for alcoholism and matched control boys were used.

The 23 normal control subjects (NC) were boys who were matched for socioeconomic status, education, and age to the high risk (HR) subjects. The NC group had a mean age of 12.4 years (SD = 2.3). They were included only if they had no exposure to alcohol or other substances of abuse, and had no history of alcoholism, or other major psychiatric disorder in first or second degree relatives. Except for alcohol history in the fathers, the same exclusion criteria were used in the NC group as for the HR group. All participating subjects were paid volunteers.

Auditory brainstem potentials were recorded in both groups of children in a manner identical to that used in our study of brainstem potentials in chronic alcoholics.[17] Clicks (0.5-msec duration) were generated by a Grass click-tone generator (S10 CTCMA) and presented monaurally through earphones (TDH-39) at a rate of 10 clicks per second for a total of 2000 clicks. Each ear was tested separately and in random order across all subjects. Stimulus intensity was 70 db above threshold. Recordings were obtained between a vertex electrode and the ipsilateral earlobe, with an electrode on the forehead serving as the ground. The potentials were amplified 100,000 times and were subjected to a digital filter with a bandpass of 100 Hz to 2 KHz.[25]

The computer sampled the electrical activity as a rate of 40 KHz for 11 msec following the click. The initiation of sampling was delayed by 1 msec in order to eliminate the stimulus artifact from the display. We measured the latency of the first five positive peaks including the interpeak latencies between peak I and each successive peak. The interpeak latency between peaks I and V is inversely related to the conduction velocity in the ascending pontine segment of the auditory pathway and is an index of brainstem transmission time (BTT).[26]

RESULTS

The brainstem potentials for one NC subject and one HR subject are shown in Fig. 1. The mean peak latencies for the HR and NC groups are indicated in Table 1. The differences in mean latencies for the three peaks (I-III-V) and three interpeak (I-III, III–V, and I–V) latencies between the two groups of subjects were assessed with the use of a two-way analysis of variance with repeated meas-

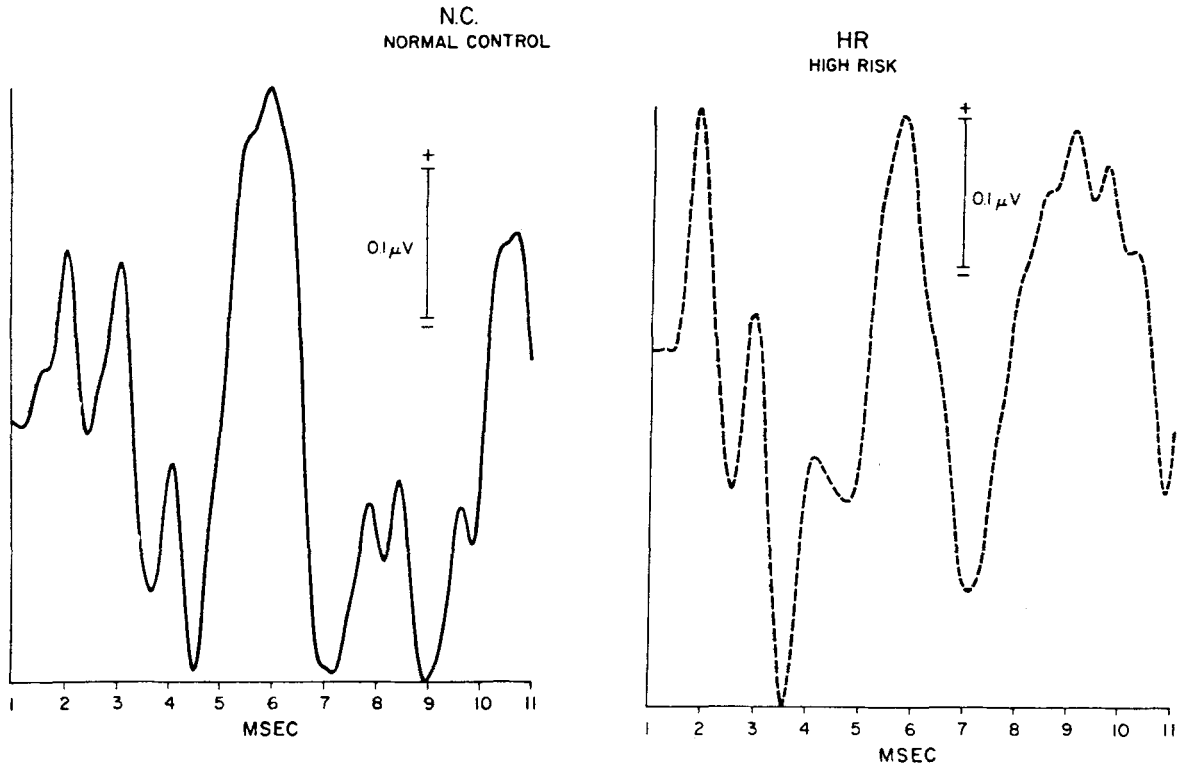

Fig. 1. Auditory brain stem potential obtained from a single control subject (left) and a single individual at risk for alcoholism (right).

Table 1. Auditory Brainstem Component Latencies

	Right ear			Left ear		
Mean latencies	I	III	V	I	III	V
Normal control	1.75	4.17	5.82	1.90	4.15	5.72
	±0.39	±0.71	±0.97	±0.34	±0.92	±0.96
High risk	1.82	3.90	5.92	1.85	3.92	5.80
	±0.41	±0.68	±1.21	±0.62	±1.08	±1.41

ures with an appropriate correction yielding a conservative number of degrees of freedom.[27]

The statistical analyses did not yield significant differences between groups for any of the latency or interpeak latency measures. Furthermore, there was no significant difference between ears for either group of subjects.

DISCUSSION

Our findings indicate that the auditory brainstem potentials obtained from sons of alcoholic fathers do not differ significantly from those obtained from matched control subjects. Both the individual peak latencies and the brain stem transmission time are quite similar in the high risk individuals and normal controls.

The lack of a statistically significant difference in brainstem potentials between HR and NC subjects is quite interesting in light of our previously reported difference in the P3 component of the ERP between HR and NC subjects.[24] Our neurophysiological investigations with subjects at high risk for alcoholism indicate that while there is a significant decrease in the amplitude of the P3 component, the brainstem potentials in the high risk boys do not differ from those in control subjects.

These findings may shed light on differences in etiology of evoked potential results obtained in alcoholic patients which indicate both P3 deficits and brainstem latency delays. The presence of prolonged brainstem transmission time in abstinent alcoholics and the absence of such deficits in children at risk suggest that brainstem deficits do not antecede the development of alcoholism but may reflect the consequence of chronic alcohol abuse and/or nutritional deficits in alcoholic patients.

It is important to note that we have recently observed improvement in the brainstem transmission time of hospitalized alcoholic patients. We recorded brainstem potentials in hospitalized, medication-free alcoholics, abstinent for a period of 3 weeks. We noted that brainstem transmission time was significantly delayed in the alcoholic patients as compared to a group of matched normal control subjects. We were able to retest some of the alcoholics who remained hospitalized for an additional period of 3 months. Upon retesting, we found that the auditory brainstem potentials recorded in the alcoholics manifested brainstem transmission times which were no longer statistically different from those observed in normal controls.[3] The low P3 voltages which we have reported in boys at high risk for alcoholism are not only present in abstinent alcoholics but do not recover after 4 months abstinence.[3]

The presence of P3 deficits in both abstinent alcoholic patients and children at high risk for alcoholism do suggest that this neurophysiological aberration may antecede the development of alcoholism. While our studies indicate that P3 deficits are present in high risk subjects not exposed to alcohol,[24] it certainly does not vitiate the possibility that chronic alcohol abuse may further impair the neural generators of the P3 component.

The ability to utilize identical neurophysiological tools in assessing brain dysfunction in abstinent alcoholics and high risk individuals should prove most valuable in separating the deleterious effects of alcohol on brain functions from brain deficits which antecede the development of alcoholism. Moreover, because evoked potential waveforms are influenced by genetic factors[21–23] and are known to be aberrant in abstinent alcoholics, this technique may prove valuable in the search for potential biological predisposing factors.

The identification of suitable biological markers that are genetically transmitted may be of great significance in identifying individuals before the onset of the disease. Furthermore, reliable biological markers may provide fundamental information concerning the etiology of alcoholism.

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