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Auditory Brainstem Potentials in Chronic Alcoholics

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Abstract. *Auditory brainstem potentials were recorded from abstinent chronic alcoholics and control subjects. The latencies of peaks II, III, IV, and V were significantly delayed in the alcoholic patients compared to control subjects. Brainstem transmission time was longer in alcoholics than in controls. This study provides systematic evidence that chronic alcohol abuse results in brainstem deficits suggesting possible demyelination of auditory tracts.*

Chronic alcoholism is known to result in aberrations of the central nervous system. At the structural level, these deficits have been studied with the use of neuropathological methods (*1*), pneumoencephalography (*2*), and computerized tomography (*3*). At the functional level, these changes have been examined with neuropsychological tests (*4*), electroencephalography (*5*), and cerebral blood flow studies (*6*). More recently, event-related potentials (*7*) have been used to assess the functional integrity of the brains of alcoholic patients. These electrophysiological studies have demonstrated functional deficits reflected in specific components of the event-related potential (ERP). The N1-P2 component of the ERP has been found to be depressed in chronic alcoholics, regardless of whether the response is to a relevant or irrelevant stimulus modality (*8*). Furthermore, abnormal P300 components have been reported in abstinent chronic alcoholics (*9*). Investigations of the structural (*1–3*) and functional (*4–9*) brain aberrations in alcoholics have produced consistent findings indicating that chronic alcohol abuse affects primarily the cerebral cortex and leaves relatively intact the primary sensory pathways.

Potentials generated in the auditory nerve and brainstem auditory pathway consist of seven positive waves occurring at specific latencies (*10*). Each peak is presumed to reflect the activity of different neural sites, with the first wave generated in the auditory nerve, the second in the cochlear nucleus, and the third in the region of the superior olivary complex. The fourth wave is postulated to emanate from the lateral lemniscus and the fifth peak from the inferior colliculus (*11, 12*). The neural sites responsible for the activity of the last two peaks are at present unknown. Investigators have reported that the time interval between peak I of the compound auditory nerve response and peak V of the inferior colliculus in the midbrain may prove valuable as a measure of brainstem transmission time (BTT) (*13*).

Several studies have demonstrated that a single dose of alcohol causes significant increases in the auditory BTT in rats (*14, 15*), cats (*15*), and man (*16*). However, functional brainstem deficits have not been reported in alcoholic patients practicing abstinence. We now report that transmission time in the auditory brainstem pathways of alcoholic patients is significantly slower than that in control subjects.

Seventeen hospitalized male alcoholic patients with a mean age of 38 ± 2.1 years (± standard deviation) were tested in this study. All patients met the Research Diagnostic Criteria (*17*) for alcoholism. Alcoholic patients with a history of hepatic encephalopathy, a history of

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Table 1. Mean latencies (± standard deviation) of auditory brainstem potentials of peaks I through V and the latency of each peak with respect to peak I for the alcoholic and control groups. The level of statistical significance (P) between the alcoholic and control groups is indicated for each measure (N.S., not significant).

Subjects	Mean latencies for peaks					Interpeak latencies			
	I	II	III	IV	V	I and II	I and III	I and IV	I and V
Controls	1.84 ± 0.22	2.73 ± 0.29	3.57 ± 0.23	4.95 ± 0.34	5.88 ± 0.39	0.88 ± 0.22	1.72 ± 0.24	3.11 ± 0.40	4.04 ± 0.43
Alcoholics	1.82 ± 0.22	3.04 ± 0.39	4.15 ± 0.51	5.77 ± 0.51	6.81 ± 0.58	1.22 ± 0.45	2.33 ± 0.62	3.95 ± 0.56	4.99 ± 0.59
P	N.S.	.02	.001	.001	.001	.01	.005	.001	.001

head injury, seizures not related to alcohol withdrawal, or abuse of other psychoactive drugs were not included in the study. The patients had been drinking heavily for an average of 16 years and a minimum of 6 years. All patients were totally abstinent for a minimum of 3 weeks and medication-free for a minimum of 2 weeks.

Seventeen age-matched and education-matched males were used as control subjects. They were recruited from among hospital employees and paid for their participation. All control subjects were prescreened for drinking and medical histories and were medically examined prior to the experiments; only subjects who were occasional "social drinkers" and were free of medical problems and medication were accepted for the study. Auditory brainstem potentials were evoked monaurally with the use of 2000 stimuli consisting of 0.5-msec clicks presented through earphones (TDH 39) at a rate of ten stimuli per second. Each ear was tested randomly across all subjects. Stimulus intensity was 70 dB above threshold. Monopolar recordings were taken 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 2000 kHz (*18*). Brain electrical activity was sampled at a rate of 40 kHz (one point every 25 μsec) for 10 msec following the onset of the click. We measured the latency of the first five peaks including the interpeak latencies (BTT) 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.

Since there was no significant difference between ears for either group of subjects the data for both ears were pooled. The differences in mean latencies for the five peaks and four interpeak latencies between the two groups of subjects were assessed initially with the use of a two-way analysis of variance with repeated measures, and an appropriate correction being applied to the degrees of freedom (*19*). The individual group means were further assessed with the use of individual t-tests.

The brainstem potentials for one control subject and one alcoholic subject are shown in Fig. 1. The statistical analysis yielded significant differences between groups [$F(1, 32) = 30.51$, $P < .01$] and between trial factors [$F(1, 32) = 111.08$, $P < .001$]. The interaction between groups and trial factors was also significant [$F(1, 32) = 10.15$, $P < .01$]. Peak I did not differ significantly between patients and controls. Peak II differed between groups ($P < .02$) as did peaks III, IV, and V ($P < .001$). Interpeak latencies were all significantly different as follows: between I and II ($P < .01$), I and III ($P < .005$), I and IV ($P < .001$), and I and V ($P < .001$).

These findings provide systematic electrophysiological evidence of increased neural transmission time in the brainstem of alcoholic patients who show no clinical signs of corticobulbar or corticospinal tract deficits. Our data indicate that while the most peripheral part of the auditory pathway is not affected (peak I), there is a significant increase in latency of each succeeding peak. This significant slowing in neural transmission time reflects a decrease in conduction velocity not elicited by deficits at the peripheral organ, but suggesting pathological changes in the medulla and the pontine formation.

Various morphological abnormalities of the auditory brainstem potential have been described in patients with neurological disorders, and electrophysiological deficits have been found to be related to specific neuroanatomical lesions (*12*). Interpeak latencies of the auditory brainstem potential are stable and not influenced by factors such as attention or motivation (*20*). A significant slowing in conduction velocity of the auditory brainstem potential was reported in two patients with quadriparesis and multiple cranial nerve deficits. These patients had a long history of alcohol abuse and were suspected of central pontine myelinolysis (*21*). The pathological changes usually involve the central part of the base of the mid- to upper pons and are characterized histologically by loss of myelin sheaths and oligodendroglia whereas nerve cells, axis cylinders, and blood vessels remain relatively intact. Demyelination of the auditory tracts and nuclei at the level of the caudal and mid-pons adjacent to the basis pontis has been shown to result in a significant increase in BTT (*22*). This demyelination cannot readily be identified by clinical diagnosis, and in most cases its presence is only detectable during postmortem examinations of the brain.

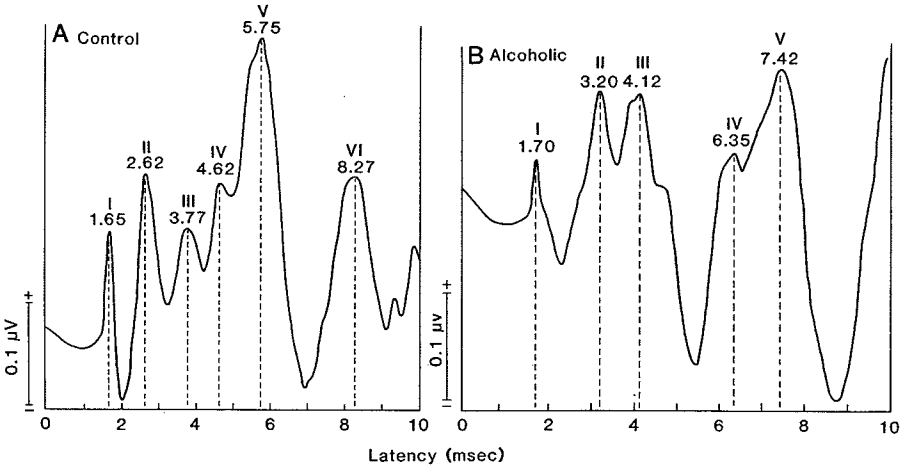

Fig. 1. (A) Auditory brainstem potential for one control subject indicating the latencies of peaks I to VI. (B) Auditory brainstem potential for one alcoholic subject, with the latencies of peaks I to V indicated. Wave VI is delayed beyond 10 msec and therefore is not shown.

Our data provide evidence for the involvement of brain areas other than neocortex in chronic alcoholism. The increase in neural transmission time within the auditory brainstem may reflect a direct pathological process of demyelination; this effect has been suspected in alcoholic patients (*23*) and observed in rats fed on alcohol for long periods (*24*). These results could also be caused indirectly by the aberrant fluidizing effects of chronic alcohol intake on cell membranes (*25*), which may result in edema. The use of auditory brainstem potentials may provide critical prognostic information about the progress of brainstem deficits in chronic alcoholics and their potential recovery with prolonged abstinence.

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