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Journal

Electroencephalography and clinical neurophysiology, 54(4)

ISSN

0013-4694

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Publication Date

1982-10-01

DOI

10.1016/0013-4694(82)90205-x

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AUDITORY BRAIN STEM RESPONSES IN CHRONIC ALCOHOLIC PATIENTS¹

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(Accepted for publication: May 28, 1982)

In acute alcohol intoxication, dizziness, vertigo, nystagmus and ataxia may indicate brain stem involvement. Among the neurological complications of alcoholism, brain stem lesions are present in Wernicke-Korsakoff syndrome, cerebellar degeneration, and central pontine myelinolysis (Courville 1954; Neuburger 1957; Adams et al. 1959; Victor et al. 1959, 1971; Lynch 1960). In spite of these known effects of alcohol or alcoholism on the brain stem, study on the prevalence of brain stem abnormalities in the general population of alcoholic patients has been ignored.

Perhaps one of the main reasons for the dearth of studies on brain stem functions associated with acute or chronic alcohol abuse was the unavailability of non-invasive objective methods. In recent years, however, techniques for recording short-latency auditory brain stem response (ABR) became available. These techniques allow study of the functional integrity of the brain stem in neurological disorders (Starr and Achor 1975; Starr 1977). Clinical and pathological studies have shown that a variety of neurological diseases involving the brain stem structures results in amplitude and/or latency changes of the ABR (Starr and Hamilton 1976; Stockard and Rossiter 1977; Chiappa et al. 1980).

Previously, we have used the ABR to study the effects of acute alcohol intoxication, tolerance to alcohol and alcohol withdrawal (Chu et al. 1978; Squires et al. 1978a, b). We now have extended our studies of the ABR to chronic alcoholic patients in order to determine the prevalence of brain stem abnormality and to correlate ABR findings with

clinical history, neurological status and laboratory data.

Methods

Patients with a history of chronic excessive alcohol consumption were selected for study if the following medical conditions were absent: (1) neurological diseases other than those complicating alcoholism, (2) cardiovascular diseases or hypertension with histories of transient neurological symptoms, (3) history of significant head trauma or anoxia-ischemia, (4) neurological disorders in the presence of neoplasms, (5) collagen vascular diseases, (6) blood dyscrasia, and (7) severe bilateral neurosensory or conductive hearing loss. The duration of heavy alcohol drinking ranged from 6 to 50 years with a mean of 25 years.

ABR tests were carried out in a quiet room with patients placed in comfortable supine positions. On rare occasions, chloral hydrate, 500 mg or 1 g, was administered to facilitate muscle relaxation. Electrodes were attached at the vertex (Cz) and mastoids, with the ipsilateral mastoid serving as the reference and the contralateral mastoid as the ground. Monaural auditory stimuli consisted of condensation clicks derived by activating TDH 39 earphones with 0.1 msec square wave pulses. The click rate was 11/sec and the intensity was 65 dB nHL (normal hearing level). Occasionally, higher intensities of 75 or 85 dB nHL were used when the components of the ABR could not be adequately identified. Brain electrical activity was amplified by approximately 10^5 with a bandpass of 100–3 kHz and averaged over 2000 click presentations for 10.24 msec. To evaluate high frequency hear-

¹ This research was supported by grants from NINCDS (NS-11876) and NIAAA (1-K02-AA-0049-01).

ing, an intensity-latency function of wave V was routinely acquired at a stimulation rate of 70/sec and click intensities of 35–75 dB nHL. Patients with moderate-to-severe hearing impairment were excluded from the study.

Recording of the ABR was not conducted during acute alcohol intoxication and withdrawal including seizures and delirium tremens, and in cases of hepatic or Wernicke's encephalopathy. In such cases, ABR was studied at least 4–6 weeks after the acute neurological episodes. The majority of patients were studied because of their histories of alcohol abuse or alcohol-related neurological complications.

The ABR was considered abnormal when the I–V, I–III and III–V intervals were respectively equal to or greater than 4.5 msec, 2.6 msec and 2.4 msec (mean $\pm$ 2.5 S.D.) for patients less than 50 years of age and 4.6 msec, 2.7 msec and 2.3 msec (mean $\pm$ 3.0 S.D.) for patients greater than 50 years of age (Starr and Achor 1975; Beagley and Sheldrake 1978; Rowe 1978; Stockard et al. 1979; Chiappa et al. 1980; Rosenhamer et al. 1980). If wave I could not be identified, the patient was not included in the study.

The majority of the patients had EEG and computerized tomographic (CT) scan as part of the neurological work-up. The classification of neurological complications of alcoholism by Victor (1975) was adapted. Acute alcohol intoxication and withdrawal syndromes other than alcohol withdrawal seizures and delirium tremens were excluded from analysis.

Results

The ABR was obtained from 66 alcoholic patients. Fifty-one patients were male and 15 were female, with a mean age of 44.8. Seventeen patients had no history of neurological complications of alcoholism and the remaining 49 patients had a history of at least one alcohol-related neurological disease. Monaurally evoked ABRs were obtained from both ears in 59 patients. Among 7 patients who had only unilateral ABRs, 4 patients had severe unilateral hearing loss on the other side,

and 3 patients had technically unsatisfactory ABRs on one side.

The overall incidence of abnormal ABRs was 41%, i.e., 27 out of 66 patients. Of these, abnormal ABRs defined by a significant delay in the I–V interval occurred in 25 patients (Fig. 1 and Table I). The distribution of the I–V intervals for the total patient population is presented in Fig. 2. The mean interval of the patient population was 4.36 msec ($\pm$ 0.35) which is prolonged when compared to the mean of 4.0 msec in normal subjects (Starr and Achor 1975; Stockard and Rossiter 1977; Rowe 1978; Chiappa et al. 1980). Note that the majority of abnormal I–V intervals were between 4.5 and 5.0 msec, and the longest value was 5.8 msec. Among the 25 patients with abnormal I–V intervals, the I–III interval was prolonged in 5, the III–V interval in 10, and both intervals in 1 (Table I). In addition, two patients with normal I–V conduction times had a prolonged I–III interval.

The ABR abnormalities were bilateral in 6 patients and unilateral in 21. Six of the 7 patients from whom only a unilateral ABR was obtained had abnormal potentials. The incidence of abnormal ABRs for male patients was 43%, while that for female patients was 38%.

The incidence of abnormal ABRs with respect to age shows at least a 3-fold increase above 30 years of age and a tendency for an abnormal ABR to be more prevalent with further increase in age (Table II). Difficulty was encountered in determining the incidence of abnormal ABRs in the various types of alcoholic neurological diseases as only 25 patients had a single neurological complication. However, when neurological complications not involving the CNS such as neuropathy and myopathy were excluded, there were 32 patients with only one neurological complication. For alcoholic patients who did not have any neurological complications, the incidence of abnormal ABRs was only 12% (Table III). A similar incidence was also observed in patients with only alcohol withdrawal seizures. Alcoholic patients with cerebellar degeneration had the highest incidence of abnormal ABRs (83%), followed by Wernicke-Korsakoff syndrome (50%), hepatic encephalopathy (50%), dementia (50%) and delirium tremens (25%). The

A. No Neurological Complications

B. Dementia

C. Cerebellar Degeneration

D. Wernicke-Korsakoff Syndrome

Fig. 1. Auditory brain stem responses in patients without a history of alcoholic neurological complications (A), with dementia (B), cerebellar degeneration (C), and Wernicke-Korsakoff syndrome (D).

TABLE I

Auditory brain stem responses in 66 alcoholic patients. The numbers are those of patients.

	I-V interval	
	Normal	Abnormal
A. Normal I-III and III-V intervals	39	9
B. Abnormal I-III interval	2	5
C. Abnormal III-V interval	0	10
D. Abnormal I-III and III-V intervals	0	1

TABLE II

The incidence of abnormal ABRs with respect to the age of patients. The numbers are those of patients.

Age	ABR		
	Normal	Abnormal	Percentage
20-29	8	1	11
30-39	11	6	35
40-49	4	4	50
50-59	10	7	41
60-69	6	8	57
70-79	0	1	?
Total	39	27	41

Fig. 2. Distribution of the I-V interval of the ABR in the patient population.

incidence of abnormal ABRs increased *pari passu* with increase in the number of neurological complications the patients had (Table IIIB). There was a 3-fold increase in abnormal ABRs in patients having one alcoholic neurological disease. An extremely high incidence of abnormal ABRs was observed in patients with 3 or more neurological complications.

The relationship between ABRs and abnormalities in EEGs and CT scans is presented in Table IV. Thirty-nine percent of the EEGs obtained from 49 patients were abnormal, showing in most cases mild to moderate diffuse slowing. None of the EEGs had epileptiform activity, but 3 EEGs

showed predominantly unilateral slowing. There was only a slight increase in the incidence of abnormal ABRs (43% vs. 37%) when the EEG was abnormal compared to when it was normal. A CT scan was obtained from 52 patients and 24 (46%) had abnormal findings consisting of either diffuse cerebral atrophy or both cerebral and cerebellar atrophies. The incidence of abnormal ABRs in patients with abnormal CT scans was almost 6 times greater than when the CT scans were normal (70% vs. 11%). All the patients with both cerebral and cerebellar atrophies in CT scans had abnormal ABRs.

TABLE III

The incidence of abnormal ABRs with respect to the type (A) and the number (B) of neurological complications of alcoholism. The numbers are those of patients.

	ABR		
	Normal	Abnormal	Percentage
<i>A. Type of neurological complications</i>			
Alcohol withdrawal seizure	9	1	10
Delirium tremens	3	1	25
Hepatic encephalopathy	1	1	50
Dementia	3	3	50
Wernicke-Korsakoff syndrome	2	2	50
Cerebellar degeneration	1	5	83
<i>B. Number of neurological complications</i>			
0	15	2	12
1	15	10	40
2	4	5	56
3	2	7	77
4	1	4	80
5	0	1	?
	39	27	41

TABLE IV

The incidence of abnormal ABRs with respect to EEG and CT scan. The numbers are those of patients.

	ABR		
	Normal	Abnormal	Percentage
<i>A. EEG</i>			
I. Normal	22	13	37
II. Abnormal	8	6	43
<i>B. CT scan</i>			
I. Normal	25	3	11
II. Abnormal	7	17	70
1. Cerebral atrophy	7	11	61
2. Cerebral and cerebellar atrophy	0	6	100

Discussion

This study shows that brain stem abnormalities in chronic alcoholic patients, as defined by prolonged interwave intervals of the ABR, are common. Even excluding the patients with Wernicke-Korsakoff syndrome and cerebellar degeneration, which are known to affect the brain stem, there were still 17 of 56 patients with abnormal ABRs

(30%). This finding suggests that many alcoholic patients without a clinical history of brain stem involvement may have brain stem lesions.

One limitation in this study was the small number of patients in each of the various subgroups of alcoholic neurological complications. Caution is needed to interpret the incidence of ABR abnormality in patients with delirium tremens, dementia, hepatic encephalopathy or Wernicke-

Korsakoff syndrome (Table IIIA). The incidence of abnormal ABRs in patients with alcohol withdrawal seizure is not different from that for patients without a history of alcoholic neurological complications, suggesting that alcohol withdrawal seizure is not an important factor associated with brain stem lesions. The data also indicate that alcoholic patients with cerebellar degeneration have a high incidence of brain stem abnormalities. The incidence of abnormal ABRs in cerebellar degeneration in this study correlates with that reported by Rosenhamer and Silfverskiöld (1980), who observed that 10 of 13 alcoholic patients (77%) with slow tremor and cerebellar ataxia displayed a significant increase of the I–V interval of the ABR.

Our data further indicate that the incidence of brain stem abnormalities is affected by the patient's age and the number of alcoholic neurological complications. Alcoholic patients below age 30 and those without a history of neurological complications had a low incidence of abnormal ABRs. There was at least a 3-fold increase in the incidence of abnormal ABRs in all age groups above age 30. A 3–4-fold increase in abnormal ABRs was also observed in patients who had a history of one or two alcoholic neurological diseases. Moreover, brain stem abnormalities were extremely common when alcoholic patients had three or more neurological complications.

One unexpected finding in this study is that the CT scan correlated with the ABR results. When CT scans were normal, the incidence of abnormal ABRs was similar to that for patients without any alcoholic neurological complications. In contrast, there was a marked increase in the incidence of brain stem abnormalities when CT scans showed diffuse cerebral atrophy, particularly when accompanied by cerebellar atrophy. There was no correlation between EEG findings and ABR results. The high correlation between abnormal ABRs and cerebral atrophy in CT scan suggests that the pathological process or processes responsible for diffuse cerebral atrophy are widespread, possibly involving the brain stem as well. Contrary to Avdaloff's (1978) report that all patients with alcohol withdrawal seizures have cortical atrophy in CT scan, our study shows that only 2 out of 10 patients with alcohol withdrawal seizures have

similar CT scan findings. The incidence of cerebral atrophy in CT scan in this study (46%) is higher than that reported by Fox et al. (1976) who observed 4 of 12 alcoholics (32%) with enlarged ventricles, but lower than that by Cala et al. (1978) who found that cerebral atrophy was present in 19 of 26 alcoholics (73%) studied.

Although brain stem lesions in Wernicke-Korsakoff syndrome, central pontine myelinolysis and cerebellar degeneration are well described in neuropathological studies (Adams et al. 1959; Victor et al. 1959, 1971), the prevalence of brain stem abnormalities in alcoholic patients has not yet, with few exceptions, been systematically investigated either by pathological examination or by electrophysiological methods. In a study by Rosenhamer and Silfverskiöld (1980) on 13 chronic alcoholics with cerebellar ataxia, 10 had abnormally prolonged I–V intervals in the ABRs. Beigleiter et al. (1981) have shown that the mean latencies of ABR waves II, III, IV and V of 17 alcoholic patients were significantly delayed, but it is not clear if those abnormalities in the ABR were seen in every patient. The pathological study by Lynch (1960) on 11 alcoholic patients showed that it was not uncommon to see some degree of demyelination in heavily myelinated areas, e.g. corona radiata and the brain stem. Neuronal loss in the basal ganglia, pontine and olivary nuclei was also noted. Findings characteristic of Wernicke's encephalopathy, Marchiafava-Bignami disease or central pontine myelinolysis were rare (Neuburger 1957; Lynch 1960). These pathological studies seem to suggest that abnormal ABRs in alcoholic patients may be related to both demyelination and neuronal loss in the brain stem.

It is obvious from our study using an electrophysiological measure of auditory brain stem function that many clinically asymptomatic alcoholic patients have brain stem abnormalities. Thus, in patients suspected of brain stem lesions because of the finding of an abnormal ABR, it is clinically important to define the history of alcohol abuse in order to clarify the significance of the ABR findings. Our data also suggest that the ABR and CT scan are particularly useful in investigating the extent of CNS abnormalities in alcoholic patients.

Summary

Auditory brain stem responses (ABRs) were obtained from 66 chronic alcoholic patients. Forty-one percent of the patients had abnormal ABR indicated by prolonged interwave intervals. The incidence of brain stem abnormalities was related to age, the type and number of alcoholic neurological complications, and cerebral atrophy in computerized tomographic (CT) scan. There was a progressive increase in the incidence of abnormal ABRs with age and the number of alcoholic neurological diseases. Among the neurological complications of alcoholism, patients with cerebellar degeneration had the highest incidence of abnormal ABRs (83%). There was a high correlation between cerebral atrophy in CT scan and abnormal ABRs. The data suggest that laboratory methods such as the ABR and CT scan are useful in evaluating the extent of CNS abnormalities in alcoholic patients.

Résumé

Réponses auditives du tronc cérébral chez des patients alcooliques chroniques

On a enregistré les réponses auditives du tronc cérébral (RATC) chez 66 patients alcooliques chroniques. Quarante et un pour cent des patients ont présenté des RATC anormales par allongement des intervalles entre composantes. L'incidence des anomalies était liée à l'âge, au nombre et au type de complications neurologiques dues à l'alcool et à l'atrophie cérébrale révélée par le scanner à tomographie computerisée. Les RATC anormales augmentaient avec l'âge ainsi que le nombre des atteintes neurologiques dues à l'alcoolisme. Au nombre des complications neurologiques de l'alcoolisme, les patients présentant une dégénérescence cérébelleuse ont montré le plus haut pourcentage de RATC anormales (83%). Une étroite corrélation existait entre l'atrophie cérébrale en CT scanner et les RATC anormales. Ces données suggèrent que les examens de laboratoire tels que les RATC et les CT scanners sont utiles pour évaluer l'étendue des anomalies du SNC chez des patients alcooliques.

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