

Visual evoked responses in chronic alcoholics

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SUMMARY Visual evoked responses (VERs) were recorded on 52 chronic alcoholic patients without Wernicke-Korsakoff syndrome, 22 of whom had cerebellar ataxia, and eight chronic alcoholics with Wernicke-Korsakoff syndrome. Abnormal VERs were found in 23% of patients without and 37% of patients with Wernicke-Korsakoff syndrome. The main VER abnormalities of all the alcoholic groups were prolonged latency and reduced amplitude of the P100 component. Improvement followed a six month period of abstinence. VERs may be useful in the early detection of alcohol induced brain damage, and in following the progress of patients with the condition.

Lesions of the visual pathways are known to be present in some chronic alcoholics.^{1,2} However, little is known about the frequency of subclinical involvement of the visual pathway in patients with milder forms of alcohol-induced brain damage, or the capacity for recovery with prolonged abstinence.

The recording of visual evoked responses (VERs) is a sensitive technique for the detection of subclinical lesions of the visual system.^{3,4} Abnormal VERs have been reported in asymptomatic chronic alcoholics,^{5,6} but the number of patients studied has been small. Although the effects of acute withdrawal on visual evoked responses have been established,⁷ studies of the effects of prolonged abstinence have not been described.

We report a study of the VERs in 52 chronic alcoholics without Wernicke-Korsakoff syndrome, 24 of whom were followed up for 6 months, and in eight chronic alcoholics with Wernicke-Korsakoff syndrome. The aim of our study was to examine the incidence and nature of VER abnormalities in alcoholic patients with and without Wernicke-Korsakoff syndrome, and to evaluate the effect of abstinence from alcohol.

Subjects and methods

Controls

The control subjects were 42 male volunteers whose ages ranged from 22 to 76 years (mean 45.9 years). Informed consent, drinking, smoking and medical histories were obtained. Only healthy subjects who abstained or drank less

than 20 g/day and were not on drug treatment were accepted for study.

Chronic alcoholics without Wernicke-Korsakoff syndrome

The group consisted of 52 males who had a history of an alcohol consumption of 50 to 200 g/day for 10 to 30 years but who had no history or clinical features of Wernicke-Korsakoff syndrome. Ages ranged from 25 to 63 years (mean 47.4 years). Thirty-six patients smoked cigarettes, ranging from 10 to 70 per day (median 22). They were further divided into two groups; group I (30 patients; age 25-59, mean 43.5 years) had no evidence of cerebellar degeneration; group II (22 patients; age 27-63, mean 51.6 years) had truncal and gait ataxia compatible with alcoholic cerebellar degeneration.⁸

A minimum abstinent period of 2 weeks was required before VERs were recorded.

Chronic alcoholics with Wernicke-Korsakoff syndrome

The group consisted of eight alcoholic patients admitted to hospital in whom the clinical diagnosis of Wernicke-Korsakoff syndrome was confirmed by neurological assessment. Their ages ranged from 50 to 70 years (mean 60.8 years) and all were males. They had a drinking history ranging from 10 to 35 years with a daily intake of 50 to 250 g. Five patients smoked cigarettes, ranging from 10 to 30 per day (median 15). The initial VER was performed within 14 to 30 days (mean 22 days) of admission to hospital during which time they were completely abstinent from alcohol.

Ophthalmological examination

Ophthalmological examination was conducted on all subjects prior to the recording of evoked responses. It included examination of the distant and near visual acuities (with and without corrective lenses), colour and stereoscopic vision, peripheral and central visual fields, eye movements, pupils and the fundus.

Patients with refractive errors were referred to ophthalmologists for corrective lenses before the VERs were performed. Those who had persistent abnormal distant (worse

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than 6/9 with Snellen chart) or near (worse than N6 with Cuprox chart) visual acuities, defective peripheral and central visual fields, cataract, vitreous abnormalities or optic atrophy were not accepted for VER study.

The visual evoked responses (VERs)

The montage for VER recording consisted of a transverse chain of five active electrodes placed 5 cm above theinion and 5 cm apart on either side of the midline electrode. These were all referred to a mid-frontal electrode placed at 12 cm from the nasion. The ground electrode was placed at the submental position.

The subject sat facing a translucent screen which was 60 cm from the stimulated eye and subtended a visual angle of 32°C. The stimulus consisted of a black and white checkerboard pattern which was back projected via a moveable mirror onto the screen, so that the individual squares subtended an angle of 55 minutes and the luminance levels were 0.8 cd/m² for the black checks and 40 cd/m² for the white checks respectively. Pattern reversal was produced once every 560 ms by a rapid displacement (10 ms) of the checkerboard pattern using the mirror reversal technique. The amplitude of the pattern displacement was adjusted to be equal to one square width. A small fixation point in the form of a red light emitting diode was provided at the centre of the screen and fixation of the subject during the averaging procedure was strictly supervised. Runs with poor fixation or lack of concentration were noted and repeated. All recordings were made monocularly with the non-stimulated eye covered by a pad.

The responses recorded were amplified by a Devices (UK) D100/D150 amplifying system with a bandwidth between 1 kHz and 0.5 Hz and a sensitivity of 50 µV/V before averaging by a D200 Digitimer analyser which was triggered by the pattern reversal. The averaged response to 128 reversals was recorded for each run which was repeated at least once in order to ensure the reproducibility of the results. The peak latency of the major positive wave (the P100 component) was measured to the nearest one millisecond while the amplitude was measured from the preceding negative peak, or from the baseline if there was no obvious preceding negative peak. Half field stimulation was employed if the P100 component showed a bifid trough (PNP complex) or if its ampli-

tude was so small that the wave could not be identified with certainty.

The criteria for defining an abnormal VER were: (a) Latency to the major positive peak (P100) greater than 2.5 standard deviations above the mean for control subjects, (b) An interocular latency difference for the P100 component greater than 2.5 standard deviations above the mean for control subjects. This criterion applied only to those patients in whom the absolute latency for both eyes was within the normal range, (c) An absent response, unilateral or bilateral.

Follow up studies

Of the 52 patients without Wernicke-Korsakoff syndrome, 24 were followed up with a second examination at 6 months after the first study. They were divided into two groups according to their drinking histories after the first test; a non abstinent group (16 patients) and an abstinent group (eight patients). Of the eight patients with Wernicke-Korsakoff syndrome, three were followed up for 6 months. Of these three patients who had a second examination performed, two remained abstinent and one resumed drinking before 6 months. The same procedures for VER recordings were repeated. A change of latency 10 ms was regarded as significant.⁹

Patients were instructed to exhale into an alcohol meter before the recordings to ensure that no tests were done under the influence of recent alcohol intake.¹⁰

Statistics

The data were stored in a disc using a VAX 780 mini-computer and were analysed by means of the Scientific Information Retrieval and Statistical Packages of Social Science (SPSS) software packages.

The non-paired *t* test was used to compare the means between groups and the paired *t* test to compare the initial and follow-up results in the alcoholic group. The differences between means was considered significant when *p* < 0.05.

Results

Controls

The major positive peak (P100 component) was

Table 1 VER in control subjects and chronic alcoholics

	Controls	Non-Wernicke-Korsakoff syndrome alcoholics		Wernicke-Korsakoff syndrome alcoholics
		I	II	
No. of male subjects	42	30	22	8
Age				
Range	22-76	25-59	27-63	50-70
Mean	45.9	43.5	51.6	60.8
P100 component				
Latency (ms)	97.2 ± 3.3	99.4 ± 5.2 p < 0.05	100.3 ± 7.0 p < 0.05	104.6 ± 7.1 p < 0.005
Amplitude (µV)	7.9 ± 3.0	6.3 ± 3.2 p < 0.05	5.0 ± 2.8 p < 0.0005	3.7 ± 1.3 p < 0.0005
ILD (ms)	1.9 ± 1.9	4.0 ± 4.2 p < 0.05	2.5 ± 2.5 NS	2.8 ± 2.6 NS

Mean values are expressed with standard deviations.

NS = not significant (*p* > 0.05).

ILD = interocular latency difference.

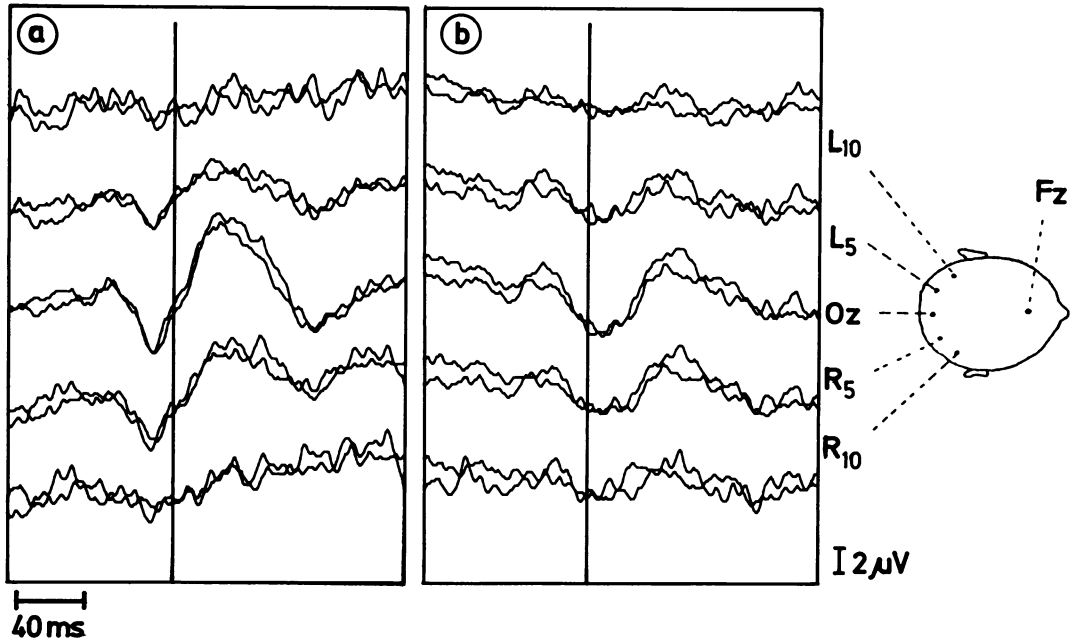


Fig 1 Pattern-reversal visual evoked responses to full field stimulation in a control subject (a) and a chronic alcoholic patient (b). Note the prolonged latency and reduced amplitude of the P100 component in B. Cursor indicates the upper limit of the normal P100 latency (106 ms).

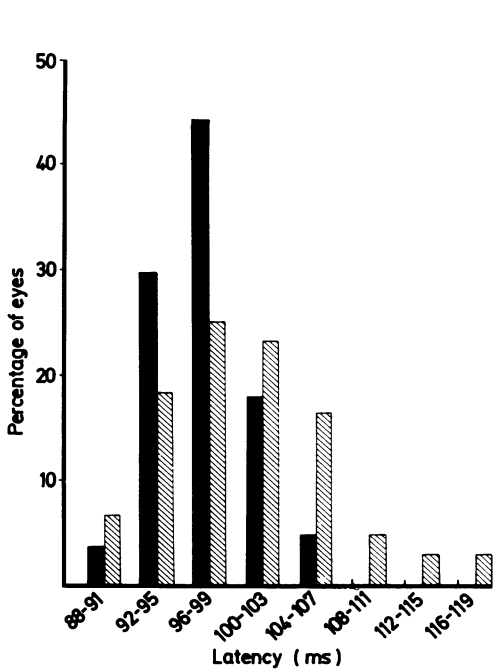


Fig 2 Distribution of values for P100 latency in control subjects (solid bars) and chronic alcoholics (hatched bars).

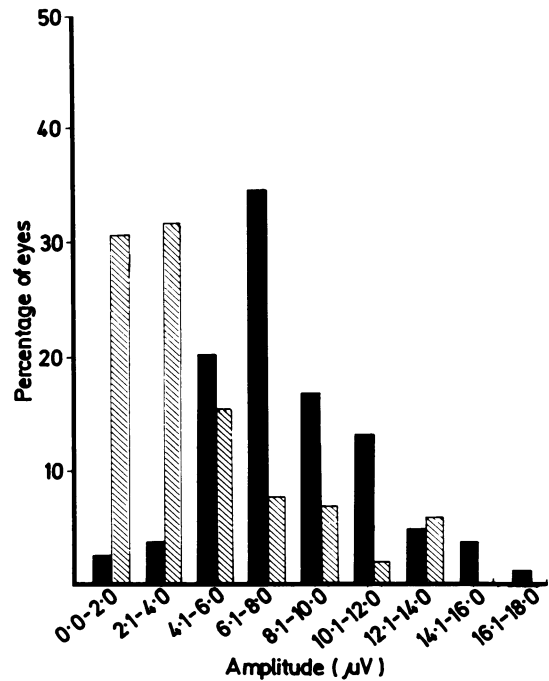


Fig 3 Distribution of values for P100 amplitude in control subjects (solid bars) and chronic alcoholics (hatched bars).

Table 2 Types of VER abnormalities in subjects with and without Wernicke-Korsakoff syndrome

	Non-Wernicke-Korsakoff syndrome alcoholic I n = 30	II n = 22	Wernicke-Korsakoff syndrome alcoholics n = 8
Normal VERs	23	17	5
Abnormal VERs	7 (23%)	5 (23%)	3 (37%)
Bilateral	0	2	3
Unilateral	5	3	0
Types of P100 abnormalities			
Prolonged latency (ms)	5	5	3
Prolonged ILD (ms)	2	0	0
Absent response	0	0	0

ILD = interocular latency difference

present in the VERs of all the controls. The mean +2.5 SD for the latency of the P100 component was 106 ms and for the interocular latency difference was 7 ms (table 1). There was no significant effect of age on the latency of the P100 component in the males.

Chronic alcoholics

The characteristic abnormality in all patient groups was a mild increase in latency and reduction in amplitude with a normal configuration of the response (fig. 1). Half-field stimulation, when performed, confirmed that the delayed response was P100. The distribution of the latency and amplitude of the P100 component in both control and patient groups is shown in figs 2 and 3.

Chronic alcoholics without Wernicke-Korsakoff syndrome

Of the 52 patients, 12 (23%) had abnormal VERs. The patients were further divided into two groups:

Group I No evidence of cerebellar degeneration.

Of the 30 patients, seven (23%) had abnormal VERs. There were five patients with prolonged P100 component latencies and two with prolonged interocular latency differences. The increases in latency ranged

from 108 ms to 119 ms. All of the abnormalities occurred unilaterally (table 2). There was significant prolongation of the latency ($p < 0.05$) and reduction of the amplitude of the P100 component ($p < 0.05$) for the whole group. The interocular latency difference was also significantly increased ($p < 0.05$) (table 1).

Group II Evidence of cerebellar degeneration.

Of the 22 patients, five (23%) had abnormal VERs. All of the five patients had prolonged P100 component latencies which occurred unilaterally in three and bilaterally in two (table 2). The increases in latency ranged from 107 to 117 ms. There was significant prolongation of the latency and reduction of the amplitude of the P100 component for the whole group ($p < 0.05$ and $p < 0.0005$ respectively). However, the interocular latency difference was not increased ($p > 0.05$) (table 1).

Chronic alcoholics with Wernicke-Korsakoff syndrome

Of the eight patients, three (37%) had abnormal VERs. All of the three patients had prolonged P100 component latencies bilaterally (table 2). The increases in latency ranged from 107 ms to 122 ms. There was significant prolongation of the latency and reduction of the amplitude of the P100 component for the whole group ($p < 0.005$ and $p < 0.0005$ respectively). The interocular latency difference was not increased ($p > 0.05$) (table 1).

Table 3 Follow-up studies of non-Wernicke-Korsakoff syndrome alcoholic group

	1st Test	2nd Test
Non abstinent group		
No of subjects	16	16
Normal VERs	15	13
Abnormal VERs	1	3
P100 component		
Latency (ms)	98.6 ± 6.5	98.9 ± 5.7
Amplitude	6.1 ± 3.5	5.7 ± 2.5
Abstinent group		
No of subjects	8	8
Normal VERs	7	8
Abnormal VERs	1	0
P100 component		
Latency (ms)	100.5 ± 5.7	98.2 ± 7.1
Amplitude (μV)	4.0 ± 1.8	5.0 ± 1.7

FOLLOW UP STUDIES

Chronic alcoholics without Wernicke-Korsakoff syndrome (table 3)

Non-abstinent group Of the 24 patients followed up for 6 months, 16 continued drinking. One of the 16 patients had abnormal VERs at the initial study, but three had abnormal VERs at the follow up study. Of the 32 eyes studied the latency decreased (≥ 10 ms) in two (6.3%) and increased (≥ 10 ms) in one (3%). There was no significant change in the mean latency and amplitude of the P100 component between the two examinations.

Abstinent group Of the 24 patients followed up for 6 months, eight remained abstinent from alcohol. The only patient with abnormal VERs at the initial study returned to normal at the follow up study. Of the 16 eyes studied the latency decreased (≥ 10 ms) in three (18.6%) and did not increase in any eyes. However, there were no significant changes in the latency and amplitude of the P100 component between the initial and the follow up studies for the whole group.

Chronic alcoholics with Wernicke-Korsakoff syndrome The three patients with abnormal VERs were followed up with a second examination at 6 months. Of the four abnormal VERs (two pairs of eyes) in the two patients who were abstinent, two returned to normal (latency decreased ≥ 10 ms) at the second study. The VERs of the third patient who continued drinking remained abnormal at the second study.

Discussion

The characteristic visual disorder associated with chronic alcoholism is alcohol amblyopia in which there is impairment of central vision.^{1,2} Abnormal VERs have been reported in alcoholics with this condition¹¹⁻¹³ and also in patients who have no evidence of visual impairment.^{5,6}

In the present study, the incidence of abnormal VERs in chronic alcoholics without a history of Wernicke-Korsakoff syndrome was 23% (12 of 52 patients). This proportion is slightly greater than that reported by Posthuma and Visser (15%)⁵ and Ahmed and Hines (13%).⁶ The study also indicated that the incidence of VER abnormalities (23%) was the same for patients with or without the complication of cerebellar degeneration and that the incidence was higher (37%) in chronic alcoholics with a history of Wernicke-Korsakoff syndrome. Despite the small size of the abstinent group, the follow-up studies demonstrated that there was a general trend for the VERs to return to normal after ceasing alcohol consumption.

The main features of the VER abnormalities of all the alcoholic patient groups were prolonged mean latency and reduced amplitude of the P100 component. The mild increase in latency (the longest was 122 ms) and the normal configuration of the response suggest that the abnormality was due to delay of the P100 component, rather than block in central macular derived fibres, with a persistent P135. This conclusion was supported by the results of half-field stimulation, when performed. The P100 component of the VER results mainly from the effect of foveal stimulation.¹⁴ Abnormalities of the P100 component therefore usually suggest a conduction defect in the optic fibres especially in those which are responsible for central vision. These VER findings are consistent

with the pathological changes of alcohol amblyopia in which the papillo-macular bundles are affected.^{1,2} The fact that abnormal VERs were found in visually asymptomatic alcoholic patients suggests that there might be a subclinical form of alcohol amblyopia.

Although the incidence of abnormal VERs was similar for both Group I and II patients of the alcoholics without Wernicke-Korsakoff syndrome, the extent of the abnormalities was different. Patients with cerebellar degeneration had more bilateral VER abnormalities than patients without cerebellar degeneration. The lack of interocular latency difference of the P100 component in the former group suggests that the lesions are of a diffuse nature and may occur either prechiasmally or postchiasmally. By contrast, patients without cerebellar degeneration had only unilateral abnormalities suggesting that the lesions are predominantly unilateral, most likely occurring in the prechiasmatal region at the optic nerves or the retina. In the classical description of the visual defect in alcohol amblyopia, Traquair¹⁵ reported that in the early stages one eye may be affected before a defect could be detected in the other. Although both eyes are usually affected symmetrically, asymmetrical fields, unilateral defects and asymmetrical pathological changes have been reported in the condition by other workers.^{1,16} It seems likely that Group I and II patients merely represent patients who are in different stages of the development of the disorder.

The pathogenesis of the conduction delay in the VER of chronic alcoholics remains uncertain. It may be a consequence of nutritional deficiency affecting the structure and function of the optic nerve,^{12,17} or the effect of ethanol on neurotransmitter release¹⁸ or cerebral amine metabolism.^{19,20} Whatever the mechanism, the finding of abnormal VERs in patients with alcohol-related brain damage suggests that they may be useful in the detection of early changes, and in following the progress of patients with the disorder.

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