Short report

Involvement of central nervous system in diabetes mellitus

ASHOK VERMA, MS BISHT, GK AHUJA

From the Department of Neurology, All India Institute of Medical Sciences, New Delhi, India

SUMMARY Brainstem auditory evoked responses were recorded in 22 diabetic patients with a variable duration of illness (mean 5.8 years) and 14 normal healthy controls of comparable age. The initial 10 millisecond components, found to be most consistent and reproducible, were analysed. Variations in the form of individual wave latency, interpeak latencies and V wave amplitude were compared in both the groups. No difference was found in any of the parameters. It was concluded that central neural pathways are not involved at least initially in diabetes mellitus.

The peripheral and autonomic neuropathy, occurring in diabetic patients is well known. Whether there is also a specific central nervous system involvement has not been well documented. Woltman and Wilder¹ concluded from pathological material that diabetic neuropathy is a disease of peripheral nerves and that degeneration in the CNS is unimportant. However, it is reasonable to ask whether such a ubiquitous metabolic derangement and diffuse angiopathy might involve any part of the nervous system. Recent studies²⁻⁷ showed the involvement of brain parenchyma in patients with long standing diabetes mellitus.

Neuropathy, with subjective symptoms and permanent signs usually appears only after many years of diabetes when incapacitating complications may also be present in other organs. However, physiological evidence of dysfunction in the CNS may be the earliest finding in clinically normal individuals. Recently, with the refinement of evoked potential techniques detailed exploration of sensory pathways in CNS has been possible. We present the results of a study in which brain stem auditory evoked responses (BAER) were sampled in diabetic patients and non-diabetic controls without clinical evidence of peripheral neuropathy or hearing

impairment. Short latency evoked potentials (the initial 10 ms) from brainstem were recorded as they are less influenced by arousal and other uncontrollable factors. Conduction speed in peripheral and central auditory pathways in diabetics was evaluated and compared with normal healthy controls.

Material and methods

The diabetic group comprised 22 insulin treated inpatients selected from the medical wards. Their ages ranged from 15 to 65 years, with a mean of 30 years. Fifteen patients were male and seven were female. Length of illness ranged from six months to 25 years, with a mean duration of 5.8 years. Patients were excluded if they suffered from any intercurrent disease which might affect the nervous system such as stroke or uraemia due to nephropathy. No patient in this group was being treated with anticonvulsants, methyl dopa, nitrofurantoin, reserpine or any medication which might be expected to interfere with functioning of CNS. Fourteen normal controls were obtained from healthy persons without history of diabetes. Their ages ranged from 15 to 60 years, with a mean of 29 years. In the control group 10 were male and four were female. All reported normal hearing and none was taking any medication which could be expected to affect cortical functioning. Normal hearing in both the groups was ascertained by clinical evaluation including tuning fork tests.

The BAER recordings were made in a shielded, sound attenuated room under standard conditions using "Nicolet-1170" clinical averaging system. The stimulus was a 100 μ s rarefaction click, delivered at 70 dBHL. The rate of stimulation was set at 11.1 Hz. Percutaneous silver disc electrodes were placed at the vertex (C_z) and both mastoids, with the common reference electrode always being placed on the mastoid contralateral to the ear stimulated.

Address for reprint requests: Dr GK Ahuja, Department of Neurology, All India Institute of Medical Sciences, New Delhi-110029, India.

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Amplifier band width was 150–3000 Hz. A total of 2048 responses, collected in the first 10 ms duration were averaged. Latencies of individual waves from stimulus, inter-peak latencies in milliseconds and V wave amplitude (μV) measured to the following trough were compared with those in controls. None of the patients was hypoglycaemic at the time of testing.

Results

WAVE LATENCIES FROM STIMULUS

The table shows individual wave latencies in milliseconds measured from the stimulus in diabetic and control groups. No statistical difference was found in any of the wave latencies, although three patients in the study group did reveal delayed central conduction (V wave latency >6 ms), in the presence of normal peripheral conduction (wave I and II latencies). Two of them were 52 and 60 years old with illness of more than 15 years duration. The third one was 18 years old, and diagnosed to be diabetic one year prior to testing.

INTER-PEAK LATENCY

In control group, latencies between waves I–III, III–V and I–V from right and left ears were: $2.10 \pm 0.19/2.12 \pm 0.21$ ms, $1.80 \pm 0.15/1.85 \pm 0.20$ ms and $3.89 \pm 0.19/4.01 \pm 0.40$ ms respectively. In the diabetic group these were $2.05 \pm 0.17/2.09 \pm 0.17$ ms, $1.85 \pm 0.15/1.89 \pm 0.16$ ms and $3.96 \pm 0.34/3.95 \pm 0.28$ ms.

Comparison of findings in both the groups revealed no difference (*t* test $p > 0.05$).

V WAVE AMPLITUDE

Among individual wave-amplitudes, that of V wave was found to be consistently reproducible. It was determined $0.26 \pm 0.73/0.26 \pm 0.84$ μV and $0.24 \pm 0.95/0.25 \pm 0.72$ μV in diabetic and control groups respectively from both the ears. Comparison between two groups was not significant ($p > 0.05$).

Table Mean latencies in milliseconds of individual waves of BAER from stimulus. Standard deviations follow mean values.

Wave no.	Non-diabetic <i>n</i> = 14	Diabetic <i>n</i> = 22	<i>t</i> value
Right ear			
I	1.64 ± 0.09	1.59 ± 0.15	1.12
II	2.65 ± 0.09	2.68 ± 0.18	−0.58
III	3.72 ± 0.14	3.71 ± 0.15	0.20
IV	5.07 ± 0.21	5.00 ± 0.31	0.74
V	5.53 ± 0.14	5.61 ± 0.37	−0.77
Left ear			
I	1.66 ± 0.09	1.64 ± 0.14	0.48
II	2.69 ± 0.10	2.68 ± 0.18	0.19
III	3.71 ± 0.13	3.73 ± 0.16	−0.39
IV	5.06 ± 0.24	5.06 ± 0.41	0.00
V	5.56 ± 0.17	5.61 ± 0.30	−0.57

Discussion

The peripheral neuropathy associated with diabetes mellitus is responsible for a myriad of syndromes. When autonomic nerves are involved such diverse abnormalities as postural hypotension, impotence, intractable diarrhoea and urinary retention may result. Whether a specific involvement of central nervous system also occurs, has been questioned. Major text books on diabetes either disregard cerebral involvement or minimise its existence.^{8,9} However, a suggestion has been made recently that sub-clinical involvement occurs in diabetic patients.^{3–7,10}

In the present study the fact that the latencies of waves I and II were identical and normal in both groups suggest that eighth nerve transmission was normal in diabetics. Furthermore subsequent waves, thought to originate from brainstem nuclei in auditory pathways were, in general, comparable with the normal healthy controls. These findings contradict those of Donald,⁷ who observed normal peripheral but delayed central conduction in diabetics. However, in the latter series the mean duration of illness (16 years) was much greater than that in our patients (mean duration 6 years). Significantly enough, three diabetics in the present study did reveal delayed central conduction (V wave latency >6 ms) in the presence of normal peripheral transmission. Two of them had illnesses of more than 15 years duration, and it is possible that it could be due to long standing metabolic dysfunction. In the third patient who was young and had diabetes detected only a year earlier, the possibility that delayed central conduction was due to discrete clinically silent lesions in the brain stem can be argued. In the literature, there is sharp disagreement about the relationship of duration and control of diabetic status to complications. Olsson *et al*¹¹ and Reske-Nielsen *et al*¹² on the basis of detailed pathoanatomic studies, concluded that brain involvement is common in long standing diabetes. Other studies^{13,14} have reported that complications may be totally unrelated to the diabetic status, and in fact patients may have angiopathy years before they develop carbohydrate intolerance. Central conduction timings in the brain stem could neither be related to age of the patient nor to severity of diabetes.

Recent studies⁵ show a relationship between diabetes and premature aging. Diabetic neuropathy could represent to a limited extent an exaggerated normal aging process.¹⁵ It is reasonable to predict that nervous system involvement might be more obvious in aged diabetics. In the present study a relative younger age of patients (mean 30 years) and short duration of illness (mean 6 years) could be the reason for absence of subtle dysfunction in central

nervous pathways.

On the basis of our study, we conclude that impulse conduction in the eighth nerve and the central neuraxis is intact and normal, at least initially, in diabetes mellitus. The exact nature and relationship of subsequent brain involvement in longstanding diabetes requires further investigation. It would be of interest to attempt to correlate objective tests of peripheral neuropathy with central conduction delays, if it exists, in a large group of diabetic patients.

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