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An Investigation of Central Nervous System Conduction Properties in Diabetes Mellitus Using Brainstem Auditory and Somatosensory Evoked Potentials

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This is to certify that the thesis prepared by Randy L. Anderson entitled An Investigation of Central Nervous System Conduction Properties in Diabeties Mellitus Using Brainstem Auditory and Somatosensory Evoked Potentials has been approved by his committee as satisfactory completion of the thesis requirement for the degree of Master of Science.

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Abstract

AN INVESTIGATION OF CENTRAL NERVOUS SYSTEM CONDUCTION PROPERTIES IN DIABETES MELLITUS USING BRAINSTEM AUDITORY AND SOMATOSENSORY EVOKED POTENTIALS

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In this study brainstem auditory evoked potentials (BAEPs), median nerve conduction velocities (CV) and early somatosensory evoked potentials (SEPs), were employed as indices of neural conduction properties in a group of young insulin dependent diabetics (five males and five females) and a group of nondiabetic controls (five males and five females). The median nerve CV was determined from 64 summated nerve responses recorded at the elbow. The nerve was stimulated at the wrist using 0.2 msec square wave electrical pulses. The SEP was recorded from scalp electrodes using the same median nerve stimulation technique as for the CV measure. The BAEPs were produced by recording responses to 70 dB SL clicks delivered to the right ear at a rate of 10 per second. Measures of central transmission time were determined from each of the EP modalities. The time interval between BAEP waves I and V determined the BAEP CTT. SEP waves P9 to P14 determined the earliest SEP CTT measure.

Comparisons between the two diagnostic groups yielded the following results: The diabetic group evidenced a significant ($p = 0.02$) slowing

of the median nerve, 53 meters per second for the diabetic group versus 59 meters per second for the nondiabetic group. With height covaried out, only the SEP P14 latency showed a significant diagnostic group difference. More interesting were the findings for the principal SEP CTT measure. The diabetic group had significantly ($p = 0.01$) longer CTTs from P9 to P14, 5.0 msec as opposed to 4.2 msec for the nondiabetic group. The diabetic group also had significantly ($p = 0.03$) longer CTTs for the BAEP, 4.2 msec versus 4.0 msec for the nondiabetic group. Although the magnitude of the diagnostic group differences are small, the median nerve CV, SEP CTT, and BAEP CTT measures indicate that diabetic neuropathy is pervasive, occurring centrally, as well as peripherally, as early as young adulthood in juvenile onset, insulin dependent diabetics.

Introduction

A number of studies have documented abnormal peripheral conduction velocity in persons with diabetes mellitus (Horowitz & Ginsberg-Fellner, 1979; Noel, 1973; Oester, Zalis, & Radriquez, 1972; Gregerson, 1967). Diabetic neuropathy is known to affect both sensory and motor nerves, producing abnormalities ranging from muscle paralysis to asymptomatic neurophysiological abnormalities such as reduced conduction velocity (Porte, Graf, Halter, Pfeifer, & Halar, 1981; Ward, Fisher, Barnes, Jessop, & Baker, 1971). In contrast, there is little information available regarding the effects of diabetes on the central nervous system (CNS). The available information comes predominantly from postmortem identification of intracranial anatomical alterations in diabetes (DeJong, 1977). In many of these cases, death resulted from pathology unrelated to diabetes. In the cases studied where death was related to diabetes, there were multiple, possibly confounding complications involving other organ systems. This information gap is partly due to the relative difficulty of measuring CNS function.

This project is an attempt to determine if metabolic abnormalities inherent in diabetes might affect CNS function as well as peripheral nervous system function. The success of scalp recorded evoked potentials in other applications suggests that they should provide accurate information about changes in function of the central nervous system as a result of diabetic neuropathy.

Brainstem evoked potentials (EPs) are electrical manifestations of the brainstem, in the nanovolt range, occurring in response to discrete stimulation of one of the sensory modalities. The EP electrical energy is volume conducted from the brainstem nuclei of origin, up through the brain mass to the scalp where it may be detected using scalp electrodes. Since the EPs occur on the background of ongoing EEG activity that is in the microvolt range, it is necessary to summate EP responses from many stimulus presentations in order to visualize the response. With serial summation, theoretically random background EEG activity (noise) tends to subtract out, while the stimulus response (signal) that is temporally locked to the stimulus presentation, adds up. In short, the summation process makes the EP response more prominent by improving the signal to noise ratio.

In this study, brainstem auditory evoked potentials (BAEPs) and early somatosensory evoked potentials (SEPs) were recorded as indices of CNS brainstem function in previously diagnosed young adult insulin dependent diabetics. The BAEPs were recorded in response to brief click stimuli. The SEPs were recorded in response to median nerve stimulation at the wrist.

Two previous studies have been reported in which the SEP was used as a measure of diabetic neuropathy (Noel, 1973; Oester et al., 1972). However, it was used only as an index of peripheral conduction from the site of stimulation up to wave N18 of the SEP (see Fig. 1, middle trace). In this research, an attempt has been made to use the SEP as a measure of both central and peripheral neuropathy.

The BAEP has proven to be an excellent comparative measure of CNS neuropathy since its peripheral component, wave I, is easily delineated

from the central components (Starr, 1978; Starr & Achor, 1979; Salamy & McKean, 1976; Salamy, McKean, & Buda, 1975). The integrity of the auditory receptor organ is verified in each participant using pure tone audiometry. Thus, differences in BAEP components are attributable to the neural pathways. Apparently, no other studies have been reported using the BAEP as a measure of diabetic neuropathy.

Representative Median Nerve Response,
Somatosensory Evoked Potential, and
Brainstem Auditory Evoked Potential

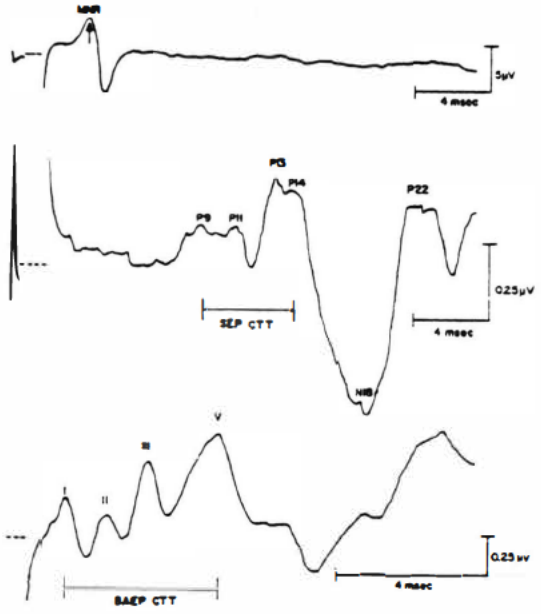

Figure 1: Representative samples of EPs collected in this study. Positive is up in all traces. All responses were amplified by 5 x 10^4, filtered at 10 Hz and 3000 Hz. The top trace is of 64 summated responses of the median nerve recorded at the elbow. The latency of the median nerve response was recorded as the peak of the initial positivity. The trace represents 25.5 msec of recording time (bin width 100 usec). The amplitude scale is 5 uV. The middle trace is the SEP. It is the summation of 1024 scalp recorded stimulus responses recorded from 1 cm posterior and 1 cm inferior to C_4. The SEP CTT measurement segment is shown below the trace. The trace represents 25.5 msec of recording time (bin width is 100 usec). The amplitude scale is 0.25 uV. The lower trace is the BAEP. The trace is the summated responses of 1024 stimulus presentations. The right ear responses were recorded from vertex referenced to the right mastoid. The amplitude scale is 0.25 uV. The trace represents 12.5 msec of recording time (bin width is 50 usec).

Literature Review

Brainstem Auditory Evoked Potentials

Use of the brainstem auditory evoked potential (BAEP) for highly specific localized neurologic evaluation is dependent upon determination of the neuroanatomical correlates of each waveform. There are four methods used to identify neural generators of EP waveforms: depth recording, lesion-making experiments, deductions from clinical cases, and potential field analysis. The first two methods are most always limited to nonhuman subjects, whereas the latter two yield less specific findings. Thus, it is necessary to use results from the first two methods to verify results of the second two, and vice versa. This process has led to a general consensus as to the neural origins of waves I through V of the BAEP.

Wave I arises from the potential volley along the acoustic nerve. Wave II arises from the cochlear nuclei (first central synapse in the pathway). Wave III arises in the region of the superior olivary complexes. Wave IV arises from tracts and nuclei of the lateral lemniscus. Wave V arises at the level of the inferior colliculi (Chiappa, Gladstone, & Young, 1979; Fabiani, Sohmer, Tait, Gafni, & Kinarti, 1979; Starr & Achor, 1979; Salamy & McKean, 1976; Buchwald & Huang, 1975).

There is some speculation about the finality of these BAEP origins or at least the implied one-to-one correspondence between given peaks and neuroanatomical structures. Discrete lesions can affect the amplitudes

of several BAEP components with no effect on latency (Starr & Achor, 1979). Also, isocontour maps show a distribution of potential fields throughout the brainstem during the occurrence of wave II (Starr & Achor, 1979). Thus it appears that several neural generators contribute simultaneously to the generation of individual BAEP components, whereas some auditory structures do not contribute at all to the generation of the BAEP (Starr & Achor, 1979).

Despite the complexity of neural origin, the BAEP is very stable within and between individuals. Further, the prominence of the BAEP components makes them fairly easy to score (see Fig. 1, lower trace). Typically, the latency of each peak is taken as the point of highest amplitude over the peak. Discrepancies sometimes arise due to morphological variation in the IV-V complex. The qualitative patterns in appearance of the IV-V complex have been described by Chiappa et al. (1979). These patterns are essentially permutations of the combined factors of the relative height and presence or absence of the two waves:

Pattern	Morphology
A	A single peak in the range of V;
B	2 peaks; wave IV lower than V;
C	2 peaks; IV higher than V;
D	IV as a shoulder on V;
E	V as a shoulder on IV;
F	IV and V equal.

In this study, wave IV was scored as missing if the BAEP showed the A pattern. The BAEP shown in Fig. 1 is representative of Pattern A. Wave IV was scored in Pattern D cases only if the slope of an imaginary tangent line to the curve appeared to reach zero over several consecutive digital points.

Table 1 shows representative BAEP latency and amplitude data taken from previous publications. One of these studies was designed to examine

Table 1

Representative Brainstem Auditory Evoked Potential Data

Publication	I	II	III	IV	V	CTT
			Latencies (msec)			
Salamy & McKean, 1976	1.57 ± 0.14	2.73 ± 0.19	3.64 ± 0.24	4.82 ± 0.23	5.55 ± 0.26	3.99 ± 0.21
Harkins, McEvoy, & Scott, 1978	1.73 ± 0.11	2.84 ± 0.13	3.77 ± 0.11	no report	5.70 ± 0.19	3.97*
Michalewski, et al., 1980 (males only)	1.90 ± 0.26	3.02 ± 0.22	3.98 ± 0.28	5.32 ± 0.24	5.96 ± 0.16	4.06*
Michalewski, et al., 1980 (females only)	1.78 ± 0.12	2.96 ± 0.12	3.82 ± 0.16	5.31 ± 0.27	5.79 ± 0.08	4.01*
Starr, 1977	1.5	2.7	3.8	4.7	5.5	3.8 ± 0.2
			Amplitudes (uV)			
Starr & Achor, 1975	0.28 ± 0.08	0.16 ± 0.09	0.26 ± 0.07	0.11 ± 0.10	0.30 ± 0.06	
Scott & Harkins, 1978	0.24 ± 0.04	0.17 ± 0.05	0.29 ± 0.03	no report	0.50 ± 0.06	
Michalewski, et al., ** 1980 (males only)	0.31 ± 0.26	0.41 ± 0.22	0.43 ± 0.16	0.80 ± 0.31	1.10 ± 0.34	
Michalewski, et al., ** 1980 (females only)	0.32 ± 0.14	0.50 ± 0.18	0.35 ± 0.15	1.17 ± 0.45	1.50 ± 0.42	

* CTT calculated by difference from reported data.
** Calculated as the difference between wave peak and preceeding negativity.

sex differences in the BAEP (Michalewski, Thompson, Patterson, Bowman, & Litzelman, 1980). While the females in the Michalewski study tended to have shorter latencies for all BAEP components, only the wave V latency sex difference was statistically significant ($p < 0.05$). At least one other study had previously reported a sex difference in wave V latency (Stockard, Stockard, & Sharbrough, 1978).

The Michalewski study (1980) also reported significantly larger amplitudes for waves IV, V, VI, and VII among their female participants. However these findings are presented here only for relative comparison between the two sex groups since the Michalewski study calculated amplitudes as the difference between each wave peak and its preceeding negativity. For this study and the other two in Table 1, the amplitude of each component was measured from each positive peak to the subsequent negativity.

Several studies have used components of the BAEP to obtain a measure of transmission time through a segment of the CNS (Fabiani et al., 1979; Starr, 1978; Starr & Achor, 1979; Salamy & McKean, 1976; Salamy et al., 1975). Such a measure is typically referred to as central transmission time (CTT). The most widely used BAEP CTT measure is the time interval between the peak of wave I and the peak of wave V. This measure provides a neurological evaluation of the brainstem auditory pathway that is relatively independent of click intensity and receptor factors (Starr & Achor, 1979).

Peripheral Conduction Velocities

Abnormalities of peripheral conduction over the primary afferent neurons of the specific somatosensory system have a direct influence on SEP latencies and amplitudes. Therefore, it is necessary to assess the

integrity of the stimulated peripheral nerve in order to use the SEP to evaluate putative abnormalities of the central somatosensory system (Starr, 1978). This assessment is typically done by recording the peripheral nerve volley over a given segment of the nerve with bipolar electrodes and calculating the conduction velocity in meters per second. The nerve volley is evoked using the same stimulus as for the SEP recording. The recorded waveform is a triphasic potential that is initially positive, then strongly negative, and ending with a slow positive component (see Fig. 1, upper trace). The negative phase is produced by action potentials passing beneath the recording electrodes. The positive phases can be obscured if the surface recording location is far from the nerve fiber (Cracco, Cracco, & Anziska, 1979). The onset latency of the negative component is typically used in calculation of median nerve conduction velocity (CV) (Desmedt & Cheron, 1980b; Noel, 1973). This method measures the CV of the fastest conducting afferent (large diameter, myelinated) fibers (Greene, Brown, Braunstein, Schwartz, Asbury, & Winegrad, 1981).

Somatosensory Evoked Potentials

SEPs are typically elicited with electrical pulses of 0.1 to 0.5 msec duration delivered to the skin over the median nerve just proximal to the wrist. The electrode arrangement is bipolar with the cathode 2 to 3 cm proximal to the anode (Desmedt & Cheron, 1980b; Cracco et al., 1979; Starr, 1978). Stimulus rate is usually 3 to 5 pulses/sec at 50 volts. Stimulus rate and duration are important in determining the type of nerve fiber being stimulated. Faster or longer pulses tend to trigger the slower conducting A-delta and C fibers associated with pain sensation (Schmidt, 1978) and reduce SEP resolution. Stimulus intensity is less

critical since currents lightly above threshold elicit maximal response amplitudes (Starr, 1978). SEPs are most frequently recorded from the parietal scalp (over somatosensory cortex) with a reference electrode on the earlobe, neck, or forehead. A noncephalic reference electrode is sometimes preferred because of its greater "neutrality" with respect to the recording electrode (Desmedt & Cheron, 1980b). However, the noncephalic reference is subject to greater myogenic contamination.

SEPs offer the opportunity to evaluate the function of the entire somatosensory system (Cracco et al., 1979). However, the utility of the SEP is dependent on precise relationships between neural generators and SEP waveforms (Desmedt & Cheron, 1980b; Starr, 1978). Unfortunately, these relationships are currently much less precise than those of the BAEP. Not only are the neural generators somewhat speculative, but also identification of SEP waves is different in existing publications (e.g., Starr, 1978 reports a P12 but not P11 or P13).

Ignoring the peak latency variations due to variations of armlength, the early SEP to median nerve stimulation has three major positive waves and one major negative wave within 20 msec of stimulus onset. The first positivity is around 9 msec (P9), the second around 11 msec (P11). The third positivity typically has two lobes, one around 13 msec (P13) and the other around 14 msec (P14). A large negativity occurs around 19 msec (N18), usually with small positive waves "riding" on it. Another large positive wave follows N18 at around 22 msec (P22) (Desmedt & Cheron, 1980b; Cracco et al., 1979) (see Fig. 1, middle trace). P22 is not seen in several of the taller participants in this study because its duration is greater than the post stimulus measurement time of 25.5 msec.

P13 has an extremely variable morphology between individuals. It may predominate over P14 or be altogether missing (see Fig. 2). P13 and P14 can be extremely difficult to differentiate because of the variable morphology of P13 and the latency "shifts" introduced by variations in armlength across individuals. This interpretation problem is further complicated in the presence of neuropathy. The general influence of neuropathy is to increase peak latencies and decrease amplitudes, as a result of demyelination, fiber loss, and/or decreased metabolic integrity (Cracco et al., 1979; Starr, 1978). Finally, stimulation of the median nerve excites some motor axons that may contaminate the SEP.

Recently, the identification of the SEP waves has been clarified by considering " . . . the conduction distances and anatomical features of each of the three neurones making up the central somatosensory pathway in adult man, and (attempting) to relate interpeak delays of SEP far-fields to actual conduction times along these neurones," (Desmedt & Cheron, 1980b, p. 394).

The Desmedt & Cheron (1980b) procedure uses electrical stimulation of the index and middle fingers in order to stimulate only sensory fibers. The median nerve volley is then recorded at the wrist, the axilla, Erb's point, and at the entrance to the spinal ganglion (C6-C7), as well as from the scalp. Further, the scalp SEP is recorded with a noncephalic reference (on the unstimulated forearm) to substantially reduce pick up of the early far fields at the reference electrode. Their results show clearly that P9 occurs before the arrival of the nerve volley at Erb's point but after its arrival at the axilla. Thus, the P9 wave of the scalp recorded SEP establishes that P11 arises from passage of the afferent volley through the ascending dorsal column. The P11 onset

Possible Morphological Differences in
Somatosensory Evoked Potentials P13 and P14

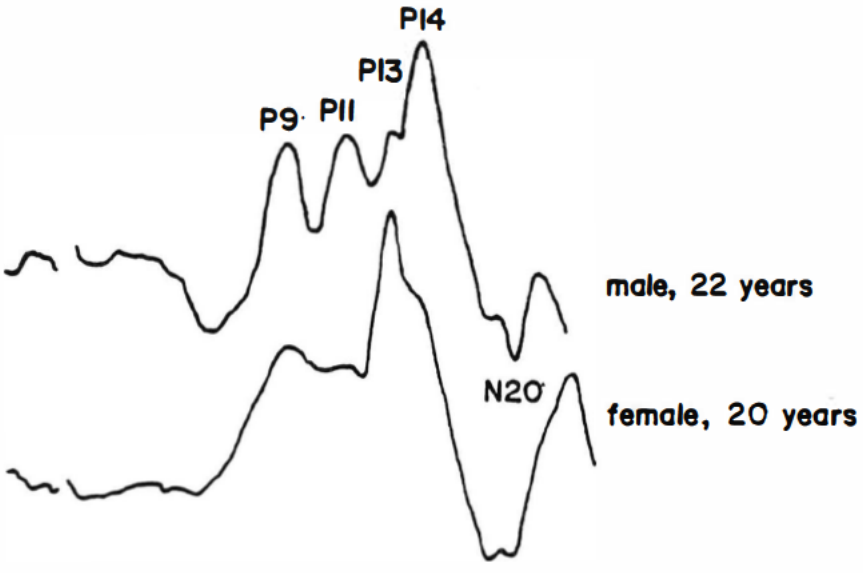

Figure 2: Two SEPs that demonstrate potential morphological differences in P13 and P14. The upper SEP is from a 22 year old male, the lower from a 20 year old female. The small arrow designates stimulus onset. The entire figure is redrawn from Desmedt & Cheron (1980c). They made no mention of the subjects' heights. The subjects would have to be of virtually identical body size, especially arm length, for the peak designations to be correct.

corresponds precisely with the arrival of the peripheral nerve volley at the spinal cord (Desmedt & Cheron, 1980b).

After careful consideration of the geometry of the ascending central somatosensory pathway, Desmedt & Cheron (1980b) were able to establish that the P13 and P14 generators are below the thalamus but above the foramen magnum. It appears that the lemniscal volley has just begun to activate the ventro-basal thalamic neurones at P14 onset (Desmedt & Cheron, 1980b). This conclusion is in agreement with a report by Greenberg, Mayer, Becker, & Miller (1977) that this wave has no thalamic or cortical component because they have recorded it in five patients with electrical and clinical brain death. Desmedt & Cheron (1980b) conclude that N18 is the response of cortical projection of the afferent volley. Thus, the descending (positive up) limb of N18 can be used as a marker for estimating the cortical SEP latency. Desmedt & Cheron (1980b) believe that N18 is related to postsynaptic potentials elicited in apical dendrites of pyramidal neurones.

Diabetic Neuropathy

The term, diabetic polyneuropathy, describes a multiplicity of neuronal degenerative anomalies associated with diabetes mellitus. Peripherally, the major manifestation of diabetic neuropathy is reduced conduction velocity in sensory and motor nerves. The presence of neuropathy in long standing insulin dependent diabetics is not universal (Pirart, 1978). However histological and electrophysiological evidence suggests that the reduced CV is the result of demyelination and subsequent loss of nerve fibers (Noel, 1973) beginning well before clinical manifestations (Greene et al., 1981). The degree of glycemic control and duration of diabetes are major determinants of the progression of the degenerative

process (Porte et al., 1981; Greene et al., 1981; Horowitz & Ginsberg-Fellner, 1979; Pirart, 1978; Skyler, Lasky, Skyler, Robertson, & Mintz, 1978; Ward et al., 1971; Gregerson, 1967). Indeed, careful management of blood glucose has been shown to reverse the degenerative process to some extent (Ward et al., 1971) with the potential reversal probably limited by the degree of large fiber loss (Greene et al., 1981).

Diabetic neuropathy sometimes involves weakened neuromuscular transmission mechanisms (Miglietta, 1973), altered pupillary reflexes (Hreidarsson, 1981) as well as reduced skin sensitivity to temperature, pin prick, proprioception, and vibration (Greene et al., 1981). While it is well established that these and other processes affected by diabetes are the result of primary neuronal changes, it is not certain whether the central mediation of these processes is affected. Neuromuscular transmission mechanisms are affected in some diabetics resulting in a decline in muscle action potentials with high stimulation frequency (20-50 per second) (Miglietta, 1973). The decline in neuromuscular transmission is observed in some diabetics despite their having normal CVs (Miglietta, 1973). Some motor fibers are apparently immune to this decrement, such as those serving the fingers (Miglietta, 1973). Abnormalities of pupil unrest are known to occur during hyperglycemia (Hreidarsson, 1981). Since the control of pupillary unrest is of central origin (see Hreidarsson, 1981), it is possible that the abnormalities associated with hyperglycemia are directly related to the effects of hyperglycemia on the central autonomic nervous system (Hreidarsson, 1981).

Electroencephalographic studies show a higher incidence in diabetics of abnormally slow and abnormally fast waves (DeJong, 1977). These

abnormalities appear to be associated with recurrent hypoglycemia (DeJong, 1977).

Gupta and Dorfman (1981) have reported longer spinal conduction times in a heterogeneous group of diabetics, but no difference in supraspinal (cervical cord to cortex) conduction. They used an indirect method of calculating spinal transit time and supraspinal transit time (Dorfman, 1977) from the SEP. They suggest that the supraspinal segment of the somatosensory pathway is more resistant to diabetic neuropathy.

In cases of diabetic neuropathy, sensory nerve potentials show reduced amplitude, a less well defined shape, and increased latency of the initial peak (Noel, 1973). Lesions of the central somatosensory pathway are expected to affect the appearance of the SEP in the same three ways (Oester et al., 1972).

The central purpose of this investigation was to determine, in the most direct way possible, if a group of young adult insulin dependent diabetics evidence altered neuronal function within the CNS, as measured with scalp recorded EPs.

Methods

Subjects

Persons between the ages of 20 and 30 were recruited for participation in this study using fliers posted around the university campus. When potential participants reported to the EP lab, the entire testing procedure was explained, followed by an opportunity to ask questions. Written consent was then obtained from each participant. All were paid $5.00 per hour of participation. Responses to the screening questionnaire were used to exclude individuals who had a potentially confounding medical history. The questionnaire identified two such cases, both diabetics. The first had diagnosed peripheral neuropathy that had produced temporary paralysis of the legs, as well as a history of neurologic seizures. The second individual was approximately 80 pounds over recommended body weight for his height and build.

After completion of the screening questionnaire, a urine sample was collected from each participant. Each sample was tested immediately for presence of glucose and ketones (AMES^{R} KETO-DIASTIX). No member of the nondiabetic group had previous evidence of diabetes nor did any show positive urinalysis results. All diabetics showed presence of urine glucose on either the first urine sample or a second sample taken halfway through EP testing (see Table 2). Therefore, these tests verified the self-report diagnostic classification of the diabetics. None of the 20 participants showed urine ketones in either urine sample.

Table 2

Urine Glucose Test Results

	First Urinalysis mg/dL	Second Urinalysis mg/dL
DIABETICS:		
Female	0.07 $\pm$ 0.06	1.00 $\pm$ 0.82
n	3	4
Male	0.75 $\pm$ 0.96	0.71 $\pm$ 0.87
n	4	4
NONDIABETICS:		
Female	0	N/A
n	5	
Male	0	N/A
	5	

An audiogram was completed on each participant to establish hearing efficacy. The audiograms were collected in a quiet room using a Beltone portable audiometer. None of the 20 participants showed a hearing deficit greater than 30 dB at any of eleven frequency bands between 125 Hz and 8000 Hz (see Fig. 3). Furthermore, the two groups did not differ significantly over any of the eleven frequency bands, nor did hearing threshold to the BAEP click stimulus show a significant group difference. One nondiabetic individual was excluded from participation based on the audiogram. This individual had hearing thresholds of 45 dB over three frequency bands in both ears.

All ten diabetic participants met the following inclusion criteria: 1) insulin dependent from first diagnosis; 2) no previously diagnosed neuropathy; 3) body weight within ten pounds of ideal for height and build (Metropolitan Life Insurance statistics); 4) no history of any other metabolic or neurological disease. The diabetic group had a mean age fo 23.9 $\pm$ 3.4 years (range of 20 to 30 years) and consisted of five males and five females. The mean duration since diagnosis was 7.8 $\pm$ 5.8 years (range of 2.5 to 17 years). The nondiabetic control group also had five males and five females. Mean age for this group was 26.1 $\pm$ 3.3 years (range of 20 to 30 years).

Procedure

Stimuli for the BAEPs were 70 dB SL condensation phase click sounds generated by passing 0.1 msec square wave electrical pulses through TDH-49 headphones. Stimulation was to the right ear at a rate of ten per second. BAEPs were recorded from vertex (Cz) referenced to the right mastoid process, with a ground electrode clipped to the right earlobe

Mean Threshold Levels from Audiometric Tests

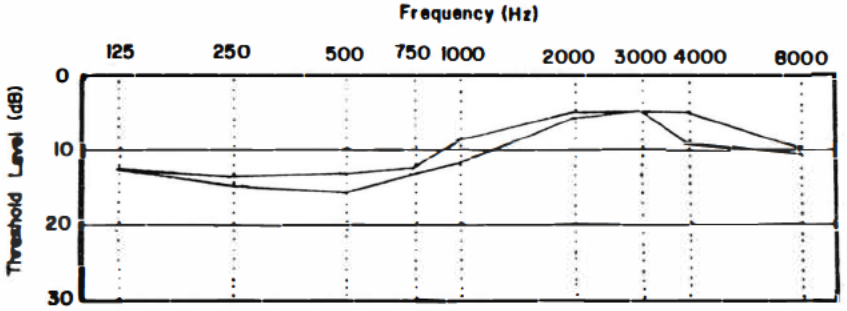

Figure 3: Mean threshold levels of audiogram test frequency levels, by diagnostic group. The mean audiograms meet at 125 Hz and 3000 Hz, however, they do not cross. The lower audiogram is from the diabetic group, the upper from the nondiabetic group. The diagnostic groups are not significantly different at any of the frequency levels tested.

(Scott & Harkins, 1978; Harkins, McEvoy, & Scott, 1978; Picton, Hillyard, Krausz, & Galambos, 1974).

Stimuli for the SEPs and the median nerve CV measures were 0.5 msec square wave electrical pulses delivered three per second to the left median nerve just proximal to the wrist. The cathode was two cm proximal to the anode. A ground electrode was placed on the inner surface of the forearm midway between the wrist and elbow. Stimulation voltage was 50 volts. The thumb twitch motor threshold established stimulus intensity for each case (Starr, 1978). The stimuli were generated by a Grass S88 stimulator, a stimulus isolation unit, and a constant current unit connected in series.

SEPs were recorded from a parasagital electrode placed over the contralateral hand representation area of somatosensory cortex (one cm inferior and one cm posterior to C4 of the International 10-20 system of cephalic electrode placement). The cephalic electrode was referenced to a nuchal electrode between cervical vertebrae five and six (Harkins & Dong, 1980).

The electrophysiological responses being measured were amplified by a Grass P511J preamplifier set at a gain of 5×10^4 with filters at 10 Hz and 3000 Hz. A Nicolet 1074 signal summator was used to process the EEG for EPs and to determine the mixed nerve CV to median nerve stimulation. A bin width of 100 usec was employed for collecting the SEPs and the CV measures. Bin width was 50 usec for the BAEPs. During summation, the EEG was continuously monitored. Processing was stopped when muscle or other artifacts were apparent (Chiappa et al., 1979). For both EP modalities, four consecutive traces of 1024 stimulus presentations each were overlapped to permit determination of response stability. The

median nerve CV measure was determined from two repeated traces of 64 stimulus presentations each. Once collected, the EPs were plotted out from the signal summator using an X-Y plotter. The important points were designated and the corresponding digital values for latency and amplitude of each point were taken from the signal summator memory. The digital values were then entered into VCU's IBM 370 computer, along with other data on each participant, for subsequent processing using the Statistical Analysis System (SAS).

Results

Separate three-way analyses of variance (diagnosis x sex x diagnosis-sex interaction) were performed on all dependent variables except those of the audiograms and urinalysis results. The analyses of variance were performed using the ANOVA procedure of SAS. Correlations were performed using the CORR procedure of SAS. In the following account of the results, statistically significant differences between the diabetics and nondiabetics are referred to as diagnostic group differences, whereas statistically significant differences between females and males are referred to as sex group differences.

As a check for equivalent auditory reception in each diagnostic group, the group means for each frequency band of the audiograms were compared using t-tests. There was no significant diagnostic group difference at any of the levels tested (see Fig. 3). The analysis of variance for a difference in click stimulus threshold also showed no diagnostic group significance (see Table 3) (n's may vary throughout all tables because of missing values). Thus it appears that any group differences in the BAEP measure did not result from an influence of diabetes on the auditory receptor.

There was also no diagnostic group difference in sensory or motor threshold to the electrical stimulus, evidencing the absence of any symptomatic deficits in the diabetics (see Table 3). The females as a group had significantly lower sensory thresholds than did the males. However, motor thresholds showed no significant sex group difference.

Table 3

Stimulus Response Parameters, Height and Weight Data

	Click Threshold (dB)	Sensory Threshold (mA)	Motor Threshold (mA)	Height	Weight
DIABETICS:					
Female	9 ± 4	0.5 ± 0.05	4.7 ± 2.11	63.7 ± 2.1	123.6 ± 5.9
n	5	4	4	5	5
Male	11 ± 4	0.7 ± 0.46	5.8 ± 2.20	69.6 ± 1.8	145.4 ± 12.7
n	5	5	5	5	5
NONDIABETICS:					
Female	13 ± 9	0.4 ± 0.10	4.8 ± 2.11	64.1 ± 2.5	120.8 ± 9.8
n	5	5	5	5	5
Male	12 ± 4	0.8 ± 0.25	5.7 ± 0.97	71.8 ± 0.4	173.2 ± 14.2
n	5	5	5	5	5
DIAGNOSIS:					
F	0.9	0.1	0.01	2.4	6.3
P	0.35	0.79	0.93	0.14	0.02
SEX:					
F	0.04	5.26	1.3	64.9	55.8
P	0.85	0.04	0.27	0.0001	0.0001
DIAGNOSIS & SEX INTERACTION:					
F	0.3	0.6	0	1.1	9.5
P	0.58	0.45	1.00	0.30	0.007

Summary statistics for the BAEP latencies are presented in Table 4, along with the results of the ANOVA comparisons for each of the four groups. The component latencies are slightly slower in the diabetics. However, the differences do not show significance. At wave V the diabetics are about 0.2 msec slower than the nondiabetics ($p = 0.06$). The differences are small relative to the standard deviations, however the trend is consistent. Figure 4 illustrates the accumulation of diagnostic group latency differences over the interwave intervals from wave I to wave V.

The BAEP amplitudes were measured as the height of each waveform from its right base up to its peak. This distance measure was converted to microvolt (uV) units using a calibration square wave pulse of known voltage that was summated in the same way as the scalp recorded responses. Summary statistics for the BAEP amplitudes are presented in Table 5. Amplitudes for waves I, III, and V were tested for group differences. Females tended to have slightly larger wave V amplitudes ($p = 0.05$), however, there was no significant diagnostic group difference (see Michalewski et al., 1980)

CTT for the BAEP was calculated by subtracting wave I latency from wave V latency (Starr, 1978; Starr & Achor, 1979; Salamy & McKean, 1976; Salamy et al., 1975). Summary statistics for the measure are presented in Table 6. Mean BAEP CTT for the diabetic group is about 0.2 msec longer than for the nondiabetics, just as for wave V latency (diabetic mean = 4.2 msec, nondiabetic mean = 4.0 msec). The diagnostic group difference shows significance ($p = 0.03$). The slower CTT suggests that diabetes may have begun to affect the metabolic integrity of the brainstem auditory pathway. However, the absence of any difference in the overall

Table 4

Brainstem Auditory Evoked Potential Latencies
(msec)

	I	II	III	IV	V	VI	VII
DIABETICS:							
Female	1.43 ± 0.13	2.59 ± 0.11	3.71 ± 0.13	4.90 ± 0.20	5.59 ± 0.33	6.91 ± 0.17	8.63 ± 0.18
n	4	4	4	3	4	4	3
Male	1.49 ± 0.14	2.63 ± 0.10	3.66 ± 0.11	4.65 ± 0.05	5.67 ± 0.06	7.31 ± 0.35	8.95 ± 0.65
n	5	5	5	3	5	4	5
NONDIABETICS:							
Female	1.51 ± 0.09	2.51 ± 0.21	3.64 ± 0.30	4.60 ± 0.13	5.40 ± 0.11	6.48 ± 0.45	8.64 ± 0.32
n	5	4	5	4	5	5	4
Male	1.47 ± 0.03	2.52 ± 0.04	3.60 ± 0.16	4.70 ± 0.25	5.50 ± 0.22	7.17 ± 0.43	8.58 ± 0.25
n	5	5	5	5	5	5	2
DIAGNOSIS:							
F	0.4	2.6	0.5	1.2	4.1	0.4	0.7
p	0.56	0.13	0.49	0.30	0.06	0.56	0.41
SEX:							
F	0.03	0.2	0.2	0.4	1.3	4.1	0.7
p	0.87	0.68	0.64	0.52	0.28	0.06	0.42
DIAGNOSIS & SEX INTERACTION:							
F	1.2	0.1	0.04	2.6	0	0.04	0.2
p	0.29	0.77	0.84	0.14	1.00	0.85	0.66

Bar Graph of Cumulative Brainstem Auditory Evoked Potential
Interwave Transmission Times

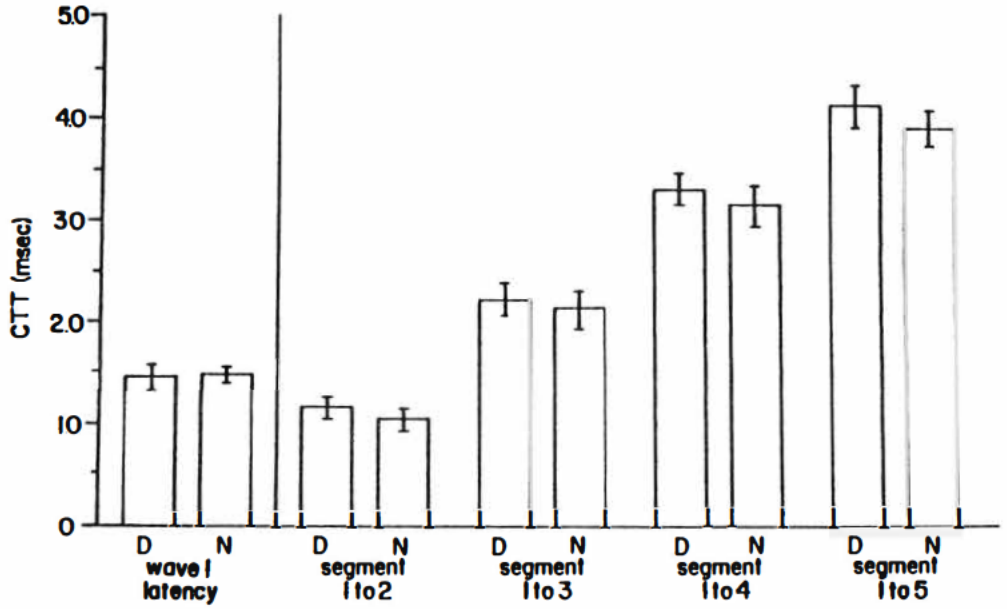

Figure 4: Display of the accumulation of interwave transmission time differences over the entire BAEP. The diagnostic group difference reaches significance over the longest segment, wave I to wave V. * Inaccurately designated P12 rather than P11 and P13.

Table 5

Brainstem Auditory Evoked Potential Amplitudes

(uV)

	I	III	V	Ratio of V to I
DIABETICS:				
Female	0.36 ± 0.22	0.28 ± 0.13	0.58 ± 0.15	2.79 ± 3.14
n	4	4	4	4
Male	0.31 ± 0.08	0.28 ± 0.13	0.50 ± 0.12	1.67 ± 0.65
n	5	5	5	5
NONDIABETICS:				
Female	0.27 ± 0.06	0.18 ± 0.007	0.70 ± 0.21	2.71 ± 1.18
n	4	3	4	4
Male	0.26 ± 0.13	0.28 ± 0.12	0.48 ± 0.12	2.19 ± 1.30
n	4	4	4	4
DIAGNOSIS:				
F	1.0	0.5	0.4	0.1
P	0.33	0.49	0.52	0.76
SEX:				
F	0.2	0.5	4.5	1.0
P	0.67	0.48	0.05	0.34
DIAGNOSIS & SEX INTERACTION:				
F	0.1	0.7	1.1	0.1
P	0.77	0.42	0.32	0.72

Table 6

Central Transmission Times and Median Nerve Conduction Velocities

	BAEP I to V (msec)	SEP P9 to P14 (msec)	SEP P14 to N18 (msec)	Median Nerve CV (m/sec)
DIABETICS:				
Female	4.16 ± 0.33	4.78 ± 1.08	4.52 ± 0.65	49.8 ± 5.3
n	4	4	5	5
Male	4.18 ± 0.10	4.90 ± 0.22	4.74 ± 0.61	55.9 ± 5.7
n	5	4	5	3
NONDIABETICS:				
Female	3.89 ± 0.12	3.80 ± 0.35	5.38 ± 0.44	59.3 ± 5.8
n	5	5	5	4
Male	4.03 ± 0.21	4.31 ± 0.21	5.82 ± 0.99	59.3 ± 4.0
n	5	4	5	5
DIAGNOSIS:				
F	5.5	8.1	9.6	7.4
p	0.03	0.01	0.007	0.02
SEX:				
F	1.1	2.0	1.1	2.3
p	0.32	0.18	0.31	0.15
DIAGNISOS & SEX INTERACTION:				
F	0.2	0.2	0.1	1.2
p	0.66	0.69	0.73	0.29

appearance of the BAEP suggests that no morphological changes have occurred.

The median nerve CV measure was calculated by dividing the distance between the stimulating electrodes and the recording electrode by the latency of the nerve volley, recorded at the elbow (see Fig. 1) (Cracco et al., 1979). The latency of the nerve volley was taken as the peak of the initial positivity, which corresponds to the onset of the negative component. Some of the median nerve volley recordings, while sufficient for latency determinations, are of poor quality because the recording electrode was not always directly over the nerve fiber. Use of a mobile recording probe would have permitted more precise location of the nerve. The median nerve CV results are summarized in Table 6 along with the CTTs. As expected, median nerve CV was significantly slower among the diabetics, indicating the presence of peripheral neuropathy ($p = 0.02$) (diabetic mean = 52.8, nondiabetic mean = 59.3). The diagnostic group means differ by about 6.5 m/sec.

Summary statistics for SEP latencies are presented in Table 7A along with analysis of variance results. The diabetics have slightly longer latencies for the first three components with only the P14 difference showing significance. However, the P14 diagnostic group difference is relatively dramatic ($p = 0.003$) (diabetic mean = 14.8, nondiabetic mean = 13.9). P14 is delayed by about 0.9 msec in the diabetic group. This difference disappears at N18, suggesting a reduction in terminal branching of the thalamocortical radiations (Desmedt & Cheron, 1980c), (diabetic mean = 19.3 msec, nondiabetic mean = 19.4 msec). Figure 5 illustrates the changing relationship of the diagnostic group latency differences over the interwave intervals from P9 to P22.

Table 7A

Somatosensory Evoked Potential Latencies

(msec)

	P9	P12*	P14	N18	P22
DIABETICS:					
Female	9.71 ± 0.94	12.23 ± 0.42	14.52 ± 0.23	19.04 ± 0.72	22.72 ± 0.93
n	4	4	5	5	5
Male	9.90 ± 0.74	12.40 ± 0.98	14.92 ± 0.67	19.66 ± 1.23	23.25 ± 1.03
n	4	3	5	5	4
NONDIABETICS:					
Female	9.14 ± 0.73	11.15 ± 0.83	12.94 ± 0.83	18.32 ± 0.90	22.63 ± 0.59
n	5	4	5	5	4
Male	10.18 ± 0.33	12.82 ± 0.58	14.64 ± 0.43	20.46 ± 1.10	22.95 ± 1.06
n	4	5	5	5	2
DIAGNOSIS:					
F	0.5		12.5	0.01	0.2
P	0.51		0.003	0.93	0.65
SEX:					
F	3.1		15.9	9.4	1.0
P	0.10		0.001	0.007	0.34
DIAGNOSIS & SEX INTERACTION:					
F	1.6		6.1	2.8	0
P	0.23		0.03	0.11	1.00

* Incorrectly designated as P12 rather than P11 and P13.

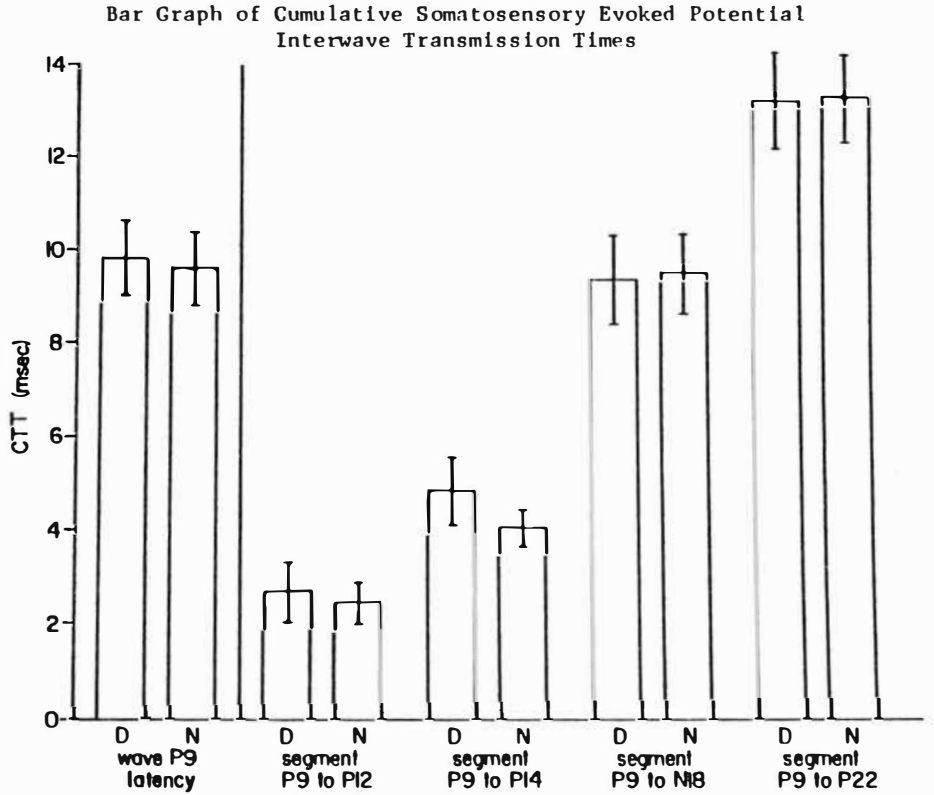

Figure 5: Display of the accumulation of interwave transmission time differences over the entire SEP. The diagnostic group difference reaches significance only for the P9 to P14 segment in this figure. (The P14 to N18 segment is significantly shorter among the diabetic group, however this segment is hidden in the P9 to N18 segment depicted here.)

The difference in P9 latencies is unexpectedly small given the difference in median nerve CV between the two groups (see Table 6). If P9 originated at the level of the axilla (Desmedt & Cheron, 1980b), the median nerve CV difference would be expected to produce about a 0.9 msec delay in P9 latency in the diabetics, given an arm length of 45 cm. A group arm length difference may have been responsible for the 0.7 msec discrepancy (0.9(expected) - 0.2(actual) = 0.7). The nondiabetic males tended to be taller and heavier than the diabetic males while the female participants were more homogeneous in height and weight. The differences are reflected in the diagnostic group means given in Table 3. This height discrepancy may have influenced the SEP latencies. Since height is related to arm length, there is reason to expect that height may have biased the SEP latencies in the taller nondiabetics, thereby disguising the influence of diabetes on the SEP latencies of the shorter diabetics. As an attempt to account for the height influence, analyses of co-variance were repeated on the SEP latencies with height covaried out (see Table 7B). Since the females were homogeneous with respect to height, it is interesting to note the larger difference in P9 latencies between the two groups of females. The P9 difference (0.7 msec) is more congruent with the median nerve CV findings.

Summary statistics for SEP amplitudes are presented in Table 8. SEP amplitudes were calculated as they were for the BAEP amplitudes, with the exception of N18. N18 amplitude represents the vertical displacement from the lowest point of N18 up to the highest point of P22. The diabetics have dramatically lower amplitudes for P14 and N18 ($p = 0.004$ and $p = 0.007$, respectively). These measures of the descending (P14) and ascending (N18) limbs of the N18 wave are probably closely related. Thus, the

Table 7B

Somatosensory Evoked Potential Latencies with Height Covaried Out

(msec)

	P9	P14	N18	P22
HEIGHT:				
F	12.1	8.1	12.8	1.8
p	0.003	0.01	0.002	0.21
DIAGNOSIS:				
F	0.8	10.9	0.1	0.2
p	0.47	0.001	0.88	0.81
SEX:				
F	0.9	0.3	0	0.01
p	0.36	0.57	0.95	0.94
DIAGNOSIS & SEX INTERACTION:				
F	1.1	5.0	1.8	0.1
p	0.31	0.04	0.20	0.76

Table 8

Somatosensory Evoked Potential Amplitudes

(uV)

	P9	P12	P14	N18
DIABETIC:				
Female	0.21 ± 0.30	0.05 ± 0.01	3.41 ± 1.17	2.81 ± 0.77
n	2	3	5	5
Male	0.22 ± 0.13	0.23 ± 0.25	2.83 ± 0.83	2.03 ± 0.70
n	4	3	5	4
NONDIABETIC:				
Female	0.21 ± 0.17	0.32 ± 0.15	4.85 ± 0.41	4.20 ± 2.00
n	4	4	5	4
Male	0.36 ± 0.05	0.10 ± 0.08	4.31 ± 1.23	5.24 ± 0.45
n	4	5	5	2
DIAGNOSIS:				
F	0.6		11.4	10.7
P	0.44		0.004	0.007
SEX:				
F	0.9		1.7	0.3
P	0.38		0.21	0.62
DIAGNOSIS & SEX INTERACTION:				
F	1.0		0	1.7
P	0.35		1.0	0.23

P14 and N18 amplitude measures may actually reflect the same thing: a relatively smaller negative displacement of the lowest point of N18 among the diabetics. No other SEP amplitudes showed any significant group difference.

Summary statistics for two SEP CTT measures are presented in Table 6. The P9 to P14 measure is the conduction time from the peak of the first component of the early SEP up to the peak of the most prominent early positivity. The P14 to N18 measure is the conduction time from the most prominent early positivity up to the most prominent early negativity, corresponding to the brainstem-to-thalamocortical transition (Desmedt & Cheron, 1980b). Like the BAEP CTT, both of the SEP CTT measures show a significant diagnostic group difference. However, the directions of the two SEP CTTs are opposite. The diabetics have a longer CTT from P9 to P14 while the P14 to N18 segment is shorter in this group. Recall that the diabetics also had significantly reduced amplitudes on the descending and ascending limbs of N18. As with the smaller P14 and N18 amplitudes among the diabetics, the shorter P14 to N18 segment might also reflect a reduction in terminal branching of the thalamocortical radiations.

A plot of each participants' BAEP CTT versus his/her SEP CTT (P9 to P14) shows a strong linear trend (see Fig. 6). This relationship implies that the longer CTTs observed in the diabetics occur together in both modalities and reflect a mild but pervasive metabolic influence of diabetes throughout the CNS. The plot reflects to a degree the same findings as the analyses of variance tests for the CTTs. However, correlations of the BAEP CTT and the SEP CTT, by diagnostic classification, reveal additional information about the relationship. There is a

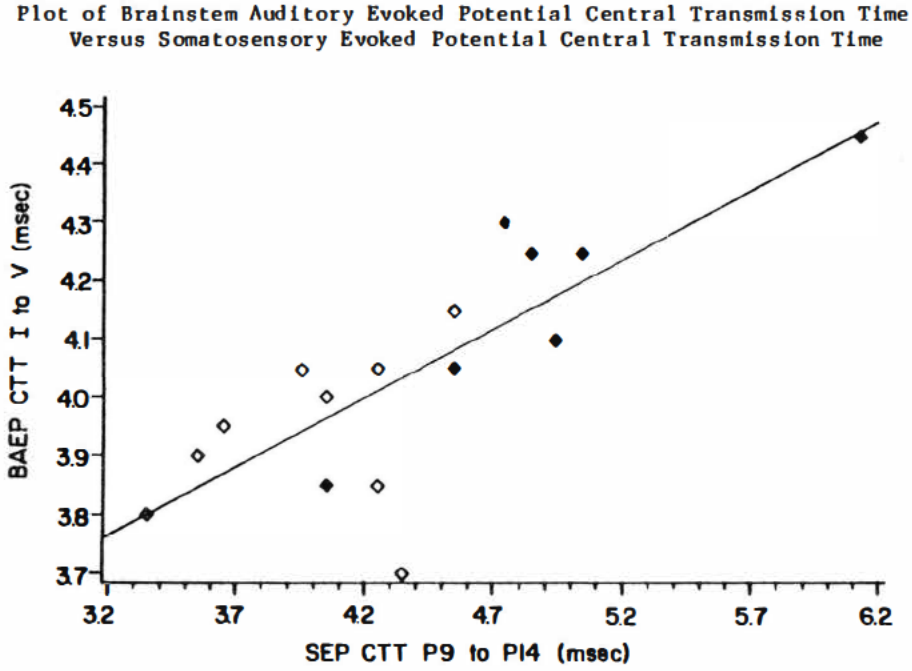

Figure 6: Plot of BAEP CTTs versus SEP CTTs. Note the apparent linear relationship between the two measures. The diabetics are depicted by the solid diamonds, the nondiabetics by the unfilled diamonds. Among the diabetics, there is a significant correlation between the two measures ($r = 0.86$, $p = 0.01$). The correlation among the nondiabetics is not significant ($r = 0.31$, $p = 0.42$).

significant correlation between the two CTTs among the diabetics ($r = 0.86$, $p = 0.01$), but not among the nondiabetics ($r = 0.31$, $p = 0.42$).

The degree of peripheral nerve diabetic neuropathy has been shown repeatedly to be inversely related to the degree of glycemic control (Greene et al., 1981; Porte et al., 1981; Horowitz & Ginsberg-Fellner, 1979; Pirart, 1978; Skyler et al., 1978; Ward et al., 1971; Gregerson, 1967). Better blood glucose control is associated with less peripheral neuropathy. Looking at Fig. 6, it appears that the large BAEP CTT -- SEP CTT correlation among the diabetics is a result of the greater dispersion of the diabetics along the regression line. This finding suggests that not all the diabetics show a diagnostic effect. Furthermore, the dispersion may be related to the degree of glycemic control, as it is at the peripheral level. The demonstration of a relationship between CTTs and glycemic abnormality would verify that longer CTTs in diabetics are a result of glycemic abnormality and validate the use of EPs to diagnose CNS diabetic neuropathy.

Discussion

The diabetic group in this study evidenced significant slowing of median nerve conduction velocity, indicative of peripheral nerve diabetic neuropathy. Furthermore, the three CTT measures reported in this study each showed a significant diagnostic group difference, suggesting a detrimental effect of diabetes on CNS function. However, the direction of the diagnostic group difference was not the same for the three CTT measures. The BAEP CTT (wave I to wave V) and the SEP CTT (P9 to P14), both of early brainstem origin, were significantly longer in the diabetic group,probably reflecting slowed central conduction. The SEP CTT (P14 to N18), of midbrain origin, was significantly shorter in the diabetics, possibly reflecting a reduction in thalamocortical radiations (Desmedt & Cheron, 1980b). More definitive statements of the meaning of these findings await the resolution of measurement problems and a better knowledge of the neural origins of the EP waveforms.

The group means for the SEP CTTs suggest a serious question concerning accurate designation of the P14 component in the nondiabetics. As an extension of the nomenclature, the anticipated CTT from P9 to P14 is about 5 msec. The anticipated CTT from P14 to N18 is about 4 msec. These values appear essentially reversed in the nondiabetics, with P9 to P14 being about 4 msec, and P14 to N18 being over 5 msec (Table 6). One could argue that the component designated as P14 in the nondiabetics is actually P13 and that the diagnostic group difference in the CTTs merely

reflects the "misdesignation". Desmedt & Cheron (1980b) have pointed out how P13 can be incorrectly designated as P14 (see Fig. 2) when P13 is inordinately large and predominates over P14. To further exacerbate the uncertainty a small P15 is sometimes present on the descending limb of P14, mimicking the P13-P14 condition in the lower SEP of Fig. 2 (Desmedt & Cheron, 1980b; Starr, 1978; Greenberg et al., 1977). It is possible that the naming of P15 is actually an error of misinterpreting the P13 and P14 waves in taller individuals.

The issue of correct designation is much more complex than just mere variation in wave morphology. Given a CV of 60 m/sec, an average of about 0.17 msec is required for each cm of conduction distance over the median nerve. Desmedt & Cheron (1980c) have attributed differences of as much as 2 msec in P9 onset latency to intrasubject differences in arm length. Thus, it is not unreasonable that the P9 wave could have a peak latency of as low as 7 msec or as high as 11 msec among normal individuals with identical median nerve CVs, because of inter-individual differences in the length of the nerve pathway. The polarity-latency combination nomenclature is only a representation of mean peak latencies from large samples where height is ignored as a factor. It is unreliable as a rigid guideline for designation of SEP components.

When comparing SEPs from a group that is heterogeneous with respect to height, the largest component of height-related variation in peak latencies arises from the longest segment of the stimulated pathway, that is, from the stimulation site up to the axilla (vicinity of P9 origin). However, it is important to realize that this component is not the only component of height related variation in peak latencies. It is reasonable to assume that height is related to body size and that it

tends to be distributed proportionally over the entire vertical axis. Therefore, it is expected that taller individuals would tend to have a greater chest girth also. Assuming that one-half of chest girth closely corresponds to the nerve pathway length from the axilla to the point of spinal entry (onset of P11), it is expected that taller individuals should have a greater conduction time between the peaks of P9 and P11. However, this component of height related variation in peak latencies is smaller than that of the first segment (stimulus onset up to peak of P9) because the nerve segment is shorter. An analogous argument applies for the remaining peak-to-peak segments of the SEP. The two major points can be generally stated as follows: 1) not only is height directly related to SEP latencies, but also it is related to the interpeak latencies. Thus, the height effect cannot be subtracted as an overall constant from each peak latency. However, 2) the height related variation in interpeak latencies should be proportional to the length of the nerve segment between the two peaks involved. Thus, the height factor should be less significant for shorter caudal segments of the nerve pathway than it is for longer rostral segments. These relationships are problematic when the SEP is used to determine impaired CNS function because the putative disease effect will be similar to the height effect. Therefore, the height effect must be accurately assessed in order to draw sound conclusions concerning group differences in peak latencies and interpeak distances, as they reflect neural processes. Clearly, the covariance approach employed in this study was effective in dealing with height related variation in the SEPs. However, the covariance approach was limited in that the height related variation may have hampered correct designation of the component peaks. Where peaks P9, P11, and P13 are

involved, the height related variation is best controlled by recording the nerve volley at the axilla (origin of P9) and over cervical vertebrae 6 and 7 (onset of P11) (Desmedt & Cheron, 1980b). These recordings allow accurate designation of the scalp recorded P9 and P11 by essentially having recorded the potential from two points that give the same latencies as the scalp recorded SEP. Such a tight designation of P9 and P11 reduces the difficulty in accurately designting P13 and P14 thereby making the differences induced by any disease factor more detectable.

In this study, the scalp recorded SEPs were extensively evaluated to insure accurate designation of the components. Since axilla and neck EPs were not recorded, the scalp SEP peaks were designated based on their overall appearance and to a degree, on the anticipated nominative peak latencies. Knowledge of the diagnostic group classification was not considered during the initial scoring. The data were then entered into the computer for calculation of summary statistics. Outlying observations were then checked for validity. Finally, the SEPs were rescored a second time from scratch with any scoring differences thoroughly reconsidered by Dr. Harkins and myself. In light of the new information concerning P11 and P13 (rather than P12), the SEPs will be rescored a third time prior to any further publication.

More research needs to be done to clarify the components of the SEP, their origins, and factors influencing their appearance. Unlike the BAEP, it is not possible to clearly interpret the SEP findings presented here until such information is available. Nonetheless, there are some notable consistencies. The BAEP CTT, PCV, and SEP CTT (P9 to P14) for the diabetic group are all in the expected direction. Thus, it appears that, among diabetics, conduction times tend to be longer throughout the

nervous system. These findings are analogous to age differences observed by Desmedt & Cheron (1980 a & c) in a group of octogenarians. Gupta and Dorfman (1981) have observed a similar trend in a heterogeneous group of diabetics, except they found no differences at the supraspinal level. However, their technique involved estimation of several parameters that would be affected by diabetic neuropathy. It is not clear whether assumptions involved in these estimations remain valid in cases of diabetic neuropathy (see Dorfman, 1977 for technique of estimating conduction time based on the F-wave motorneuron backfiring phenomenon).

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Vita

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