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Sensory Nerve Conduction Studies in the Diagnosis of Diabetic Sensorimotor Polyneuropathy: Electrophysiological Features

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Abstract. [Purpose] To analyze the electrophysiological characteristics of diabetic sensorimotor polyneuropathy (DSPN), also known as DPN, and to determine sensitive indicators of the disease using sensory nerve conduction studies (SNCSs). [Methods] SNCSs of the median, ulnar, and sural nerve were performed on 120 patients diagnosed with DSPN and compared with those of 77 healthy controls. We performed analysis to detect abnormal conduction velocities and the distal amplitude of the compound nerve action potential (CNAP). In addition, we determined the optimal cut-off values for the diagnosis of DSPN. [Results] More severe abnormal nerve conduction was found in the lower limbs than in the upper limbs. The severity of the abnormal nerve conduction was more apparent in the distal CNAP amplitude than in the conduction velocity. [Conclusion] Our findings suggest that SNCSs of the lower limb nerve seem to be more sensitive at detecting DSPN than SNCSs of the upper limb. In particular, the sural nerve is the best indicator for the early detection of DSPN.
Key words: Diabetic sensorimotor polyneuropathy, Sensory nerve conduction studies, Sural nerve

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INTRODUCTION

Diabetic sensorimotor polyneuropathy (DSPN) is a slowly progressive disorder and the most common complication of chronic diabetes mellitus[1–6)]. The pathophysiology of DSPN is multifactorial and involves genetic, environmental, behavioral, metabolic, neurotrophic, and vascular factors[2,6)]. DSPN can affect any part of the nervous system. This nerve disorder, which is usually considered to appear in the late stages of diabetes mellitus, has a negative influence on both morbidity and quality of life[7–11)]. The incidence and prevalence of DSPN is showing a steady upward trend worldwide[7,12)]. Early diagnosis of the disease is very important for effective management. The diagnosis of DSPN is associated with specific clinical symptoms and signs and is detected via nerve conduction studies (NCSs), the quantitative sensory test, and the quantitative autonomic test[2,8,13)]. A NCS is one of the most sensitive tests because it can detect DSPN prior to the occurrence of clinical symptoms and it is widely considered as an excellent test even in the prognostic assessment of the disease through follow-up study[14–16)]. NCSs can be divided into motor, sensory, mixed, and late response (H-reflex and F-wave) tests through which the function of the peripheral nerves can be assessed objectively and quantitatively[17–21)]. Sensory NCSs (SNCSs) are usually used in the early detection of subclinical diabetes or in the differential diagnosis and screening of DSPN[22,23)], because the sensory nerves are generally damaged prior to motor nerve damage of the peripheral nerves[24–26)].

With the aim of detecting the most sensitive indicator for the early diagnosis of DSPN, this study searched the main electrophysiological characteristics of DSPN using comparative analysis of the results of SNCSs with a control group. In contrast to earlier studies, this study analyzed the severity of neuropathy through stepwise analysis of major parameters of SNCS and abnormal manifestations of the segment. Then, we determined the most sensitive indicator for the early diagnosis of DSPN. In addition, this study aimed to derive electrophysiological reference values for SNCSs, which could aid the early diagnosis and early prevention of DSPN by yielding a cut-off value of DSPN.

SUBJECTS AND METHODS

We studied diabetic patients (n=120), diagnosed via hematological examinations, with signs and symptoms of diabetic neuropathy including paresthesia, weakening of muscular strength, and loss of tendon reflexes. The control subjects (n=77) were diagnosed as normal in NCSs and had no other medical history of diabetes or clinical signs or symptoms.

For the SNCSs, the median nerve and the ulnar nerve of the upper limb were examined by segment; the sural nerve

of the lower limb was also examined. For each patient, both the upper limbs and one lower limb were examined or one upper limb and both lower limbs were examined. The nature of the tests, including the electrical stimulation, was explained to each patient, and great care was taken to ensure that the patients were in a comfortable posture. The amplitude of the compound nerve action potential (CNAP), also called the sensory nerve action potential (SNAP), and the sensory nerve conduction velocity (SNCV) obtained by the signal averaging techniques were analyzed by segment. The distal CNAP amplitude was determined by measuring the amplitude from the negative peak to the positive peak and expressed in microvolts. The SNCV (m/sec) was measured using the peak latency. The median nerve and the ulnar nerve were examined using orthodromic methods, and the sural nerve was assessed using antidromic methods. All of the patients were studied using the same electromyography (EMG) unit. The NCSs were performed using standard EMG equipment (Nicolet, U.S.A, Viking IV). Round attachment type surface 20-mm electrodes were used, and the measurements were based on Oh's method and reference values[27]. We used a band-pass filter of 20 Hz ~ 3 KHz, a sweep speed of 1 msec, and a sensitivity of 20 μV.

Three categories of abnormal manifestations of the distal CNAP amplitude were analyzed: any abnormality, abnormalities > 10%, and abnormalities >50%. The data were compared with the normal reference value for SNCS. The median and ulnar nerve CNAPs were based on the distal CNAP amplitude, which was obtained from subjects wrists by stimulating the fingers of the last terminal segment. The mean ± SD of the distal CNAP amplitude of three evoked CNAPs was calculated. The mean ± SD of the SNCV by segment type was analyzed for each SNCS. The abnormal manifestations of the median and ulnar nerves were analyzed in three categories: any abnormality, abnormalities >10%, and abnormalities >50%. The data were compared with the normal reference value of SNCV. The median and ulnar nerve SNCVs were based on the distal SNCV (finger - wrist segment). The rate at which the CNAP was not evoked was analyzed for each sensory nerve type. The CNAP frequency was compared with that of nerves without left-right distinction, and the CNAP standard that did not show an evoked potential was regarded as the distal CNAP. The reference value that separated the two groups was determined by the type of nerve and the parameter using comparative results of all of the measurements of the control and the DSPN groups.

The results of the SNCSs were analyzed using the SAS 9.1 for Windows, and statistical significance was accepted at values less than 0.05. The Chi-square test was used to determine the cut-off value. The Chi-square test or Fisher's exact test was used to determine the statistical significance of the frequency of abnormal manifestations and of the no potential by the parameter types of a sensory nerve.

RESULTS

The number and type of nerves studied for the control group and the DSPN group are shown in Table 1. The control group comprised 40 males and 37 females (mean age: 48.4 ± 13.0), and the DSPN group comprised 71 men and 49 women (mean age: 59.6 ± 11.7). There were statistically significant differences between the DSPN and control groups for all of the distal CNAP amplitudes (Table 2). In particular, there was tendency for the ulnar and sural nerve values to be higher than that of median nerve in an abnormal finding. Similarly, the mean value of the distal CNAP amplitude of the median nerve in the DSPN group was 14.7 ± 10.7 μV, which was higher than the normal reference value for the median nerve and different from that recorded for the ulnar and sural nerves (Table 4). The abnormal manifestations were then compared by the type of nerve and stage of SNCV in a distal segment (finger to wrist) (Table 3). The results revealed significant differences between the DSPN and control groups for all of the nerves, except for abnormal values greater than 50% of the ulnar nerve. In particular, there was a clear difference in the values for the sural nerve between the DSPN group and the control group in all three categories of abnormality ($p<0.0001$). The mean value of the SNCV of the distal segment of the median nerve in the DSPN group was 33.7 ± 10.4 m/s, which is remarkably lower than the normal reference value of the proximal segment (Table 4). The mean value of the SNCV in the DSPN group was noticeably low when compared with the normal reference value for the same segment of the ulnar nerve. The distal CNAP was not evoked in fewer than 5% of sensory nerves of the upper limb in the DSPN group, but there was no statistically significant difference from the control group. In contrast, there was a clear difference from the control group for the sural nerve in the DSPN group (Table 5). The cut-off value was determined by comparing the type of nerves and the major parameters of the control and DSPN groups. The cut-off values for the distal CNAP and conduction velocity between the fingers and the wrist were 24.5 μV and 44 m/sec, respectively, for the median nerve and 12.0 μV and 42 m/sec, respectively, for the ulnar nerve. The cut-off values for the distal CNAP and conduction velocity of the sural nerve were 9.0 μV and 37 m/sec, respectively.

Table 1. Demographic data of control and DSPN groups

Sensory nerve	Control (n)	DSPN (n)
Median	91	149
Ulnar	89	125
Sural	132	226

Both upper limbs and one lower limb or one upper limb and both lower limbs of subjects were measured. DSPN, diabetic sensorimotor polyneuropathy.

DISCUSSION

DSPN, which is a representative type of diabetes complication and also the most common systemic polyneuropathy, can be diagnosed using an electrophysiological test. It is well known that neuropathy is present prior to the appearance of clinical symptoms[28]. Therefore, early diagnosis is considered to be very important, and there has been much research on electrodiagnostic testing. To inves-

Table 2. Comparison of the electrophysiological characteristics of the distal compound nerve action potential amplitude.

Sensory nerve	EOA	Control (%)	DSPN (%)
Median	abn.	91/0 (0%)	149/55† (36.9%)
	> 10%	91/0 (0%)	149/52†(34.9%)
	> 50%	91/0 (0%)	149/32† (21.5%)
Ulnar	abn.	89/1 (1.1%)	125/81† (64.8%)
	> 10%	89/1 (1.1%)	125/73† (58.4%)
	> 50%	89/1 (1.1%)	125/32† (25.6%)
Sural	abn.	132/3 (2.3%)	226/149† (65.9%)
	> 10%	132/3 (2.3%)	226/139† (61.5%)
	> 50%	132/3 (2.3%)	226/83† (36.7%)

EOA, Extent Of Abnormality from reference value. abn, abnormal; DSPN, diabetic sensorimotor polyneuropathy. †p<0.0001.

Table 3. Comparison of the electrophysiological characteristics of the conduction velocity of the finger to wrist segment.

Sensory nerve	EOA	Control (%)	DSPN (%)
Median	abn.	91/4 (4.4%)	149/116† (77.9%)
	> 10%	91/0 (0%)	149/81† (54.4%)
	> 50%	91/0 (0%)	149/11* (7.4%)
Ulnar	abn.	89/0 (0%)	125/76† (60.8%)
	> 10%	89/0 (0%)	125/21‡ (16.8%)
	> 50%	89/0 (0%)	125/6 (4.8%)
Sural	abn.	132/2 (1.5%)	226/124† (54.9%)
	> 10%	132/0 (0%)	226/75† (33.2%)
	> 50%	132/0 (0%)	226/36† (15.9%)

EOA, Extent Of Abnormality from reference value. abn, abnormal; DSPN, diabetic sensorimotor polyneuropathy. * p<0.05, ‡ p=0.0001, † p<0.0001.

Table 4. Comparison of the sensory and mixed nerve conduction study data of the control and DSPN groups

Parameter		Normal value	Control	DSPN
Median sensory nerve	dCNAP Amp.	10 <	42.5 ± 16.8	14.7 ± 10.7
	SNCV (F-W)	41.26 <	47.4 ± 3.6	33.7 ± 10.4
	SNCV (W-E)	49.39 <	55.1 ± 3.3	47.2 ± 5.3
	SNCV (E-Ax)	53.95 <	58.4 ± 3.5	51.3 ± 4.0
Ulnar sensory nerve	dCNAP Amp.	10 <	24.0 ± 1.0	8.7 ± 6.0
	SNCV (F-W)	39.26 <	46.4 ± 3.1	37.2 ± 9.3
	SNCV (W-E)	47.46 <	56.2 ± 3.3	47.0 ± 5.9
	SNCV (E-Ax)	48.18 <	56.5 ± 3.9	47.8 ± 6.6
Sural nerve	CNAP Amp.	6 <	19.2 ± 8.1	5.2 ± 4.8
	SNCV	34.68 <	42.6 ± 3.2	29.5 ± 13.5

Mean ± SD. dCNAP, distal compound nerve action potential; Amp., amplitude (μV); SNCV, sensory nerve conduction velocity (m/sec); F-W, finger to wrist segment; W-E, wrist to elbow segment; E-Ax, elbow to axilla segment.

tigate the main electrophysiological characteristics of DSPN, we analyzed abnormal manifestations by stage based on type of major parameter and segment of SNCS for different sensory nerves. We then analyzed the severity of the neuropathy and also attempted to detect a sensitive indicator for the diagnosis of DSPN. Moreover, we aimed to identify a cut-off value that could be used as an electrophysiological reference value in SNCSs for the early diagnosis of DSPN. The results of the abnormal manifestations by stage in the SNCSs are shown in Tables 2 and 3. There was clear evidence of the manifestation of systemic polyneuropathy, which had invaded the entire upper and lower limbs. The DSPN group showed significant differences from the control group for all the nerves. In particular, the amplitude of the distal CNAP (Table 2) and the SNCV (Table 3) of all of the nerves in the DSPN group differed significantly (p<0.05~p<0.0001) from the normal reference value. This finding implies that SNCSs can play a role in the differential diagnosis of the DSPN. A stepwise analysis of the abnormal manifestations attempted to identify the electrophysiological features of DSPN. The analysis shows that a decrease in the amplitude of the distal CNAP strongly points to diabetic neuropathy (p<0.0001), in all of the stages. The invasion of the lower limb was greater than that of upper limb. A major difference in SNCV (p<0.0001) was observed only in the sural nerve of the lower limb. In addition, no significant difference was found between the DSPN and control groups for the nerves of the upper limb with no potential (Table 5); a significant difference was found only for the sural nerve. Based on the results of the analysis of the electrophysiological features of DSPN, it appears that the nerves of the lower limb, rather than those of the upper limb, are more likely to be damaged. In addition, the findings suggest that the distal CNAP amplitude could be regarded as a slightly more sensitive indicator of DSPN than nerve conduction velocities in SNCSs. The sural nerve, therefore, appears to be a useful indicator for the early diagnosis of DSPN.

Table 5. Comparison of the No potential frequency between the control and the DSPN groups

Sensory nerve	Control (%)	DSPN (%)
Median	91/0 (0%)	149/8 (5.4%)
Ulnar	89/0 (0%)	125/5 (4.0%)
Sural	132/0 (0%)	226/36† (15.9%)

DSPN, diabetic sensorimotor polyneuropathy. † p<0.0001.

The results also show that the mean value of the distal segment (finger to wrist) of the median nerve was remarkably low compared with the normal reference value for the proximal segment or in the same segment of the ulnar nerve in a mean value analysis of the SNCV (Table 4). This finding appears to be due to carpal tunnel syndrome (CTS), which selectively invaded only the median nerve. Previous work has suggested that the median nerve could serve as an important indicator in electrophysiological analyses of DSPN[29]. However, other studies have reported that the criterion of median NCS should not be included as an electrophysiological indicator of DSPN because of the effects of CTS[30,31]. The cut-off value determined for the distal CNAP amplitude and the SNCV was somewhat strict compared with the existing normal reference values. However, there was a definite difference from a value quantitatively measured in a normal person. There is a need for more research on the values of patients who already have symptoms.

Full consideration should be given to the verification of the testing procedure and methodology, namely, the strength of electrical stimulation, the exact measurement of the inter-electrode distance, subjects' temperature and skin resistance, and the equipment setting. It is important that the electrophysiological function of the peripheral nerve is quantified and evaluated in the follow-up and the prognosis of patients.

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