Current Perception Threshold and Sympathetic Skin Response in Diabetic and Alcoholic Polyneuropathies

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Abstract

Objective **Correlation between current perception threshold and sympathetic skin response was investigated in patients with diabetic or alcoholic polyneuropathy.**

Methods **Current perception threshold was measured using Neurometer CPT/C, and the sympathetic skin response was measured using Neuropack Σ.**

Patients **Fourteen patients with diabetic polyneuropathy and 10 patients with alcoholic polyneuropathy were studied.**

Results **There was a significant negative correlation between the current perception threshold to 5 Hz stimulation and the amplitude of sympathetic skin response.**

Conclusion **Since both current perception threshold to 5 Hz stimulation and sympathetic skin response are related to C fibers, these two are considered to be impaired concurrently in diabetic and alcoholic polyneuropathies.**

(Internal Medicine 41: 819–822, 2002)

Key words: CPT, SSR, C fiber, polyneuropathy, diabetes mellitus, alcoholism

Introduction

In the current perception threshold (CPT) examination, 5 Hz, 250 Hz, and 2,000 Hz stimulation has been considered to stimulate C fibers, A-δ fibers, and A-β fibers, respectively (1–6). The CPT examination has been reported to be useful for the detection, screening, diagnosis, and management of diseases of the peripheral nervous system (5, 7–9).

On the other hand, the sympathetic skin response (SSR) involves C fibers (10–13). Our hypothesis is that CPT to 5 Hz stimulation and SSR are impaired concurrently in diabetic and alcoholic polyneuropathies. In order to verify this hypothesis, we measured CPT and SSR in patients with diabetic or alcoholic polyneuropathy.

Materials and Methods

We studied 14 patients with diabetic polyneuropathy (mean age 51±6 years, 6 males, 8 females), 10 patients with alcoholic polyneuropathy (mean age 53±7 years, 8 males, 2 females) and 24 age-matched healthy controls (mean age 52±6 years, 14 males, 10 females) with their informed consent. We diagnosed polyneuropathy when a patient had glove and stocking type sensory disturbance and/or decreased nerve conduction velocities in the four extremities. We diagnosed diabetic polyneuropathy when a patient with polyneuropathy had diabetes mellitus and did not have other causes of polyneuropathy. We diagnosed alcoholic polyneuropathy when a patient with polyneuropathy had chronic alcoholism and did not have other causes of polyneuropathy. The patients who also had other neurological diseases were excluded.

All of the patients with diabetic or alcoholic polyneuropathy in the Neurology Clinic of the Nihon University Nerima Hikarigaoka Hospital were asked for informed consent. The mean value of hemoglobin A_{1C} in the diabetic polyneuropathy group was 8.4% and none of them received insulin therapy. The mean amount of alcohol consumption in the alcoholic polyneuropathy group was 97 ml pure alcohol equivalent per day for 23 years. Disturbance in pain and/or temperature senses was present in 57% in the diabetic polyneuropathy group and 50% in the alcoholic polyneuropathy group. Disturbance in touch sense was present in 86% in the diabetic polyneuropathy group and 80% in the alcoholic polyneuropathy group. Orthostatic hypotension (more than 20 mmHg decrease in systolic blood pressure and/or more than 10 mmHg decrease in diastolic blood pressure by standing from supine position) was present in 36% in the diabetic polyneuropathy group and 30% in the alcoholic polyneuropathy group.

We used the Neurometer® CPT/C (Neurotron Inc., Baltimore, MD, USA) to measure CPT (5). The device delivers sinusoidal electrical stimuli at frequencies of 5 Hz, 250 Hz, and

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Received for publication August 27, 2001; Accepted for publication June 13, 2002

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2,000 Hz. CPT was measured at the index fingers and near the external malleolus on both sides. Patients were asked to identify the presence or absence of the stimulus through a forced choice protocol. After an initial tentative threshold was determined, we gave stimuli that varied around the presumed threshold to confirm threshold stability and replicability. To prevent guessing, results were verified with placebo stimulation. The placebo stimulation was given by turning off all current without informing the subject and presenting absent stimuli. The threshold of perception was the measured response.

We examined SSR using Neuropack Σ (Nihon Kohden, Tokyo). Skin temperature was maintained at >32°C and the subjects were kept awake and relaxed. The light of the examining room was dimmed. Exploring electrodes were placed on bilateral palms and soles, and reference electrodes were placed on the back of the hand and the back of the foot. Electrical stimulation with the intensity of at least 20 mA was applied to the frontal head (bilateral supraorbital nerves) at irregular intervals and at a frequency of approximately 1/min to avoid habituation. Twenty recordings were stored and the recording with the largest amplitude was chosen for measurement (11). The latencies and amplitudes of sympathetic skin response to electrical stimulation were measured.

We measured the sensory nerve conduction velocity of the median nerve and the sural nerve on both sides. We examined the correlation between the nerve conduction velocity and the CPT or the amplitude of SSR in each limb.

Statistical analysis was performed using Mann-Whitney's U test for comparison among the three groups, using Spearman's correlation coefficients for correlation among the CPT, the amplitude of SSR, the nerve conduction velocity and the clinical symptoms, and using χ^2 test for comparison between the right-left difference in the appearance rate of SSR and the right-left difference in the clinical symptoms.

Results

Figure 1 shows actual records of the sympathetic skin response in a patient with diabetic polyneuropathy and a healthy control. The amplitude of sympathetic skin response was smaller in the patient with diabetic polyneuropathy than in the healthy control.

Table 1 shows the comparison among the diabetic polyneuropathy group, the alcoholic polyneuropathy group and the healthy control group. The CPT to 5 Hz stimulation and the CPT to 2,000 Hz stimulation were significantly higher in the diabetic polyneuropathy group and the alcoholic polyneuropathy group than in the healthy control group. The amplitude of SSR was significantly smaller in the diabetic polyneuropathy group and the alcoholic polyneuropathy group than in the healthy control group.

The appearance rate of SSR in the diabetic polyneuropathy

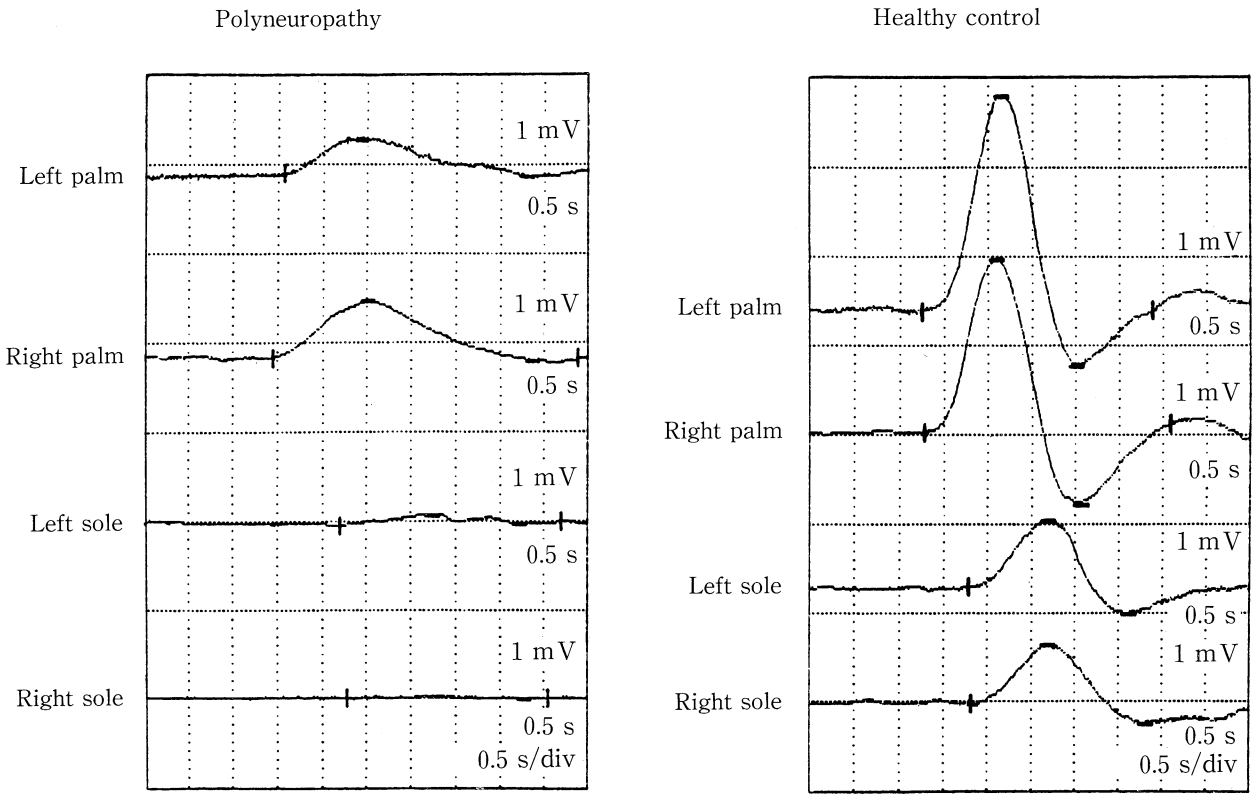

Figure 1. Actual records of sympathetic skin response in a patient with diabetic polyneuropathy and a healthy control.

Table 1. Mean and Standard Deviation of Current Perception Threshold (CPT) and Latency and Amplitude of Sympathetic Skin Response (SSR)

	CPT (CPT unit)			SSR	
	5 Hz	250 Hz	2,000 Hz	Latency (msec)	Amplitude (mV)
Diabetic polyneuropathy group					
Left hand	97±24*	107±26	371±60*	1,361±198	1.8±1.0*
Right hand	99±25*	109±29	346±71**	1,348±192	1.9±1.0*
Left foot	76±24*	80±26	319±53*	1,853±287	1.0±0.7*
Right foot	75±22*	78±25	316±55*	1,869±298	1.0±0.6*
Alcoholic polyneuropathy group					
Left hand	95±23*	104±25	343±58**	1,352±192	1.9±1.1*
Right hand	93±24*	105±28	338±64**	1,333±186	1.9±1.1*
Left foot	72±22*	79±23	308±54*	1,838±288	1.2±0.8*
Right foot	72±21*	75±25	309±52*	1,854±287	1.1±0.8*
Healthy control group					
Left hand	70±21	100±25	285±53	1,277±179	3.1±1.3
Right hand	72±23	103±28	294±59	1,290±185	2.9±1.2
Left foot	49±20	76±22	230±51	1,745±291	2.1±1.0
Right foot	48±21	74±24	233±50	1,721±273	2.0±0.9

*p<0.01 compared to the healthy control group. **p<0.05 compared to the healthy control group.

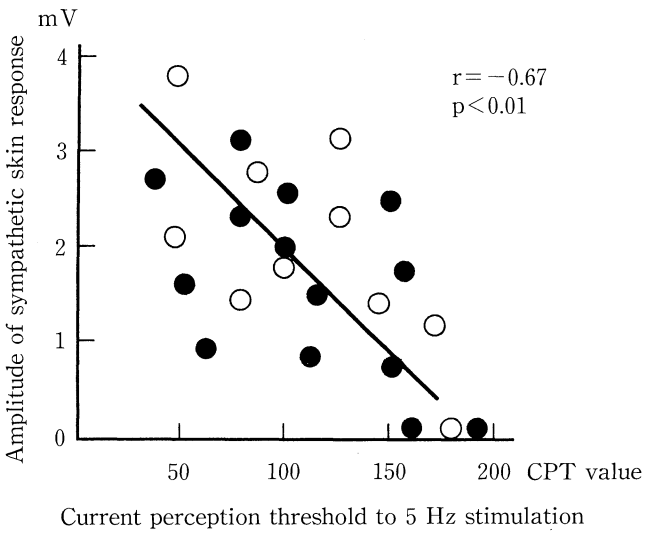

Figure 2. Correlation between current perception threshold (CPT) to 5 Hz stimulation and the amplitude of sympathetic skin response in the right hand in patients with diabetic or alcoholic polyneuropathy. Black circles indicate diabetic polyneuropathy (r=–0.65, p<0.01) and white circles indicate alcoholic polyneuropathy (r=–0.58, p<0.01).

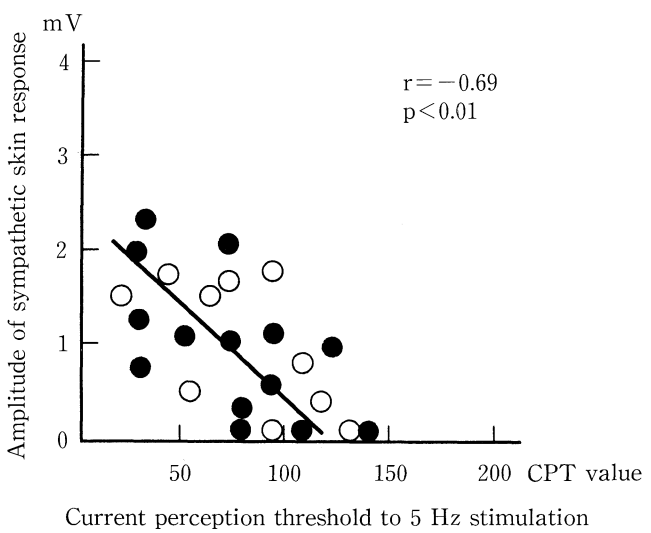

Figure 3. Correlation between current perception threshold (CPT) to 5 Hz stimulation and the amplitude of sympathetic skin response in the right foot in patients with diabetic or alcoholic polyneuropathy. Black circles indicate diabetic polyneuropathy (r=–0.66, p<0.01) and white circles indicate alcoholic polyneuropathy (r=–0.63, p<0.01).

group and the alcoholic polyneuropathy group was 79%, 80% in the left hand, 86%, 90% in the right hand, 71%, 70% in the left foot and 79%, 80% in the right foot, respectively. The appearance rate of SSR in the healthy control group was 100% in all the extremities. The appearance rate of SSR was significantly lower in the diabetic polyneuropathy group and the alcoholic polyneuropathy group than in the healthy control group.

Figure 2 shows the correlation between the CPT to 5 Hz stimulation and the amplitude of SSR in the right hand, and Fig. 3 shows the same correlation in the right foot in the dia-

betic polyneuropathy group and the alcoholic polyneuropathy group. There were significant negative correlations between the CPT to 5 Hz stimulation and the amplitude of SSR in all the extremities in the diabetic polyneuropathy group and the alcoholic polyneuropathy group. There were no significant correlations between the CPT to 250 Hz or 2,000 Hz stimulation and the amplitude of SSR in the diabetic polyneuropathy group and the alcoholic polyneuropathy group.

There were no significant correlations between the nerve conduction velocity and the CPT or the amplitude of SSR although the nerve conduction velocity showed a tendency to negatively correlate ($r=-0.42$, $p<0.1$) with the CPT to 2,000 Hz stimulation. There were no significant correlations between the CPT and the clinical symptoms although the CPT to 5 Hz stimulation showed a tendency to correlate ($r=0.38$, $p<0.1$) with the degree of the disturbance in pain and/or temperature senses in diabetic and alcoholic polyneuropathy groups. There were no significant correlations between the amplitude of SSR and the clinical symptoms although the SSR was absent in 3 out of 5 patients with orthostatic hypotension in the diabetic polyneuropathy group and in 2 out of 3 patients with orthostatic hypotension in the alcoholic polyneuropathy group. The right-left difference in the appearance rate of SSR did not show any significant correlation with the right-left difference in the clinical symptoms.

Discussion

The CPT examination has been reported to be useful in the detection of diabetic polyneuropathy and alcoholic polyneuropathy (1, 2, 7, 8).

The SSR has been used to assess the sympathetic sudomotor function (11, 14–19) and may be abnormal in diabetic polyneuropathy (19) and alcoholic polyneuropathy (14, 16, 17). The SSR was initially regarded as an all-or-none phenomenon but currently amplitude criteria have been defined since SSR techniques were refined (11). Therefore, the amplitude of SSR has been used to assess the sympathetic sudomotor function (11, 15–18) in addition to the appearance rate of SSR.

Peripheral small caliber fibers and C fibers may be involved in diabetic polyneuropathy and alcoholic polyneuropathy (14, 16, 19, 20). The significant negative correlation between the CPT to 5 Hz stimulation and the amplitude of SSR in the present study suggests that somatic C fibers and sympathetic C fibers may be impaired concurrently in diabetic and alcoholic polyneuropathies. We hope that these examinations will also be performed in other types of polyneuropathy.

In the present study, the nerve conduction velocity showed a tendency to negatively correlate with the CPT to 2,000 Hz stimulation. This may be related to the fact that both the nerve conduction velocity and the CPT to 2,000 Hz stimulation shows the function of Aβ fibers (1–6). Pain and temperature senses are related to somatic C fibers. In the present study, the CPT to 5 Hz stimulation showed a tendency to correlate with the degree of the disturbance in pain and/or temperature senses. A large number of patients should be examined to determine the significance of this correlation.

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