

Autonomic involvement in carpal tunnel syndrome – sympathetic skin response and skin temperature

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Abstract

Objective: Some studies found autonomic involvement in carpal tunnel syndrome (CTS). The purpose of this study is to investigate whether autonomic involvement is a consequence of the primary destruction of autonomic fibers or a response to sensory fibers' destruction as in complex regional pain syndrome type I.

Methods: Sympathetic skin response (SSR) and skin temperature measurements (STM) in the median and ulnar sides of both hands in 29 CTS patients (unilateral n=16) and the 23 healthy volunteers were recorded. CTS was categorized in three groups based on the results of electrophysiological tests.

Results: Mild CTS patients (n=28), moderate CTS patients (n=9), severe CTS patients (n=5) and control group (n=46) were evaluated. The temperature measurements of both the ulnar and the median sides in severe CTS patients were consistently higher than the others. The temperature of distal phalanx of the 2nd finger in patients with severe CTS were significantly higher than the control group and the mild CTS patients ($p<0.05$). Other temperature recordings, SSR latency or amplitude values did not present significant differences between groups ($p>0.05$).

Conclusion: Autonomic involvement in CTS may be speculated that the compression severe enough to result in permanent electrophysiological changes may lead to an irritation in A delta and C fibers that can trigger a reflex sympathetic response when it reaches a certain level of intensity. This hypothesis may also help explain the presence of positive autonomic findings such as increased temperature or hyperemia.

Keywords: Carpal tunnel syndrome, autonomic involvement, sympathetic skin response, skin temperature measurements

INTRODUCTION

Entrapment neuropathies have been described as rarely causing autonomic involvement and studies examining the incidence of autonomic involvement in carpal tunnel syndrome are relatively scarce in number (1-12). Contrary to some reports on the presence of autonomic involvement, others have failed to detect such involvement (2-12). Furthermore, it has not been fully elucidated whether autonomic impairment is primarily due to the injury of autonomic nerves or whether it actually represents a response to the injury inflicted upon the sensory nerves similar to the case with reflex sympathetic dystrophy (complex regional pain syndrome (CRPS) Type I).

On the other hand, sympathetic skin response (SSR) and skin temperature measurements are effective and simple means for assessing the sympathetic sudomotor activity (1, 13-16). In previous studies with CRPS patients, an altered sympathetic skin response has been reported to occur in approximately 58% to 62% of the patients (13, 14). In another study, the reported sensitivity and specificity of abnormal skin temperature measurements in patients with CRPS were 32 - 71% to 64 -100% (15, 16). In the study by Verghese et al., the corresponding figures for sensitivity and specificity were 34% and 89%, respectively (7).

This study was undertaken to assess whether the above-mentioned autonomic involvement is a consequence of the primary destruction of autonomic fibers or a response to sensory fibers' destruction as in complex regional pain syndrome (CRPS) type I.

You may cite this article as: Sorgun MH, Tugan Yıldız CB, Şener HÖ. autonomic involvement in carpal tunnel syndrome – sympathetic skin response and skin temperature. *Neurol Sci Neurophysiol* 2018; 35: 14-20.

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METHODS

Patients referred to the electrophysiology laboratory with a preliminary diagnosis of CTS with paresthesias associated with awakening in the night hours and relief with movements and who had either normal neurological findings or no other suggestion of another peripheral nervous system disorder other than CTS were diagnosed as having CTS and included in this study. Patients with polyneuropathy, plexopathy, or radiculopathy were excluded. Also excluded were patients who had systemic conditions associated with polyneuropathy or mononeuritis.

Control subjects consisted of consenting healthy volunteers or patients who were referred to the EMG laboratory with a pre-diagnosis of lumbar disk herniation with no complaints involving the upper extremities, history and examination suggesting polyneuropathy or systemic diseases (Diabetes mellitus, rheumatic diseases, hypothyroidism, sarcoidosis, amyloidosis, multiple myeloma) that may result in peripheral nervous system complications.

The age, gender, CTS symptoms, and neurological examination results were recorded in all patients.

The study procedures were commenced after ethics committee approval and obtainment of written informed consent from patients.

Prior to electrophysiological studies, all patients were kept in a room with a controlled temperature of approximately 22 to 24°C for 15 minutes after which surface temperature measurements were performed and recorded using an infrared temperature measurement device (Exergen Dermatemp Infrared Temperature Scanner®) in both hands at the distal phalanx of the 2nd finger (DF2), metacarpophalangeal joint of the 2nd finger (MCF2), distal phalanx of the 5th finger (DF5), and metacarpophalangeal joint of the 5th finger (MCF5).

The temperature of the extremities was kept at a minimum of 32°C using the infrared heater as long as required for study purposes.

Electrophysiological tests were performed using a 4-channel electromyography device (Keypoint; Medtronic, Skovlunde, Denmark) with the patient in supine position, and the forearm in extension and supination. All stimulations and recordings were performed using superficial electrodes, which were attached with electrode gel after cleansing the skin with alcohol swabs to reduce the skin resistance.

The wrist was attached to ground electrodes and superficial electrodes were used for sympathetic skin recordings. An active electrode was placed on the thenar eminences of the hands for median SSR and hypothenar eminences of the hands for ulnar SSR on the volar surface of both hands and reference

electrodes were placed on the dorsal surface of the hand, just behind the active electrodes, 4 - channel sympathetic skin test recording was performed with an instant suprasternal electrical stimulus. Impedances of active and reference electrodes were below 5 kV. Frequency limits were 0.5 Hz to 2 kHz. A rectangular, 0.1 ms duration electrical pulse at an intensity of 48±50 mA was applied to the skin over the sternal body and the analysis time was 10 s. The amplitude and latency of the potentials obtained with SSR test were recorded (17).

Carpal tunnel syndrome was empirically categorized in three groups based on the electrophysiological findings: Group I, mild CTS with median motor latency <4.4 msec, and median sensory conduction velocity >44 m/sec; Group II, moderate CTS with a median motor latency of 4.4 to 5.5 msec and/or median sensory conduction velocity 44 - 40 m/sec; and Group III, severe CTS with a median motor latency >5.5 msec and / or median sensory conduction velocity <40 m/sec.

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 16.0 version (SPSS Inc.; Chicago, IL, USA). Descriptive statistics were expressed as means / standard deviations for normally-distributed continuous variables and median/interquartile range for non-normally distributed variables. For data analysis chi-square, Student's t test, Wilcoxon Signed Ranks Test, and Kruskal Wallis test were used. P<0.05 was considered to be statistically significant.

RESULTS

Of the 29 CTS patients, 16 had unilateral and 13 had bilateral CTS. Electrophysiological tests were performed in 46 arms of 23 healthy volunteers, and in 42 symptomatic arms of 29 CTS patients. The mean age of controls and patients was 46.4±8.4 and 42.4±10.5 years, respectively (p=0.291). There were 26 female and 3 males in the CTS group, and 19 female and 4 male participants among the controls (p=0.444).

The recorded temperatures and sympathetic skin response data were assessed and analyzed among controls (n=46), and among those with mild (n=28), moderate (n=9), or severe (n=5) CTS. A comparison between control subjects and those with CTS was carried out in terms of the temperature measurements at DF2, DF5, MCF2 and MCF5. Temperatures at DF2 were significantly higher among severe CTS patients as compared to controls and those with mild CTS (p=0.015 and p=0.042, respectively). The other differences in temperature recordings were not significantly different (p>0.05) (Table 1).

In patients with unilateral CTS, the data recorded in the involved side were compared with those in the intact side. There were no significant differences between DF5 and DF2 and between MCF5 and MCF2 between the two sides (p>0.05). Again, no significant differences in DF2 and MCF2 were found between the intact and diseased hands (p>0.05) (Table 2).

Table 1. Temperature measurements in patients with CTS and in controls (°C; mean±SD)

	Controls n=46	CTS			
		Mild n=28	Moderate n=9	Severe n=5	All n=42
DF2	32.6±1.7	31.5±2.3	32.0±3.5	34.1±0.4 *p=0.015 **p=0.042	31.9±2.6
MCF2	33.0±1.7	31.8±2.4	32.7±1.9	32.3±2.2	34.1±0.8
DF5	32.3±2.1	31.0±2.5	31.6±3.2	32.9±1.0	31.3±2.5
MCF5	32.8±1.9	31.7±2.6	32.6±2.1	34.0±0.5	32.2±2.5

SD: standard deviation; DF2: distal phalanx of the 2nd finger; MCF2: metacarpophalangeal joint of the 2nd finger; DF5: distal phalanx of the 5th finger; MCF5: metacarpophalangeal joint of the 5th finger; *p: severe CTS patients as compared to controls;

**p: severe CTS patients as compared to mild CTS

Table 2. Temperature measurements in the affected and intact hands in patients with unilateral CTS (°C; mean±SD)

	Intact n=16	CTS			
		Mild n=10	Moderate n=4	Severe n=2	All n=16
DF2	32.5±2.3	32.0±2.4	32.6±2.3	34.3±0.3	32.4±2.3
MCF2	32.9±1.7	32.4±1.8	33.2±1.2	34.3±0.7	32.8±1.7
DF5	32.2±2.3	31.6±2.9	33.0±1.9	33.1±0.2	32.1±2.5
MCF5	32.9±1.6	32.5±2.2	33.1±1.5	34.1±0.6	32.8±2.0

SD: standard deviation; DF2: distal phalanx of the 2nd finger; MCF2: metacarpophalangeal joint of the 2nd finger; DF5: distal phalanx of the 5th finger; MCF5: metacarpophalangeal joint of the 5th finger

Table 3. SSR values in CTS patients and in controls

	Controls n=46	CTS			
		Mild n=28	Moderate n=9	Severe n=5	All n=42
Median nerve					
SSR latency, ms ±SD	1.7±6.5	1.6±2.1	1.4±3.1	1.5±1.2	1.5±2.4
SSR amplitude, mV±SD	1.2±0.9	1.4±1.3	2.2±2.0	1.8±0.6	1.6±1.4
Ulnar nerve					
SSR latency, ms ±SD	1.7±6.9	1.6±1.9	1.4±3.4	1.5±1.4	1.6±2.4
SSR amplitude, mV±SD	1.2±1.1	1.3±1.0	2.4±2.4	1.5±0.6	1.6±1.4

SSR: sympathetic skin response; SD: standard deviation

SSR latency and amplitude values did not differ significantly between hands with CTS and hands of control subjects ($p>0.05$) (Table 3).

In patients with unilateral CTS, the sympathetic skin test results in the diseased and intact hands were similar ($p>0.05$) (Table 4).

DISCUSSION

The objective of the current study was to examine whether the autonomic involvement in CTS is a primary or a second-

ary phenomenon. For this purpose, median and ulnar side temperature measurements as well as the latency and amplitude values of SSR potentials were assessed in 46 arms of 23 healthy volunteers and in 42 symptomatic arms of 29 CTS patients. No significant differences were found between the median and ulnar side of the involved hands in CTS patients, and between the healthy and involved sides in CTS patients. In patients with severe CTS, DF2 temperature was significantly higher than in controls as well as mild CTS patients ($p=0.015$ and 0.042 , respectively). Moreover, there was an increase in both ulnar and median skin tempera-

Table 4. SSR values in the affected and intact hands in patients with unilateral CTS

	Intact n=16	CTS			All n=16
		Mild n=10	Moderate n=4	Severe n=2	
Median nerve					
SSR latency, ms \pm SD	1.5 \pm 2.3	1.5 \pm 2.5	1.6 \pm 1.1	1.6 \pm 0.4	1.5 \pm 2.4
SSR amplitude, mV \pm SD	1.0 \pm 0.8	0.8 \pm 0.7	1.3 \pm 1.0	1.3 \pm 0.9	1.0 \pm 0.8
Ulnar nerve					
SSR latency, ms \pm SD	1.6 \pm 1.4	1.5 \pm 1.9	1.6 \pm 0.8	1.6 \pm 1.8	1.6 \pm 1.6
SSR amplitude, mV \pm SD	1.2 \pm 0.9	1.1 \pm 0.9	1.4 \pm 1.3	1.0 \pm 0.7	1.1 \pm 0.9

SSR: sympathetic skin response; SD: standard deviation

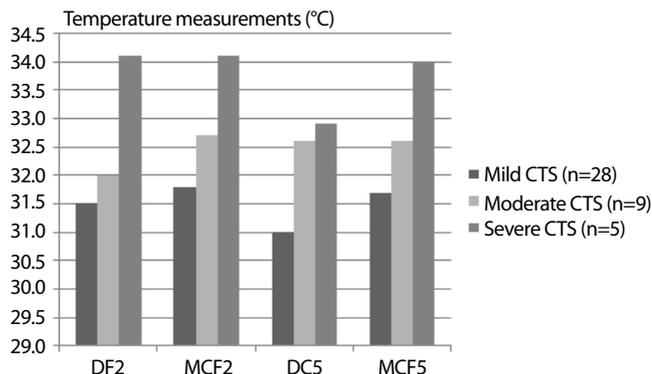
Table 5. Studies examining the autonomic involvement in CTS

References	Patients (hands)/controls(hand), no.	Methodology	Result
Aminoff MJ (2)	13/3	Plethysmography Inspiratory vasoconstrictor reflex	Abnormal Abnormal
Jordan et al. (3)	46 CTS, 32 controls	Galvanic skin response Temperature measurement	Normal
Caccia et al. (4)	21 bilateral CTS, 16 unilateral CTS	SSR area SSR amplitude and latency	Abnormal Normal
Reddeppa et al. (5)	30 CTS, 30 healthy controls	SSR area SSR amplitude and latency	Abnormal Normal
Sener et al. (6)	21 CTS, 21 healthy controls	SSR area and amplitude SSR latency	Normal Normal
Ming et al. (8)	30 CTS (38), 22 controls (41)	digital infrared termography Temperature	Abnormal Abnormal
Orlin et al. (9)	13 CTS, 10 controls	Photoplethysmography laser doppler termography	Abnormal Abnormal Abnormal
Argyriou et al. (10)	30 CTS (46), 31 severe, 15 mild/moderate	SSR latency SSR amplitude	Normal Normal
Bayrak et al. (11)	31 CTS (51), 25 controls (50)	SSR area, amplitude, latency Motor Unit Number Estimation	Normal Normal
Zyluk et al. (12)	53 unilateral CTS	Capilleroscopy SSR latency, area, amplitude	Normal Normal

tures of all severe CTS patients as compared to the milder patients'. Although the difference did not reached a statistically significance except in DF2, it is consistent for every severe CTS patient. This finding suggests that the autonomic involvement is not restricted to a single nerve territory, but regional instead.

The autonomic involvement in entrapment neuropathies have not been a major focus of attention and consequently only few studies have examined the autonomic involvement in patients with carpal tunnel syndrome (2-12). These studies utilized different methodologies to examine the autonomic involvement. Abnormalities have been detected

using a variety of methods including plethysmography, inspiratory vasoconstrictor reflex, or laser Doppler. In studies utilizing capilleroscopy, no abnormalities were observed. In another study, galvanic skin response was found to be normal. There are three studies examining the skin temperature in CTS. Of these, two reported colder hands in CTS patients than in healthy individuals. The most frequent method to examine the autonomic involvement in CTS was SSR analysis. In a total of six studies comparing SSR latency, amplitude or areas between diseased or intact hands or healthy controls, only two reported a smaller SSR area in CTS patients, while latency and amplitude values were normal in these two studies (2-12) (Table 5).

Figure 1. Changes in hand temperature measurements by CTS severity

DF2: distal phalanx of the 2nd finger; MCF2: metacarpophalangeal joint of the 2nd finger; DC5: distal phalanx of the 5th finger; MCF5: metacarpophalangeal joint of the 5th finger; CTS: carpal tunnel syndrome

In a study by Aminoff, 13 CTS patients with normal routine nerve conduction tests, vasoconstrictor reflexes were tested using pletysmography, with only 5 patients exhibiting normal responses (2). It has been proposed that the trapping effect on the median nerve at the level of wrist could have an impact on sympathetic efferent fibers (2).

Caccia et al. examined SSR responses in a total of 21 patients with bilateral and 16 patients with unilateral CTS (4). Both groups exhibited a decrease in SSR areas. In patients with unilateral CTS, a decreased SSR area was also found in the intact side, which was explained on the basis of the involvement of the efferent pathways in the autonomic reflex (4).

In the study by Reddeppa et al. the latency, area, and amplitude of SSR potentials were compared between 30 patients with CTS (21 bilateral, 9 unilateral) and 30 healthy controls (5). No SSR potentials could be obtained in 7 patients with bilateral CTS. The comparison between CTS patients and controls showed no significant differences in SSR latency or amplitude between CTS patients and controls. However, there was a significant decrease in SSR potential areas in 23 hands with CTS, where an SSR potential could be elicited. In patients with unilateral CTS, no comparison with the intact side was performed and only controls were compared (5).

In their study involving 21 patients with CTS and 21 healthy controls, Sener et al. found no differences in terms of the sympathetic skin response between the two groups (6).

Verghese et al. found autonomic involvement in 76 (55%) extremities from 47 patients, among a total of 139 extremities in 76 CTS patients (7). The types of involvement included sweating in the fingers (59%), dry hands (39%), Raynaud's phenomenon (33%), and blanching of the hand (32%). The reported sensitivity and specificity for SSR abnormality among hands with autonomic involvement were 38% and 89%, respectively, and the severity of the autonomic involvement correlated

with female gender, as well as the severity of the SSR abnormality and EMG results (7).

Argyriou et al. examined 46 hands in a total of 30 patients with idiopathic CTS and 30 healthy hands as controls (10). Of these patients, 31 had severe and 15 had mild to moderate CTS. These authors detected a higher sympathetic system score (i.e. red or purple discoloration, excessive sweating, dry hands, Raynaud's phenomenon, and swelling of the fingers) in hands with severe CTS. On the other hand, SSR latency and amplitude did not differ significantly between controls, severe CTS patients, and mild to moderate CTS patients. These authors concluded that SSR is not a sensitive marker for the autonomic involvement in CTS (10).

Bayrak et al. compared 31 patients diagnosed with CTS based on clinical and electrophysiological studies with 25 healthy controls and found no associations between sympathetic skin response, sympathetic symptom score, and electrophysiological findings (11).

In the study by Zyluk et al. SSR and capillaroscopy were performed in 53 patients with unilateral CTS who were diagnosed clinically and electrophysiologically (12). In that study, the CTS sensory conduction velocity was categorized into three groups based on the nervous conduction velocity and amplitude: mild, moderate and severe CTS. There were no significant differences between the intact or involved hands in terms of SSR or capillaroscopy parameters (12).

Jordan and Greider observed increased index finger temperatures in 6 patients describing sympathetic symptoms among a group of 46 CTS patients (3).

Ming et al., using digital infrared thermography measurements, took infrared photographs of 38 hands from 30 CTS patients and 41 hands from 22 healthy individuals (8). A significantly lower temperature was found in the median innervation zone than in ulnar innervation zone in hands with CTS. These authors proposed that one component of the carpal tunnel syndrome may involve a sympathetic nervous system pathology and that digital infrared thermography may represent a feasible and non-invasive method that may be particularly useful in the diagnosis of early CTS (8). Although significant decreases in the involved side were noted, no comparisons taking the severity of CTS into account were performed. In our study, temperatures were lower in the CTS group than in controls, although the differences did not reach statistical significance.

Orlin et al. utilized photoplethysmography and laser Doppler techniques to assess the sympathetic nervous activity as well as temperatures (9). Provocation tests were done to irritate the autonomic fibers of the median nerve within the carpal tunnel for temperature and skin perfusion assessments in 13

patients with CTS and 10 healthy controls. At the end of the study, these authors observed decreased skin temperature and increased sweating, even in those with normal electrophysiological findings, and found no difference between the two groups with respect to skin perfusion. They concluded that sympathetic fibers of the nerve were sensitive even to minor compression, and suggested that use of thermography may be a valuable diagnostic tool even in the early stages of the disease by demonstrating the presence autonomic dysfunction (9). Similar to the study by Ming et al., comparisons did not account for the differences in the severity of CTS (8). However, among all these studies, only three involved median and ulnar nerve comparisons (6, 8, 10). Similar to our findings, no SSR differences were found, and Ming et al. observed lower temperatures in hands with CTS both at the ulnar and median sides (8).

CTS patients in this study have relatively milder disease and the electrophysiological classification was based on demyelination criteria such as prolonged latency and decreased velocity. In contrast with the general characteristics of CRPS, CTS of this severity involves a relatively milder nerve tissue trauma. Therefore, although the disease is considered severe on the basis of electrophysiological criteria, the severity of the nervous injury is of a lesser degree as compared to an actual nervous injury. In this disease severity, positive autonomic signs such as increased temperature are likely, whereas in more severe CTS accompanied with severe axonal involvement and atrophy, reduced temperature may be expected. This possibility may be evaluated in further studies.

Autonomic involvement in entrapment neuropathy is a rare occurrence. Only after a certain level of nervous compression, the tiny fibers may be affected following the injury to the sensory-motor fibers with thick myelin layer. Due to the direct involvement of the sympathetic nerves, an autonomic dysfunction occurs restricted to the peripheral nervous zone (18).

On the other hand, when the extent of the peripheral nervous injury exceeds the innervation zone of that specific peripheral nerve, this may be explained on the basis of the pathogenesis of CRPS. With the peripheral nervous injury, the neuropathic pain process is triggered. After the peripheral sensitization, a maladaptive sensitization in the posterior horn and in more central areas lead to the involvement of an area that extends beyond the territory of the peripheral nerve, resulting to reflex sympathetic hyperactivity (14-16, 19). Although the pathophysiology of the CRPS has not been clearly understood, several mechanisms are thought to be involved including peripheral and central mechanisms as well as neurogenic inflammation and microvascular dysfunction (14-16, 19).

Previous studies utilized SSR and skin temperature measurements for the assessment of CRPS. Of the patients with CRPS, 58% to 62% have been found to have sympathetic skin involvement (13, 14). Again, in these patients the sensitivity and specificity of the skin temperature abnormality were 32% to 71% and 64% to 100%, respectively (15, 16).

Previous studies conducted to test the sympathetic nervous system involvement in patients with CTS utilized a variety of different methodologies with divergent results. Even in studies utilizing the same methodology, it was noted that these studies did not provide same testing condition in terms of the surface temperature of the hands or they did not provide information on these conditions, probably accounting for the observed differences in results (2-12). In three studies, patients with CTS were categorized on the basis of clinical and electrophysiological findings (10-12). However, only a single study provided a comparison between controls and CTS patients with mild, moderate, or severe disease (12).

Although change in surface temperature appears to provide specific information, the sensitivity of thermographic measurements is low. Again, despite the efforts to maintain a stable ambient temperature and despite the fact that patients were kept in a temperature-controlled room prior to testing, the effect of the changes in the body temperature may complicate the detection of temperature changes in the skin.

Another noteworthy observation of our study was the detection of higher hand temperatures in the affected hand in patients with unilateral moderate CTS, although the differences were not statistically significant. Based on this information, it may be speculated that the compression severe enough to result in permanent electrophysiological changes may lead to an irritation in A delta and C fibers that can trigger a reflex sympathetic response when it reaches a certain level of intensity. This hypothesis may also help explain the presence of certain positive autonomic findings such as increased temperature or hyperemia in CTS or certain other entrapment neuropathies. Further support for this hypothesis is provided by the fact that the change in both median and ulnar sensory zones occurs consistently in the same direction.

Although the differences which suggest a regional autonomic disorder in severe CTS patients are quite consistent the most important limitation of our study is the small number of these patients.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara University School of Medicine (119-3196).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.Ö.S., C.B.T.Y.; Design - Ö.H.S.; Supervision - Ö.H.S.; Resources - H.Ö.S.; Materials - C.B.T.Y., M.H.S.; Data Collection and/or Processing - C.B.T.Y., M.H.S.; Analysis and/or Interpretation - M.H.S.; Literature Search - M.H.S.; Writing Manuscript - M.H.S., C.B.T.Y.; Critical Review - H.Ö.S., M.H.S.; Other - H.Ö.S., M.H.S., C.B.T.Y.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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