June 2004

The Influence of Stimulation Point and Regional Body Temperature of Segmental Nerve Conduction Velocity of the Median and Ulnar Nerves in Health Subjects and Subjects with Carpal Tunnel Syndrome

Marc Steven Croteau

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THE INFLUENCE OF STIMULATION POINT AND REGIONAL BODY TEMPERATURE ON SEGMENTAL NERVE CONDUCTION VELOCITY OF THE MEDIAN AND ULNAR NERVES IN HEALTHY SUBJECTS AND SUBJECTS WITH CARPAL TUNNEL SYNDROME

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A Thesis
Submitted in Partial Fulfillment of the
Requirements for the Degree of
Master of Public Health
at the
University of Connecticut
2004
MASTER OF PUBLIC HEALTH THESIS

THE INFLUENCE OF STIMULATION POINT AND REGIONAL BODY TEMPERATURE ON SEGMENTAL NERVE CONDUCTION VELOCITY OF THE MEDIAN AND ULNAR NERVES IN HEALTHY SUBJECTS AND SUBJECTS WITH CARPAL TUNNEL SYNDROME

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Acknowledgments

This study was funded by a grant from the Harvard-NIOSH Education and Research Center Pilot Projects Research Training Program. I wish to thank David Christiani, M.D., M.P.H., M.S. and Ann Backus, M.S. for their assistance and support.

I am truly grateful to the members of The Lowell P. Weicker, Jr. General Clinical Research Center at the University of Connecticut Health Center for their tireless efforts and support. In particular, I wish to thank Priscilla Adler, Israel Cordero, Jill Zimmerman, and Joanne Lamothe for their valuable assistance.

I wish to especially thank Ulysses Diva, M.S. for his indispensable contributions and biostatistical analysis.

I am most grateful to Martin Cherniack, M.D., M.P.H. for his ongoing mentoring and direction. His creative energy is infectious. I also wish to thank Donald Peterson, PhD., for his technical guidance and support throughout this project. Finally, I wish to express my gratitude to Tim Morse, PhD., for his unwavering support and advice.

This investigation was made possible by Grant No. T42/CCT122961-01 from NIOSH. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NIOSH.
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Introduction: A Public Health Perspective

Work related musculoskeletal disorders represent the most commonly reported category of occupational disorders in the United States (Herbert, 2000). These disorders encompass over 60% of occupational illness reported to the United States Bureau of Labor Statistics (Bernard). According to the National Institute for Occupational Safety and Health (NIOSH), musculoskeletal disorders account for more than $2.1 billion in worker's compensation costs and 90 million dollars in indirect costs annually (NIOSH).

Musculoskeletal disorders made up 50% to 60% of occupational disease cases reported in the State of Connecticut for the year 2000. There were 3,827 cases reported to the CT Bureau of Labor Statistics, and 2,075 cases reported to Connecticut Worker's Compensation Commission. These figures are even more striking when one considers the well recognized underreporting associated with worker's compensation claims. For instance, capture-recapture analysis of upper extremity work related musculoskeletal disorders in Connecticut for 1995 estimates underreporting by a factor of 11:1 (Morse, 2001). Twenty-seven per cent of cases, numbering 568, reported to the CT Worker's Compensation Commission were classified as Carpal Tunnel Syndrome [CTS] (Morse, 2002). CTS is exceptionally costly when compared to other disorders. The median number of days that employees miss work
due to occupational injury and illness is regarded as a measure of the cost and severity of disease. The United States Department of Labor reports that among major disabling workplace injuries and illnesses in 1999, Carpal Tunnel Syndrome was associated with the highest median number of days away from work (BLS).

Case definition is a key starting point in determining prevalence rates, natural history, treatment outcomes, and causality in Carpal Tunnel Syndrome. However, despite its public health importance, Carpal Tunnel Syndrome has no universally accepted diagnostic clinical and laboratory criteria (Verdugo, 2004). Some studies have employed case definitions based upon a variety of symptoms and physical exam findings, others have applied various nerve conduction test findings, and others have combined a range of clinical and nerve conduction criteria (Rempel, 1998). As a result, interpreting the epidemiology of Carpal Tunnel Syndrome is encumbered by dissimilar case definitions amongst various studies. Furthermore, even with uniform case definitions, results from epidemiological studies are subject to spectrum bias (also known as case-mix bias). It is difficult to measure disease severity in a uniform way. For instance, electrophysiological test results do not correlate well with disease severity. Cohorts in different studies, therefore, may not represent the same disease spectrum. Again, this imprecision makes it difficult to assess natural history and treatment outcomes.
Background prevalence rates in a general population provide an important foundation for identifying disease causality. Unfortunately, background prevalence rates of carpal tunnel syndrome in the general population are not fully defined. In 1999, Atroshi, et al., presented a well-designed study of background prevalence that merits a detailed review. He investigated population prevalence rates in a region in southern Sweden. A survey was sent to 3000 randomly selected subjects, stratified by age and gender. A response rate of 83% (n=2466; 46% male) was achieved. Of the 2466 responders, 354 (14.4%) reported pain, numbness, and/or tingling in the median nerve distribution of the hands. Eighty-one percent (n=287) of the symptomatic responders underwent clinical examination. Thirteen subjects were excluded because of previous Carpal Tunnel Syndrome surgery, and two refused further testing. These exclusions may have served to underestimate prevalence. Clinical and electrophysiological exams were completed on 262 symptomatic subjects (35% males, mean age 52, SD 13 years). The authors then analyzed the data under a number of different case definitions. "Clinically certain carpal tunnel syndrome" was defined as the presence of recurring nocturnal and/or activity-related numbness and/or tingling involving the palmar aspects of at least two of digits I-IV. This definition usually included a positive Tinel's sign at the wrist and/or Phalen's test. Ninety-four symptomatic responders (3.8%; 95%CI 3.1%-4.6%) met the definition of clinically certain carpal tunnel syndrome. The
electrophysiological criterion used for the diagnosis of median neuropathy was a median-ulnar latency difference of 0.8 milliseconds or longer. Most authors use a 0.5 millisecond latency difference. Although a 0.8 millisecond difference represents a strict electrophysiological criterion, limbs were warmed only if skin temperatures were less than 30°C and details regarding temperature data were not reported. The prevalence of electrophysiological criteria coupled with less specific symptoms (e.g., whole hand numbness) was 4.9% (95% CI of 4.1%-5.8%). The prevalence of subjects who met both specific clinical criteria and electrophysiological criteria was 2.7% (95% Confidence Interval, 2.1%-3.4%). 3.5% of blue collar workers versus 1.7% of white collar workers met strict clinical and electrophysiological criteria. Importantly, eighteen percent (23/125) of asymptomatic controls also met electrophysiological criteria (Atroshi, 1999). This last finding has a number of implications that will be discussed further below.

Spontaneous improvements in cases of untreated carpal tunnel syndrome have been demonstrated. (Padua, 2001). In fact, incidence rates of carpal tunnel syndrome in individuals seeking care seem much lower than expected based upon the prevalence rates reported by Atroshi, et. al.. For instance, Stevens and his colleagues report an age adjusted incidence rate of 125 per 100,000 person-years from 1976 to 1980 in patients seeking care in Rochester, Minnesota (Stevens, 1988).
A number of occupational exposures are associated with an increased risk of developing carpal tunnel syndrome. Personal risk factors such as gender, obesity, and medical conditions may increase susceptibility. Epidemiologic surveillance data consistently demonstrate the highest rates of carpal tunnel syndrome among workers with high demands for intensive manual exertion (Bernard). For instance, an incidence rate of 2,570 cases per 100,000 full time equivalents has been reported in workers packing seafood (Franklin, 1984). Work demands strongly associated with carpal tunnel syndrome include forceful repetitive work and use of pneumatic tools (Silverstein, 1987). In fact, the strongest biodynamic exposure associated with carpal tunnel syndrome is vibration from use of pneumatic tools (MacKinnon, 2002). Importantly, exposure to vibratory tools can also cause a number of concurrent pathological conditions including disease within the digital nerves (Brammer, 1987; Stomberg, 1999). When evaluating symptoms related to exposure to significant low frequency vibration, it can be difficult to distinguish carpal tunnel syndrome from neurological disease within the digits (Cherniack, 1990). Therefore, carpal tunnel surgery in the context of hand-vibration syndrome should be approached with caution as outcomes may be sub-optimal. The evidence indicates that patients with carpal tunnel syndrome in the context of vibration exposure are more likely to have residual post-surgical symptoms. (Hagberg, 1991; Rosenbaum, 2002). Job functions associated with high exposure to vibratory tools include rock
drilling, grinding, and use of chainsaws. Occupations associated with high rates of carpal tunnel syndrome include meatpacking, poultry processing, automobile manufacturing, logging, rock drilling, and others (Bernard). A comprehensive review of the epidemiology of carpal tunnel syndrome and workplace exposures can be found at www.cdc.gov/niosh/pdfs/97-141.pdf (Bernard).

Carpal Tunnel Syndrome: A Clinical Perspective

Carpal tunnel syndrome is thought to result from compression of the median nerve within the carpal canal. It typically presents with numbness, tingling and discomfort in the hand. These symptoms are usually worsened by sleep, gripping, and forceful repetitive action of the hand or wrist and relieved by shaking the hand or changing posture. Absence of night symptoms should call the diagnosis into question (Oh, 2003). Sensory symptoms are characteristically distributed along the median nerve within the hand involving the palmar aspect of the thumb, index, long finger, and ring finger to a variable extent. Many patients have difficulty localizing symptoms and describe numbness and tingling within the whole hand. A minority of patients also describe proximal spread of symptoms into the forearm (Stevens, 1999). Motor involvement resulting in weakness and atrophy of the thenar muscles is usually a later finding.
Early symptoms of carpal tunnel syndrome may manifest from ectopic discharges of median nerve impulses and not slowed conduction as is commonly believed (Rosenbaum, 2002). As carpal tunnel syndrome progresses, distortion of myelin typically occurs followed by axonal disruption. It should be noted that the median nerve is a mixed nerve. It consists of sensory and motor fibers, as well as myelinated and unmyelinated fibers. Non-myelinated small fibers appear relatively resistant to compression (Lundborg, 1996). The occurrence of small fiber disease in carpal tunnel syndrome may represent a late finding, or it may represent concurrent disease. Sensory modalities that are mediated by myelinated large fibers include position sense, vibration sensation, and light touch (Wilbourn, 2002). Autonomic modalities, cold sensation, warm sensation, and pain induced by cold or hot temperatures are mediated by unmyelinated small fibers (Rosenbaum, 2002).

Although confirmatory neurodiagnostic studies are often performed, the diagnosis of carpal tunnel syndrome rests upon clinical criteria. Abnormal nerve conduction studies are more likely in patients with longer duration of symptoms, perhaps reflecting demyelination. However, abnormal studies alone do not prove that the patient's symptoms are due to carpal tunnel syndrome. Slowed nerve conduction across the carpal segment of the median nerve has been demonstrated in normal asymptomatic populations (Atroshi, 1999; Redmond, 1988; Werner, 1997). Poor case selection increases
the likelihood of false positive nerve conduction findings. Over reliance on these findings may lead to inappropriate intervention and poor outcomes.

Carpal Tunnel Syndrome and Neurodiagnostic Tests

Nerve conduction studies assess large myelinated fibers. Sensory nerve conduction test results reflect only the fastest conducting fibers. Latencies and conduction velocities provide no information regarding the number of fibers conducting impulses. Only a minority of myelinated sensory fibers need to function in order to yield normal sensory conduction tests. Therefore, the identification of focal slowing requires that virtually all of the large myelinated fibers which conduct impulses must be involved at the lesion site. If some axons conduct normally through the “damaged area,” then their rates of conduction will determine the test results (Rosenbaum, 2002; Wilbourn, 2002). In addition, the recording site and the stimulation point must bracket the lesion (Wilbourn, 2002).

It should also be noted that sensory conduction studies do not reflect the most distal segments of sensory nerves or sensory receptors even though abnormalities may be limited to those segments of the nerve (Wilbourn, 2002). For instance, damaged Pacinian corpuscles cannot be identified through nerve conduction studies, even though vibration sensation is a modality transmitted by myelinated fibers. Moreover, nerve conduction studies do not identify small fiber disease.
Motor function is also mediated through myelinated fibers. Nerve conduction studies can identify motor dysfunction. However, sensory nerve conduction studies are typically more sensitive than motor conduction studies for conditions involving demyelination such as Carpal Tunnel Syndrome (Wilbourn, 2002).

As already stated, there exists no diagnostic gold standard for Carpal Tunnel Syndrome. Rempel et. al., have published consensus criteria for the classification of Carpal Tunnel Syndrome in epidemiological studies. However, the guidelines for case definitions in epidemiological studies vary depending upon each study’s objectives. “Epidemiological case definitions” are not intended for clinical diagnosis and may range in sensitivity and specificity (Rempel, 1998).

The specificity of nerve conduction tests rests, in part, upon careful case definition. Accordingly, nerve conduction tests must be interpreted within the applicable context in order to avoid misclassification of disease. A study by Gupta and Benstead illustrates this point. In this study, inclusion criteria consisted of nonspecific symptoms of numbness and tingling involving the hand, or pain in the hand or wrist, or weakness in the median nerve distribution. Diagnosis of Carpal tunnel Syndrome was based exclusively upon electrodiagnostic criteria irrespective of symptom distribution. All subjects underwent comprehensive electrophysiological studies of their upper extremities. All cases that met electrodiagnostic criteria for “Carpal Tunnel
 Syndrome” exclusive of other upper extremity electrodiagnostic findings were then analyzed for symptom distribution. As illustrated in Figure 1, over 60% of these electrodiagnostically defined cases had paresthesias outside of the median nerve distribution. This study demonstrates the importance of accurate case definition when interpreting nerve conduction studies. Coupling nonspecific symptoms with nerve conduction tests leads to misleading results. Nerve conduction results that reveal slowed conduction in the median nerve at the wrist do not prove that the symptoms are caused by the conduction delay.

Figure 1: Distribution of Symptoms Based upon Nerve Conduction Test Results

![Pie chart showing distribution of symptoms](image)

Figure 1: Distribution of Symptoms in Subjects Meeting EDX of CTS (Adapted from Gutpa SK, 1997; Rosenbaum, 2002)

The sensitivity and specificity of nerve conduction tests depend upon a number of considerations. A major limitation in determining the sensitivity and specificity of nerve conduction studies in carpal tunnel syndrome is the lack of standardized diagnostic criteria in carpal tunnel syndrome
compounded by a wide disease spectrum in severity. Neurodiagnostic criteria may be adjusted to make testing more sensitive, often in attempts to diagnosis carpal tunnel syndrome earlier in the course of disease. However, because of biological variability in healthy populations, higher sensitivity results in greater overlap between healthy subjects and subjects with carpal tunnel syndrome. Redmond and Rivner performed nerve conduction studies in fifty “normal” subjects (30 women and 20 men) without present or past symptoms of carpal tunnel syndrome or other neurological complaints. All subjects had a negative neuromuscular exam. Testing was performed with surface skin temperatures at least 34°C. Bilateral medial and ulnar orthodromic sensory responses were obtained from palmar stimulation. Motor responses were also recorded. Twenty-three (46%) of these fifty subjects had at least one false positive electrodiagnostic test for carpal tunnel syndrome (see Table 1).

Table 1: Nerve Conduction Results in Healthy Subjects

<table>
<thead>
<tr>
<th>Nerve Conduction Abnormality</th>
<th>Percent Abnormal in Healthy Subjects</th>
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<tr>
<td>Distal Motor Latency &gt; 4.5 msec</td>
<td>2%</td>
</tr>
<tr>
<td>Median-ulnar palmar latency &gt; 0.3msec</td>
<td>8%</td>
</tr>
<tr>
<td>Residual Motor Latency &gt;2.6msec</td>
<td>14%</td>
</tr>
<tr>
<td>Median/Ulnar Sensory Action Potential Amplitude Ratio &gt;1.1</td>
<td>30%</td>
</tr>
<tr>
<td>At Least One Abnormal</td>
<td>46%</td>
</tr>
</tbody>
</table>

Table 1: (Adapted from Redmond 1988; Rosenbaum, 2002)
The above study demonstrated that a 0.4 millisecond difference between median and ulnar sensory latencies occurs in asymptomatic populations. Using this orthodromic technique, Redmond found no normal subject with a latency difference that was greater than 0.4 milliseconds. This criterion is often used clinically. In contrast, Felsenthal and Splindler using antidromic stimulation at the wrist established a median/ulnar latency difference normal cut-off of 0.5 milliseconds or less (Felsenthal, 1979).

Johnson, et. al., using antidromic stimulation at the wrist and digit IV recording, found that 93% of their normal subjects had a median/ulnar latency difference < 0.3 milliseconds (Johnson, 1981). However, the median/ulnar latency difference exceeded 0.6 milliseconds in three subjects. Perhaps the most unexpected finding was reported by Atroshi, et. al., who performed nerve conduction tests in 125 subjects who reported no hand symptoms, diabetes, rheumatic disease, thyroid disease, previous wrist fracture, or carpal tunnel surgery. The technique used in this study involved stimulation of the median and ulnar nerves antidromically at fixed points 3 cm proximal to the distal crease of the wrist, and recording at the proximal interphalangeal joint of the of the third and fifth digits respectively. Twenty-three asymptomatic subjects (18%) had a median/ulnar latency difference of 0.8 milliseconds. This finding exceeds the stringent cut-off point suggested by Salerno et., al., which was designed to reduce false positive rates (Salerno,
13. It should be noted that hands in the Atroshi study were warmed only if skin temperature was less than 30°C, a temperature that is cooler than most testing conditions. However, despite this caveat, one would not expect a differential temperature effect between the ulnar and median nerves resulting in latency differences. The impact of temperature on nerve conduction studies will be discussed further below.

Some have postulated that slowed conduction in asymptomatic populations represents pre-clinical disease. Existing evidence fails to support this contention. In interviews conducted up to ten months following their studies, Redmond found that none reported symptoms (Redmond, 1988). Werner, et. al., also addressed this question. He found that screening nerve conduction studies was not predictive of future symptomatic carpal tunnel syndrome. This case control study identified 77 cases of asymptomatic workers who met electrodiagnostic criteria for median neuropathy. In this study, electrodiagnostic criteria for abnormal findings consisted of a median/ulnar sensory peak latency difference of 0.5 milliseconds. Controls consisted of age and gender matched workers with normal conduction studies in both hands (defined as a sensory peak latency difference of < 0.2 milliseconds). Hands were warmed if surface skin temperatures were < 32°C. Testing was performed antidromically with stimulation at the wrists and recording 14 cm distally at digits two and five. A follow-up questionnaire at 10 to 24 months post-testing revealed no significant differences in symptom
rates. This finding held true even if the more stringent criterion of a 0.8msec latency difference was used (Werner, 1997).

Carpal tunnel syndrome may also be associated with normal nerve conduction studies. It is generally thought that normal nerve conduction studies are associated with a milder case-mix. Careful case definition is important in evaluating the literature addressing this phenomenon.

In 1979, Jun Kimura examined segmental conduction along the wrist palmar segment of the median nerve. In this hallmark study, the median nerve was stimulated percutaneously at one centimeter intervals along twelve points approximating the course of the nerve between the midpalm and the distal forearm. Ambient room temperatures were maintained at 26-28 °C. Whenever necessary, skin temperatures were maintained at 34 °C with an infrared heat lamp. The distal palmar crease corresponding to the distal edge of the transverse ligament was designated as reference point 0. Each distal stimulation point was assigned a minus sign corresponding to the distance in centimeters from the 0 reference point at the distal crease. Hence, stimulation at – 3 cm approximated the distal edge of the transverse ligament. Similarly, stimulation points proximal to the distal wrist crease were designated a (+) sign corresponding to the distance in centimeters proximal to the same reference point. Ring recording electrodes were placed at the proximal interphalangeal joint of the index. Antidromic sensory
measurements were obtained using onset latency. Peak latency was used only when onset latency was insufficiently clear. Focal slowing of the nerve was defined as 0.5 ms/cm and more than twice that of the other 1 cm segments. Through this technique, Kimura was able to map out the point of maximal conduction delay in cases of carpal tunnel syndrome. In the majority of CTS cases, the point of maximal delay occurred between two to four centimeters distal to the 0 reference point. Only one of forty-seven cases did the point of maximal delay occur distal to five centimeters from 0 reference point (Kimura, 1979).

In this study, Kimura also examined sensory conduction time across the carpal tunnel by comparing the latency difference between evoked potentials resulting from stimulation at the wrist and at the palm. For these purposes, the specific points of stimulation at the wrist were located three cm proximal to the 0 reference. Five centimeters distal the 0 reference constituted the palmar stimulation point. Nerve conduction velocity was determined by dividing distance by latency. Normal values were established in 122 hands from 61 patients without clinical evidence of neuropathy. The limits of normal were defined as ± two standard deviations from the mean in the control group. In this sample, sensory latency was considered to be abnormal if it exceeded 3.4 milliseconds from the wrist to digit, and 1.9 ms from palm to digit. These measurements corresponded to a conduction velocity of 43 m/s from the wrist to palm, and 42 m/s from the palm to digit.
Table 2 presents his findings (Kimura, 1979).

Table 2: Mean Nerve Conduction Test results: Cases versus Controls

<table>
<thead>
<tr>
<th>Skin Temp 34° C</th>
<th>Control Latency (ms) n=122</th>
<th>CTS Latency (ms) n=172</th>
<th>Control CV (m/s) n=122</th>
<th>CTS CV (m/s) n=172</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palm-Digit</td>
<td>1.41 ± 0.22</td>
<td>1.48 ± 0.28</td>
<td>58.1 ± 7.7</td>
<td>53.9 ± 9.0</td>
</tr>
<tr>
<td>Wrist-Digit</td>
<td>2.82 ± 0.28</td>
<td>3.70 ± 0.59</td>
<td>57.3 ± 6.9</td>
<td>38.5 ± 0.46</td>
</tr>
</tbody>
</table>

Table 2: Adapted from Kimura, J. Brain. 102, 615-635, 1979.

Kimura postulated that this technique could be used to help distinguish disease within the digital segments of the median nerve. This consideration has direct applicability in Hand-Arm Vibration Syndrome.

Vibration exposure is strongly associated with carpal tunnel syndrome (Silverstein, 1987; Stromberg, 1999). However, as previously mentioned, exposure to vibration can also cause a number of pathological conditions including disease within the digital nerves (Brammer, 1987; Cherniack, 1990; Stomberg, 1999). When evaluating symptoms related to exposure to significant low frequency vibration, it can be difficult to distinguish carpal tunnel syndrome from neurological disease within the digits. In 1994, Sakakibara examined upper extremity segmental nerve conduction using a specialized technique which he applied to workers with hand-vibration syndrome and healthy controls. The subjects consisted of twenty-one chain saw operators and five rock drillers with officially recognized hand-vibration
syndrome (n=26). Controls, numbering twenty-eight, consisted of teachers, clerks, and forestry workers that had not used vibrating tools. Segmental sensory nerve conduction was measured in the median and ulnar nerves of both upper extremities. Two pairs of recording electrodes were attached proximally and distally on Digits III and Digits V representing the median and ulnar nerves respectively. A pair of recording electrodes was also positioned in the mid-palm along the course of the median and ulnar nerves. The median and ulnar nerves were then stimulated antidromically at the wrist and around the elbow as illustrated in the figure below. The distances between recording and stimulation points were carefully measured with a tape measure. Whenever possible, the distance between the proximal and distal recording electrodes were fixed at 40 mm for Digit III and 30 mm for digit V. Limbs were kept under a heater. Surface skin temperature for the fingers ranged from 31 to 35°C. Surface skin temperature for the palm and forearm were measured at 33 to 37°C. Nerve conduction velocity from proximal-to-distal finger, from palm-to-finger, and from the elbow-to-wrist was calculated by dividing the distance in millimeters between each recording point by the onset latency in milliseconds. Nerve conduction velocities from the wrist-to-palm, from wrist-to-proximal finger, and from wrist-to-distal finger were similarly calculated.
Nerve conduction velocity in the subjects was significantly slower than velocities obtained in controls for several segments. Specifically, nerve conduction within the digits (proximal digit to distal digit) was significantly slower in the subjects compared to controls for both the median and ulnar nerves. The wrist-to-palm and wrist-to-proximal finger segments for both nerves were also slower in subjects compared to controls. Significant slowing from the palm-to-proximal digit was demonstrated for the right hand only. There were no significant differences between subjects and controls in median or ulnar nerve conduction from the elbow to wrist (Sakakibara, 1994).
Cherniack, et. al, applied a modified version of the Sakakibara technique among shipyard workers exposed to vibrating tools. The cohort consisted of 214 shipyard workers, 199 males and 15 females. The mean age of the cohort was 47.7 years, SD ± 5.57. The average number of years of vibratory tool exposure was 18.9 years. Surface skin temperatures were measured at the base of digit II using a digital thermometer. Attempts were made to maintain skin temperatures at 31°C. In contrast to the Sakakibara study, ulnar and median nerve stimulation points were limited to the wrists. Recording paired ring electrodes were placed proximally and distally on digit III and digit V. Disposable-gelled strip electrodes were fitted across the palm to record the wrist-to-palm segments of the median and ulnar nerves. Both median and ulnar wrist-to-palm and digital segments were slower than the palm-to-proximal-digit segments (Cherniack, 2004). The results are presented in Table 3.

Table 3: Mean Segmental Nerve Conduction for the Median Nerve

<table>
<thead>
<tr>
<th>Nerve Segment</th>
<th>Sensory Nerve Conduction Velocity (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wrist-palm</td>
<td>41.4 m/s (SD 8.0)</td>
</tr>
<tr>
<td>Palm to proximal digit</td>
<td>50.8 m/s (SD 9.5)</td>
</tr>
<tr>
<td>Proximal digit to distal digit</td>
<td>42.1 m/s (SD 9.3)</td>
</tr>
</tbody>
</table>

Table 3: (Cherniack, et., al., 2004)
**Serial Testing Variation in Nerve Conduction Studies**

Performing nerve conduction tests serially on the same person demonstrates variability in testing. For antidromic sensory nerve conduction, coefficients of variation range from 5.4% to 9%. The three important experimental errors in the determination of conduction velocity are temperature, measurement of distance, and measurement of latency (Oh, 2003). Measurement errors may be more problematic across short segments. Experimental error increases as distance decreases, and may be 20% with distances less than 6 cm. Uncertainty in the determination of onset latency seems to constitute the greatest source of error. However, the effects of random errors in distance measurement are also accentuated across short segments (Landau, 2003). This concern has direct applicability to the examination of conduction within digital nerves which may involve short segments.

Temperature differences within the hand may also have a significant role when comparing segmental nerve conduction from the wrist-to-palm and palm-to-digit segments. Furthermore, certain medical conditions may widen temperature differences between proximal and distal segments. For instance, segmental temperature differences may be more pronounced in hand vibration syndrome that includes vasospasm within the digits. Autonomic dysfunction may also widen temperature ranges between proximal and distal nerve segments. Of note in this regard, Verghese et. al.
found autonomic disturbance in 55% of carpal tunnel syndrome cases. Autonomic dysfunction was reported in 76/139 limbs (46 CTS cases). Of these, 59% reported finger swelling, 39% reported dry palms, 33% reported Raynaud’s phenomenon, and 32% had blanching. Clinical conditions that are independently associated with autonomic dysfunction such as diabetes or connective tissue disorders were excluded from the study. Autonomic dysfunction correlated with the severity of electromyographic findings (Verghese, 2000). Depending upon severity, autonomic dysfunction could intensify temperature variation between the palm and digits for a given individual. Under these conditions, one might expect that average nerve conduction resulting from a distal point of stimulation of relatively colder digits might be slowed.

**Temperature Effects upon Nerve Conduction Testing**

The core temperature of the body remains within a range of $37\degree C \pm 0.5\degree C$ (Engel, 1985). The neutral temperature of air in a closed room is $27-28\degree C$. This temperature range is one in which a naked human can remain indefinitely without involvement of thermoregulatory modulation through sweating or shivering. The comfort range for ambient temperatures is 20-25$\degree C$ depending upon humidity, wind velocity, clothing and mean radiation (Engel, 1985).

Skin is the principle organ that dissipates heat. In general, skin temperature increases as the body dissipates excessive heat. Skin cools when
the body preserves heat. Skin temperature also responds to ambient environmental temperatures. Under moderate environmental conditions, skin temperature depends upon autonomic regulation of blood flow through the skin (Anbar, 1994). In contrast to the core, anatomic skin temperature distribution is quite diverse. Blood flow within the fingers can vary by a factor of 600. Temperature differences in various regions of skin can be a greater than 15°C. For instance, skin temperature of the foot can be as low as 15°C (Engel, 1985). Anatomic variation in skin temperature results, in part, from regional vascular distribution and underlying fat. However, skin temperature variation also results from complex neurologically controlled local thermal regulation that is, nevertheless, influenced by the body's thermoregulatory state (Anbar, 1994). For instance, in one study, the direction of vasomotor reflex responses to painful intraneural electrical stimulation of the median nerve varied depending upon whether subjects were warm or cold at baseline (Oberle, 1988).

Vigorous activity raises body temperature. Also, the distribution of skin temperature changes with exercise. Skin temperature typically falls with the onset of exercise. There is a heat surge immediately following exercise where skin temperature rises (Clark, 1985).

The degree of hotness or coldness is measurable by a number of methods. In 1872, Wunderlich introduced fever measurements using simple thermometers. Clinically, skin temperature for nerve conduction testing is
typically measured with a contact thermometer. There are a number of limitations in measuring skin surface temperature with contact thermometry. Since skin has relatively low heat capacity and conductance, its temperature is likely to be affected on contact with a cooler or warmer object. A contact thermometer therefore results in a conductive heat transfer into the typically cooler measuring device. As a result, skin temperature cools at the point of contact. Such cooling can then result in autonomic compensatory mechanisms (Anbar, 1994).

All surfaces warmer than absolute zero radiate energy in the infrared spectrum. In fact, most of the body's excess heat is dissipated by radiation through the skin. Thermal infrared radiation provides a means for non-contact temperature measurement via infrared thermography.

Temperature is an important determinant influencing nerve conduction study results. As early as 1867, Von Helmholtz recognized that nerve conduction velocity decreases at lower temperatures (Oh, 2003). Declines in temperature prolong sensory and motor latency and decrease nerve conduction velocity; whereas they increase amplitude duration and area (Ashworth, 1998; Oh, 2003). To avoid being misled by temperature effects, nerve conduction studies are typically performed at skin temperatures between 31-33°C. Kimura performed his study at a minimum of 34°C. Warming methods typically involve exposure to infrared heat lamps, or warm bath emersion. In clinical practice, time constraints often do not
allow adequate warming. In fact, time constraints for warming have led to acceptance of wider temperature ranges than is optimal (Wallin, 2002).

Under these testing conditions, temperature corrective factors are often applied. Within physiologic ranges, nerve conduction velocity increases linearly with temperature increase. In sensory nerve conduction with surface electrodes, this rate ranges from 1.1-2.4 m/sec for every °C (Oh, 2003).

Typically, a correction factor of 1.4-2.4 m/s per °C is used for median nerve sensory conduction velocity (Ashworth, 1998). However, laboratories are expected to establish their own normative values. The application of correction factors should be consistent with the temperature level at which the laboratory obtained its normal values.

It is important to note that correction factors are based upon values obtained in normal populations. Differences in temperature effects between normal and abnormal nerves must be known in order to validate the routine use of correction factors. Studies examining the temperature effect upon diseased nerves have been inconsistent. Bolton, et. al. performed serial nerve conduction studies at cool and at warm temperatures, with a mean finger temperature of 23°C and 33°C, respectively. These authors found that the rate of change in sensory amplitude as a function of temperature was less in carpal tunnel syndrome compared to normal controls (Bolton, 1982). However, the change in value per degree rise for distal latency was the same in controls and cases of carpal tunnel syndrome. Specifically, the mean
change in value for distal latency was \(-0.09\) milliseconds per degree rise \(({}^\circ\text{C})\) in both groups (Bolton, 1982). More recently, Ashworth compared the effect of temperature on the median and ulnar nerves in subjects with "electrophysiologically confirmed" carpal tunnel syndrome. In the Ashworth study, thirty-three affected limbs were cooled with ice water, and median and ulnar nerve conduction studies were repeatedly performed as the limb re-warmed. Study temperature ranged from 23.5\(^\circ\text{C}\) to 35\(^\circ\text{C}\). The rate of change in sensory conduction velocity with re-warming was \(+0.11\) m/s/\(^{\circ}\text{C}\) in the diseased median nerve compared to \(+1.0\) m/s/\(^{\circ}\text{C}\) in the healthy ulnar nerve \((P\text{-value 0.02})\) (Ashworth, 1998). The rate of change in sensory amplitude was also less in the median nerve, but this finding was not statistically significant. Ashworth's findings suggest that application of corrective factors may not be appropriate in the setting of carpal tunnel syndrome. In contrast, however, Baysal AI, et. al. found no significant differences in temperature effects for sensory nerve conduction velocity between normal and carpal tunnel syndrome groups. These authors concluded the same temperature correction factors could be applied to carpal tunnel syndrome cases as normal individuals (Baysal, 1993). The uncertainties regarding the appropriate application of corrective factors reinforce the importance of adequate limb warming for reliability in nerve conduction studies. Differences in temperature effects between diseased and healthy nerves are not fully understood nor quantified.
Given the impracticalities of current warming methods, Wallin suggested an alternative approach to warming limbs for nerve conduction studies. He studied 114 adult females who underwent sub-maximal exercise on a bicycle ergometer in two contiguous six-minute sessions. For women under age 35, exercise resistance was set at a load of 75 watts for the initial six-minutes, than increased to a load of 100 watts for the final six minutes of exercise. In women older than 35 years of age, the initial load was set at 50 watts, and increased to 75 watts for the remaining six minutes of exercise. Heart rate was monitored with a pulsimeter. Subjective symptoms of exertion were monitored with the RPE Scale by Borg. Following exercise, subjects were covered with a heated blanket. Digital skin temperatures were measured with a temperature electrode at the distal phalanx. As demonstrated in the table below, this exercise protocol appears to have provided sustained warming for the performance of nerve conduction testing. For the majority of the subjects, digital skin temperatures increased by 7°C or more. Also noteworthy is that the dispersion of temperature values narrowed after one minute post-exercise and during nerve conduction. Only seven of the 114 subjects had a temperature below 33°C when the median nerve was tested (Wallin, 2002; see Table 4).
Table 4: Finger Temperature Response to Exercise

<table>
<thead>
<tr>
<th>Statistical Parameter</th>
<th>Temperatures During Cycling Session (°C)</th>
<th>Temperature During Nerve Conduction Testing (°C)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=114</td>
<td>Baseline</td>
</tr>
<tr>
<td>Mean</td>
<td>28.1</td>
<td>33.3</td>
</tr>
<tr>
<td>Minimum</td>
<td>20.5</td>
<td>21.6</td>
</tr>
<tr>
<td>Maximum</td>
<td>35.4</td>
<td>36.7</td>
</tr>
<tr>
<td>SD</td>
<td>4.4</td>
<td>3.8</td>
</tr>
</tbody>
</table>

Table 4: (Modified from Wallin, 2002); N= number; SD = standard deviation

Whether exercise warming proves effective in the context of nerve disease or vasospastic disease remains to be proven. Again, of interest is the warming response exercise might have in digits afflicted with vibration-induced white finger, or carpal tunnel syndrome associated with autonomic dysfunction. Depending upon severity, autonomic dysfunction could widen temperature variation between the palm and digits within a given individual. In addition, the presence of autonomic dysfunction associated with carpal tunnel syndrome may lead to variable responses to warming methods among subjects. Moreover, the degree of autonomic dysfunction may explain, in part, inconsistencies in temperature effect observed in CTS cases versus controls in some studies, and not others.

It is also important to note that autonomic dysfunction associated with carpal tunnel syndrome can be identified using thermography. However, thermography alone has low sensitivity (23%) for the diagnosis of carpal tunnel syndrome (Anbar, 1994). Small fiber disease resulting in autonomic dysfunction is a late finding. In clinical series, many patients who meet
clinical and electrophysiologic criteria for Carpal Tunnel Syndrome have normal thermography. (Rosenbaum, 2002; So, 1989)

Rosenbaum summarizes a number of well recognized caveats when considering nerve conduction studies in the context of carpal tunnel syndrome. Many of these have already been discussed.

- Biological variability creates an overlap of normal and abnormal
- Experimental error increases with attention to short abnormal segments of nerve
- The probability of an abnormal result increases if multiple tests are performed on the same patient
- Symptoms of carpal tunnel syndrome can occur whether or not nerve conduction is measurably impaired
- Nerve conduction slowing does not always measure clinical disruption of nerve function
- Mild nerve compression is a common finding in asymptomatic populations
- Axonal Interruption is a late manifestation of carpal tunnel syndrome (Rosenbaum, 2002)

The caveats enumerated by Rosenbaum further complicate the interpretation of epidemiological studies. In addition, references to neurodiagnostic tests in the medical literature rarely provide detail regarding laboratory testing conditions. A number of methodological questions in the
performance of nerve conduction studies remain open. The effect of regional
temperature variation on segmental nerve conduction is not well delineated.
The impact that temperature has in a diseased nerve is not established.
Warming methods have not been standardized. Methods and timing of
temperature measurements have not been established. These unresolved
methodological questions may account for some of the variability seen in
nerve conduction study results. The pilot study presented below examines
the aforementioned methodological question

Methods:

In order to test the hypotheses listed under “Objectives” below, we
compared segmental sensory nerve conduction for the median and ulnar
nerves within the wrists and hands under two methods of warming using two
independent nerve testing techniques in healthy individuals and subjects
with carpal tunnel syndrome. Also, surface skin temperatures were measured
via contact thermometry and infrared thermography and the results
compared. This study was approved by the University of Connecticut Health
Center’s Institutional Review Board, Reference Number 03-090. Funding
was provided by a grant from the Harvard-NIOSH Education and Research
Center Pilot Projects Research Training Program.
Objectives:

To test the following specific null hypotheses:

1. Stimulation point makes no difference in nerve conduction velocity
2. Temperature measurement method makes no difference in skin temperature
3. Warming method makes no difference in skin temperature
4. Warming method makes no difference in nerve conduction velocity

Two groups of subjects between the ages of 20 and 55 years underwent repeated bilateral sensory median and ulnar nerve conduction studies involving segments within the wrists, hands, and digits. Cases consisted of subjects between the ages of 20 and 55 years who had a clinical diagnosis of carpal tunnel syndrome and had not undergone surgical release; controls were healthy subjects. The case definition consisted of wrist or palm discomfort associated with numbness and/or tingling involving at least two digits in the distribution of the median nerve, precipitated by grasping (e.g. holding a telephone, driving) and relieved by shaking. The presence of night or early morning symptoms was also elicited. Exclusion criteria included diabetes mellitus, rheumatoid arthritis, cervical disk disease, previous carpal tunnel surgery, or other neurological disorders affecting the peripheral nervous system. Recruitment was via a series of broadcast announcements at the University of Connecticut Health Center. Candidates for participation
were screened via telephone by a physician in order to confirm that selection
criteria were met prior to enrollment into the study. Each participant
completed a brief medical questionnaire and underwent Tinel's testing at the
wrists and Phalen's test. The Tinel's Test and the Phalen's Test are
commonly performed physical exam maneuvers in suspect cases of Carpal
Tunnel Syndrome. The case definition was not based upon these physical
exam results.

Each individual subject underwent repeated nerve conduction testing
consisting of two independent nerve conduction techniques specified below.
Testing was performed in two sessions. The duration of each session was
estimated to approximate two hours. An interval of at least one hour was
required between each test session. Session One was performed using
standard warming of the upper extremities via a heat lamp. In Session One,
all subjects whose baseline skin temperatures at the palm were less than
32°C underwent heat lamp warming for 12 minutes prior to testing. The
warming method for the Session Two consisted of exercise on a stationary
bicycle ergometer for twelve minutes. Exercise resistance was adjusted to
provide a load of 50-100 watts and a targeted heart rate range of 135-145
beats per minute. Heart rate was monitored continuously with a wireless
heart monitor fastened to the subject's chest. Subjective symptoms of
exertion were elicited at two minute intervals during exercise using the RPE-
Borg Scale. A physician remained in attendance during exercise.
The ambient room temperature was measured with a digital thermometer at each session. A series of surface skin temperature measurements using a handheld digital thermometer were made proximal to the fourth digit bilaterally following a ten minute period of acclimation (categorized as baseline temperature), after a 12 minute period of active warming (categorized as post-warming temperature), and immediately following nerve conduction testing of a given limb (categorized as final temperature). Concurrently, serial infrared thermographic images of the wrists and hands were also obtained at baseline, immediately after warming (categorized as post-warming temperature), and immediately following the completion of nerve conduction testing for a given limb (categorized as final temperature). See figure 3 for an illustrative example. Thermographic images were obtained utilizing an IR SnapShot® Model 525 Imaging Radiometer with an object temperature range of 0°C to +350°C and a thermal sensitivity of <0.4°C and a measurement accuracy of ± 3%. The camera was mounted on a tripod at a fixed distance of 80 cm. The camera was calibrated for operation within an environmental temperature range between 0.0°C to 40.0°C.

Thermograms were stored on a PC card. Thermograms were transferred to a PC and analyzed using the software package, IR SnapView 2.1®. A blue red palette was used to visualize the temperature scale. Blue tones represented the coldest temperatures and red represented the warmest.
Infrared point temperature was recorded proximal to the fourth digit. Mean, minimum, and maximum infrared temperatures were recorded along lines drawn from wrist-to-digit III, wrist-to-digit V, palm-to-digit III, and palm-to-digit V. The standard deviation of temperatures along each drawn line was also recorded (see Figure 4). Temperature data was transferred to an Excel Spreadsheet.

Figure 3: Illustrative Example of Sequential Infrared Thermographic Images

- Testing Performed in Two Sessions: Lamp Warming and Exercise Warming
- Each Session Included Both Kimura and Sakakibara Techniques for Both Ulnar and Median Nerves in Both Hands
- Skin Temperatures were Measured Using a Digital Thermometer and Infrared Images for each hand at three intervals in each session

Figure 3: Illustrative example of thermographic images obtained at baseline, immediately following warming, and immediately after the completion nerve conduction testing.
Figure 4: Illustrative Example of Infrared Thermographic Temperature Measurements

Table: Temperature Measures

<table>
<thead>
<tr>
<th>Label</th>
<th>Ave</th>
<th>SD</th>
<th>Max</th>
<th>Min</th>
</tr>
</thead>
<tbody>
<tr>
<td>L1</td>
<td>30.9</td>
<td>1.59</td>
<td>33.0</td>
<td>27.0</td>
</tr>
<tr>
<td>L2</td>
<td>30.0</td>
<td>0.79</td>
<td>31.6</td>
<td>28.7</td>
</tr>
<tr>
<td>L3</td>
<td>30.6</td>
<td>1.66</td>
<td>33.0</td>
<td>27.0</td>
</tr>
<tr>
<td>L4</td>
<td>29.7</td>
<td>0.41</td>
<td>30.6</td>
<td>28.7</td>
</tr>
<tr>
<td>P1</td>
<td>31.3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DT</td>
<td>30.9</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Each subject generated twelve images and temperature tables.

Figure 4: Illustrative example of point and linear infrared temperature measurements. L1 = wrist-to-digit III segment; L2 = wrist-to-digit V segment; L3 = palm-to-digit III segment; L4 = palm-to-digit V segment; P1 = infrared point measure; D = digital thermometer measure; Ave = average temperature; SD = standard deviation; Max = maximum temperature; Min = minimum temperature.

All nerve conduction tests were performed on a Nicolet Viking Quest. Sensitivity was set at 20 μV. Low frequency filter was set at 20 Hz and the high Frequency Filter set a 3 kHz. Distances in millimeters between each recording cathode and stimulation cathode were measured and recorded. Stimuli were applied for 0.1 ms duration, and rarely at 0.2 ms duration. The initial stimulation was set at 70v with 20v increments to a maximum of 150 volts. Onset latencies were recorded. Segmental nerve conduction velocities were calculated based upon the distances between the stimulating cathode
and the recording cathode in millimeters divided by the onset latency in milliseconds.

The first nerve conduction technique consisted of a modification of the antidromic method described by Kimura. The distal crease of the wrist served as an anatomical reference point. Stimulation of the ulnar and median nerves was located three centimeters proximal to this reference point at the wrist, and five centimeters distal to this reference point within the palm. Recording ring electrodes were placed on the distal Digit III and distal Digit V. Placement was made anthropometrically in order to allow maximal distances. All distance measurements between each segment were made with a tape measure and recorded.

Figure 5: Illustration Example of Modified Kimura Technique, Median Nerve.

Figure 5: Recording Electrodes were placed at the distal third digit for median nerve testing. A1 = conduction from wrist to digit III; A2 = conduction palm to digit III; B3 = conduction from wrist to digit V; B4 = conduction from palm to digit V.
The second technique consisted of the method described by Sakakibara, et. al as modified by Cherniack, et. al. Two pairs of recording ring electrodes were placed proximally and distally on Digits III and Digits V coupled with a pair of palm strip electrodes whose anode was placed at the distal palmar crease. Each anode electrode was separated distally from its paired cathode electrode by 1/2 inch. Distance measurements were made from cathode to cathode for each segment. Antidromic responses were measured by stimulating the median and ulnar nerves at three centimeters proximal to the distal crease of the wrist. Recording took place at the mid-palm, at digit III and digit V proximally, and at digit III and digit V distally. Both techniques were performed bilaterally at each session.

Analysis of Covariance (ANOCOVA) was used to study the effects of warming method, measurement technique, disease status, and ambient temperature on segmental skin surface temperature and nerve conduction velocity. Least squares means were determined and the Tukey-Kramer method was used to adjust for multiple comparisons. The analysis was implemented in PROC GLM of SAS® v. 9.0. The dispersion of temperature measurements was studied by taking the natural logarithmic transformation of the variance of line temperature readings. The transformation was necessary to approximate normality of the distribution for purposes of comparisons. Independent and pair-wise t-test procedures (PROC TTEST of
SAS® v. 9.0) were then used to compare the mean log-variance readings between two groups (e.g. cases vs. controls, exercise vs. lamp warming, etc.). The level of significance for comparisons was set at 5%.

**Results:**

There were nine cases (eight females, one male) and ten controls (nine females, one male) representing thirty-eight limbs that were tested. All the cases described bilateral symptoms to a varying degree. Mean age for cases was 45.56 (SD 4.10); mean age for controls 47.30 (SD 4.22). There was no statistically significant difference in mean age between cases and controls. Fifty-six percent (5/9) of cases had a positive Phalen’s Sign; whereas only one control (10%) had a positive Phalen’s Sign. Tinel’s Sign at the wrist was positive in one case and in one control.

**Table 5: Demographics**

<table>
<thead>
<tr>
<th>Status</th>
<th>Mean Age (SD)</th>
<th>Positive Phalens Test</th>
<th>Positive Tinels Test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases</td>
<td>45.56 (4.10)</td>
<td>5</td>
<td>1</td>
</tr>
<tr>
<td>Controls</td>
<td>47.30 (4.22)</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

*Table 5: SD = standard deviation; n = number*
Mean Segmental Conduction Velocity Results: Cases vs. Controls

There was a significant difference between cases and controls in mean sensory conduction velocity for both the wrist-to-digit III, and the palm-to-digit V segments of the median nerve. Mean segmental conduction velocity within the ulnar nerve revealed no significant differences between cases and controls. Table 6 summarizes these results.

Table 6: Mean Segmental Conduction Velocity

<table>
<thead>
<tr>
<th>Nerve Segment</th>
<th>Mean Conduction Velocity (m/s) (SEM)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Case</td>
</tr>
<tr>
<td>Median Nerve</td>
<td>50.38 (1.013)</td>
<td>41.57 (1.700)</td>
</tr>
<tr>
<td>Wrist to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Nerve</td>
<td>53.19 (0.993)</td>
<td>50.39 (1.013)</td>
</tr>
<tr>
<td>Palm to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>52.91 (1.619)</td>
<td>53.21 (1.630)</td>
</tr>
<tr>
<td>Wrist to Digit V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>51.80 (0.958)</td>
<td>52.26 (1.011)</td>
</tr>
<tr>
<td>Palm to digit V</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 6: Mean = least square means; m/s = meters per second; NS = nonsignificant; SEM = standard error of the mean
Figure 6: Ambient Temperature Testing Conditions

Figure 6 illustrates ambient temperature recordings in Celsius for subjects two through nineteen. There was a failure to record the ambient room temperature for the first subject. Ambient room temperatures ranged from 20.2°C to 27.6°C (Mean 22.3°C, SD 1.485). The first three subjects were tested under relatively warmer room conditions. The mean ambient room temperature for cases was 21.90°C (Minimum 20.2°C, Maximum 27.6°C); the mean ambient room temperature for controls was 22.65°C (Minimum 20.3°C, Maximum 27.2°C). The difference between these means, 0.75°C, was not statistically significant. The effect of room temperature was the same across
types of warming method, point temperature measurement method, and subject classification.

Temperature Results

Figure 7 below represents a schematic of how the participants were divided into sub-groups for analysis. The temperature results in Figure 7 consist of the mean skin surface point temperature measurements obtained immediately following a twelve minute warming period (categorized as post-warming temperatures). Point temperature measurements were obtained concurrently via a handheld digital thermometer placed proximal to the fourth digit and via an infrared thermographic measurement proximal to the fourth digit.
Does method of measurement affect temperature results?

Digital and infrared surface skin temperature measurements were obtained virtually simultaneously for each sub-group at each point of measurement. Baseline temperature refers to the surface skin temperature that was obtained following a period of acclimation approximating 10 minutes. Post-warming temperatures were obtained immediately following a 12-minute active warming period. Final temperatures were obtained.
immediately following completion of the nerve conduction tests for a given limb.

There was no significant difference between mean digital thermometer and mean point infrared thermographic surface skin temperature measurements (see Table 7). Within the case-exercise-warming subgroup, the mean *post-warming temperatures* were 32.58°C and 31.15°C as measured by digital and infrared methods respectively (difference not significant). Within the case-lamp-warming subgroup, the mean *post-warming* temperatures were identical at 33.28°C and 33.28°C as measured by digital and infrared methods respectively (NS). Within the control-exercise-warming subgroup, the mean *post-warming* temperatures were 32.94°C and 32.25°C as measured by digital and infrared methods respectively (NS). Within the control-lamp-warming subgroups, the mean *post-warming* temperatures were 34.32°C and 33.04°C as measured by digital and infrared methods respectively (NS).

Final temperatures represent temperature measurements that were obtained after the completion of nerve conduction tests for a given limb. Within the case-exercise-warming subgroup, the mean *final temperatures* were 32.67°C and 33.15°C as measured by digital and infrared methods respectively (NS). Within the case-lamp-warming subgroup, the mean *final temperatures* were 31.70°C and 32.14°C as measured by digital and infrared methods respectively (NS). Within the control-exercise-warming subgroup,
the mean final temperatures were 31.91°C and 31.89°C as measured by digital and infrared methods respectively (NS). Within the control-lamp-warming subgroup, the mean final temperatures were 32.51°C and 32.30°C as measured by digital and infrared methods respectively (NS). Figure 8 presents these results in detail for each subgroup.

**Figure 8: Least Square Means Post-Warming Point Temperature Results Using Digital and Infrared Thermographic Measurements**

<table>
<thead>
<tr>
<th>Status</th>
<th>Measure Method</th>
<th>Warming Method</th>
<th>Baseline Temperature (SEM)</th>
<th>Post-warming Temperature (SEM)</th>
<th>Final Temperature (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>Digital</td>
<td>Exercise</td>
<td>32.58 °C (0.663)</td>
<td>33.28 °C (0.420)</td>
<td>32.67°C (0.412)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lamp</td>
<td>32.97°C (0.663)</td>
<td>33.28 °C (0.427)</td>
<td>31.70°C (0.419)</td>
</tr>
<tr>
<td>Infrared</td>
<td>Digital</td>
<td>Exercise</td>
<td>31.15°C (0.684)</td>
<td>32.91 °C (0.418)</td>
<td>33.15°C (0.410)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Lamp</td>
<td>32.25°C (0.663)</td>
<td>33.28 °C (0.429)</td>
<td>32.14°C (0.408)</td>
</tr>
</tbody>
</table>

Control

<table>
<thead>
<tr>
<th>Digital</th>
<th>Exercise</th>
<th>27.81°C (0.595)</th>
<th>32.94 °C (0.384)</th>
<th>31.91°C (0.378)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamp</td>
<td>29.67°C (0.595)</td>
<td>34.32 °C (0.363)</td>
<td>32.51°C (0.356)</td>
<td></td>
</tr>
<tr>
<td>Infrared</td>
<td>Exercise</td>
<td>28.54°C (0.624)</td>
<td>32.25 °C (0.390)</td>
<td>31.89°C (0.383)</td>
</tr>
<tr>
<td>Lamp</td>
<td>28.75°C (0.624)</td>
<td>33.04 °C (0.388)</td>
<td>32.30°C (0.381)</td>
<td></td>
</tr>
</tbody>
</table>

Figure 8: SEM=standard error of the mean
Figure 9 illustrates the relationship of mean temperatures between digital thermometer temperature measurements and infrared thermographic point temperature measurements.

**Figure 9: Sequential Temperature Measurements: Digital Thermometer versus Infrared Thermograph**

Does warming method effect point temperature results?

Table 7 demonstrates the overall baseline point temperature means in cases and controls. The overall mean baseline point temperature was significantly higher in cases versus controls.

**Table 7: Baseline Least Square Mean Point Temperatures**

<table>
<thead>
<tr>
<th>Status</th>
<th>Baseline Point Temperature</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>32.24°C (0.335)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Control</td>
<td>28.69°C (0.305)</td>
<td></td>
</tr>
</tbody>
</table>

*Table 7: SEM=standard error of the mean*
The case versus control difference in baseline point temperature measurements remained significant for each subgroup except the infrared/exercise subgroup (refer to Figure 8 for means in each subgroup).

Exercise and lamp warming methods did not produce significantly different mean skin point temperature measurements. The mean post-warming temperatures were 33.28°C for the case-exercise-warming subgroup and 33.28°C for the case-lamp-warming subgroup as measured by a digital thermometer. Within the case-infrared-measurement subgroups, exercise resulted in a mean post-warming skin temperature of 32.91°C in the exercise warming subgroup and 33.28°C in the lamp warming subgroup (NS). Digital thermometer measurements within controls revealed a post-warming mean skin temperature of 32.94°C in the exercise-warming subgroup and 34.32°C in the lamp-warming subgroup (NS). The control-infrared-measurement subgroups revealed mean point skin temperatures of 32.25°C for exercise warming and 33.04°C for lamp warming (NS). Figure 10 summarizes the relationships between warming methods by comparing mean post-warming surface skin temperatures for each subgroup.
Both lamp and exercise methods of warming reduced temperature variability among all sub-groups as evidenced by smaller standard errors following warming (see Figure 8 and Table 8). Table 8 summarizes the overall temperature results by warming method.

**Table 8: Least Square Means Point Temperature Readings: Warming Method**

<table>
<thead>
<tr>
<th>Warming Method</th>
<th>Baseline Temperature (SEM)</th>
<th>Post-Warming Temperature (SEM)</th>
<th>Final Temperature (SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lamp</td>
<td>30.91°C (0.318)</td>
<td>33.48°C (0.197)</td>
<td>32.16°C (0.192)</td>
</tr>
<tr>
<td>Exercise</td>
<td>30.02°C (0.321)</td>
<td>32.85°C (0.195)</td>
<td>32.41°C (0.192)</td>
</tr>
</tbody>
</table>

Table 8: SEM = Standard error of the mean
The graphs depicted in Figure 11 and Figure 12 plot surface skin temperatures for each subgroup across each measurement sequence. Figure 11 plots digital thermometer measurements. Figure 12 plots infrared thermographic measurements. These graphs illustrate the sequential measurements in surface skin temperatures for cases and controls across the testing period for lamp warming and exercise warming. The time interval for each sequence is not depicted to scale. For example, the baseline to post-warming sequence was always much shorter in duration than the post-warming to final sequence. The graphs do not depict interval duration.

Nerve conduction testing for each limb was performed during the sequence that occurred between the post-warm and final temperature readings. The plots indicate to what degree warming occurred, and how well it was sustained in each during nerve conduction testing.

The graphs in Figures 11-12 consistently indicate that surface skin temperatures were dynamic. As such, the timing of temperature measurements during the course of testing affects temperature results. Sequential post-warm to final (post-testing) mean skin temperatures were generally cooler except for the case-exercise subgroup for which mean skin temperatures continued to rise.
Figure 11: Surface Skin Temperatures Measures using a Digital Thermometer Held in the Palm Proximal to Fourth Digit.

Figure 11: $DT$=Digital Thermometer; $Mean$=Least Square Mean; Temperature Scale in Degrees Celsius

Figure 12: Mean Skin Surface Temperature from Point Infrared Readings

Figure 12: Point measurement taken proximal to fourth digit. $IR$=infrared thermographic measurement; $Mean$=Least Square Mean; Temperature Scale in Degrees Celsius
As previously indicated, environmental ambient temperatures were not controlled. The digital and infrared point temperature sequential relationships were re-analyzed in a subset of subjects who were tested under similar ambient room temperature conditions. In this analysis, the four subjects who were tested under the warmest room temperatures were excluded, leaving fifteen subjects. Subjects 1, 2, 3, and 10 were excluded. (See figure 6). Figures 13 and 14 plot the mean temperature relationships for subjects four through nine and eleven through nineteen.

**Figure 13:** Digital Thermometer Mean Surface Skin Temperature in Subset of Subjects Based upon Ambient Room Temperatures

![Graph showing mean surface temperature](image)

**Figure 13:** $DT =$ Digital Thermometer; $Mean =$ Least Square Mean; $Temperature$ Scale in Degrees Celsius
Figure 14: Infrared Thermographic Mean Surface Skin Temperature in Subset of Subjects Based upon Ambient Room Temperatures

Figure 14: *Point measurement taken proximal to fourth digit. IR=infrared thermographic measurement; Mean=Least Square Mean; Temperature Scale in Degrees Celsius*

Segmental Post Warming Infrared Temperature Measures

Infrared thermographic temperature was also measured along lines representing nerve segments (see Figure 4). Segmental linear infrared measurements revealed no significant differences in least square means between warming methods (lamp vs. exercise) for any segment (see Table 9).
Table 9: Postwarming Segmental Mean Temperature: Lamp v. Exercise

<table>
<thead>
<tr>
<th>Segment</th>
<th>Temperature °C (SEM)</th>
<th>P-Value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lamp</td>
<td>Exercise</td>
</tr>
<tr>
<td>Median Nerve</td>
<td>32.59 (0.276)</td>
<td>31.89 (0.273)</td>
</tr>
<tr>
<td>Wrist to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Nerve</td>
<td>32.90 (0.275)</td>
<td>32.41 (0.273)</td>
</tr>
<tr>
<td>Palm to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>32.08 (0.274)</td>
<td>32.06 (0.274)</td>
</tr>
<tr>
<td>Wrist to Digit V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>32.45 (0.274)</td>
<td>32.58 (0.274)</td>
</tr>
<tr>
<td>Palm to Digit V</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 9: SEM=standard error of the means; Number ~38 observations in each segment category. Mean=Least Square Mean

The graphs depicted in Figures 15-18 plot the segmental skin temperature means for each subgroup across each measurement sequence. Each data point on the graphs represents sample numbers of 17 to 20 observations. Although the graphs in Figures 15-18 suggest linear relationships, it is important to note that temperature measurements were not continuous. The actual shapes of the temperature curves between each measurement interval remain unknown. As previously stated, the graphs portray the sequence order of each interval, but do not depict the duration in time of each interval.

Baseline temperatures were warmer in cases compared to controls. The segmental infrared temperature graphs again demonstrate that
temperature was dynamic throughout the testing period. The point in time at which measurements were made affected the results.

The TTest Procedure was used to test the significance of temperature differences between each sequence. A significant difference between baseline temperature and post-warming temperature provides an indication of the warming effect. Non-significant differences in mean temperature from the post-warming to final sequence suggest that post-warming temperature levels were sustained. Non-significant differences in mean temperature between the baseline to final sequence suggest that the warming effect was un-sustained and approached baseline measurements.

Mean temperature differences from the baseline to post-warming sequence were significant in all subgroups. Mean post-warming segmental temperatures were more often sustained in the exercise warming subgroups when compared to the lamp warming sub-groups. Also, final mean infrared line temperatures of the case-exercise sub-groups corresponding to median nerve segments were actually higher than their respective post-warming temperatures.

Figure 15 depicts sequential infrared line temperature measurements along the wrist to digit III line for each subgroup.
Figure 15: Mean Line Infrared Thermographic Temperature Measurements for Wrist-to-Digit III Segment

WD3 Surface Temperatures (IR Line Means)

Figure 15: WD3=wrist-to-digit III; IR=infrared thermographic measurement; Mean=Least Square Means; I-Bar represents the standard error of the means

Regarding the wrist-to-digit III segment, temperature differences from the baseline to post-warm sequence and from the baseline to final sequence were statistically significant in the exercise warming subgroups. Temperature differences from the post-warm to final sequence were not statistically significant for the exercise warming subgroups (see Table 10). The results indicate a sustained warming effect within the exercise subgroups. In the lamp warming sessions, the mean infrared line temperatures corresponding to wrist-to-digit III revealed significant increases from baseline to post-warming, but also significant drops from post-warming to final measurements. The results indicate that post-warming temperature
levels corresponding to the wrist to digit III were not well sustained in the lamp warming subgroups (see Table 10). In fact, the mean final temperature in the case-lamp subgroup was actually lower than at baseline, although insignificantly so (see Figure 15, Table 10). Again, note that ambient room temperatures were uncontrolled.

<table>
<thead>
<tr>
<th>Measurement Sequence</th>
<th>Wrist-to digit III</th>
<th>Case Exercise P-value</th>
<th>Control Exercise P-value</th>
<th>Case Lamp P-value</th>
<th>Control Lamp P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline → Postwarm</td>
<td>0.0033</td>
<td>&lt;0.0001</td>
<td>0.0332</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Baseline → Final</td>
<td>0.0002</td>
<td>0.0002</td>
<td>NS</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>Post-warm → Final</td>
<td>NS</td>
<td>NS</td>
<td>0.0451</td>
<td>0.0003</td>
<td></td>
</tr>
</tbody>
</table>

Table 10: NS=nonsignificant

Figure 16 consists of a graph that plots the sequential mean temperature measurements in each subgroup corresponding to the palm-to-digit III segments.
The sequential relationships in the palm-to-digit III segment paralleled those of the wrist-to-digit III segment. Again, mean baseline to post-warming temperature differences corresponding to the palm-to-digit III segments were significant in all subgroups (see Table 11). Again, temperature differences from post-warm to final measurements were not statistically significant for the exercise warming subgroups (see Table 11). Again, in the lamp warming sessions, the mean infrared line temperatures corresponding to palm-to-digit III revealed significant increases from baseline to post-warming, but also significant drops from post-warming to final measurements indicating that the post-warming temperature levels were not well sustained. Again, the mean final temperature in the case-lamp subgroup was actually lower,
although insignificantly so, than the baseline temperature mean (see Figure 16, Table 11). The results indicate sustained warming along the palm to digit III segment for the exercise subgroups, but not the lamp subgroups.

Table 11: Differences in IR Line Mean Temperature for Palm to Digit III Segment

<table>
<thead>
<tr>
<th>Measurement Sequence</th>
<th>Case Exercise P-value</th>
<th>Control Exercise P-value</th>
<th>Case Lamp P-value</th>
<th>Control Lamp P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline→ Postwarm</td>
<td>0.0016</td>
<td>&lt;0.0001</td>
<td>0.0284</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline→ Final</td>
<td>0.0002</td>
<td>0.0001</td>
<td>NS</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Post-warm→Final</td>
<td>NS</td>
<td>NS</td>
<td>0.0381</td>
<td>0.0005</td>
</tr>
</tbody>
</table>

Table 11: NS=nonsignificant

Figure 17 depicts sequential infrared mean temperature measurements along the line corresponding to the wrist to digit V segment for each subgroup.

**Figure 17:** Mean Segmental Temperature Measurements Wrist-to-Digit V

*WD5= wrist-to-digit V; IR= infrared thermographic measurement; I-Bar represents the standard error of the means*
The mean temperature differences from baseline to post-warming corresponding to the wrist-to-digit V segments were significant in all subgroups (see Table 12). The temperature differences from the post-warming to final sequence were insignificant for the cases. However, the mean decrements in temperature at the post-warming to final measurement point were significant in controls (see Figure 17, Table 12). Following the above guidelines would indicate that cases, but not controls, had a sustained warming effect for infrared line temperatures corresponding to the wrist to digit V segments. However, the baseline to final sequence was also insignificant in the case/lamp subgroup, indicating an unsustained temperature effect. The case/lamp actually revealed little movement in temperature between each sequence and constitutes an exception to the guidelines.

<table>
<thead>
<tr>
<th>Measurement Sequence</th>
<th>Wrist-to digit V</th>
<th>Case Exercise P-value</th>
<th>Control Exercise P-value</th>
<th>Case Lamp P-value</th>
<th>Control Lamp P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline → Postwarm</td>
<td>0.0017</td>
<td>&lt;0.0001</td>
<td>0.0280</td>
<td>0.0005</td>
<td></td>
</tr>
<tr>
<td>Baseline → Final</td>
<td>0.0017</td>
<td>0.0003</td>
<td>NS</td>
<td>0.0110</td>
<td></td>
</tr>
<tr>
<td>Post-warm → Final</td>
<td>NS</td>
<td>0.0165</td>
<td>NS</td>
<td>0.0001</td>
<td></td>
</tr>
</tbody>
</table>

Table 12: Differences in IR Line Means for Wrist-to-Digit V Segment

Table 12: NS=nonsignificant
Figure 18 consists of a graph that plots the sequential mean infrared temperature measurements in each subgroup along lines corresponding to the palm-to-digit V segments.

**Figure 18:** Mean Segmental Temperature Measurements for Palm-to-Digit V

Mean temperature differences were significantly higher from baseline to post-warming in the palm-to-digit V segment for all subgroups. However, mean temperature differences from the post-warming to final sequence were insignificantly in only the case-
exercise subgroup. A sustained warming effect in temperatures corresponding to the palm to digit V segment was demonstrated in the exercise case subgroup only (see Table 13).

Table 13: Differences in IR Line Means for Palm to Digit V Segment

<table>
<thead>
<tr>
<th>Measurement Sequence Palm·to digit V</th>
<th>Case Exercise P-value</th>
<th>Control Exercise P-value</th>
<th>Case Lamp P-value</th>
<th>Control Lamp P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline → Postwarm</td>
<td>0.0012</td>
<td>&lt;0.0001</td>
<td>0.0483</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Baseline → Final</td>
<td>0.0009</td>
<td>0.0007</td>
<td>NS</td>
<td>0.0001</td>
</tr>
<tr>
<td>Post-warm → Final</td>
<td>NS</td>
<td>0.0032</td>
<td>0.0429</td>
<td>0.0007</td>
</tr>
</tbody>
</table>

Table 13: *NS=nonsignificant*

Figure 19 demonstrates the sequential temperature relationships by segment and warming method in cases

Figure 19: Sequential Mean Infrared Line Temperature Measurements

Figure 19: WD3= wrist to digit III; PD3= palm to digit III; WD5= wrist to digit V; PD5= palm to digit V;
Figure 20 demonstrates the sequential temperature relationships by segment and warming method in controls.

Figure 20: Sequential Mean Infrared Line Temperature Measurements

To summarize the sequential mean infrared line temperature differences:

- Exercise was associated with sustained warming within all segments corresponding to the median nerve.

- Exercise was associated with sustained warming among cases, but not controls, along segments corresponding to the ulnar nerve.

- Lamp warming was unsustained along segments corresponding to the median and ulnar nerves.
An effective warming method should reduce temperature variance in order to optimize inter-subject testing conditions. Therefore, another way to analyze the effect of warming methods is to examine the dispersion (variance) of temperature measurements at baseline, then compare the post-warming and the final reduction in variance. The final (post-testing) comparison provides an indication of how long the effect was sustained.

Figures 21-24 relate to changes in variance across each temperature measurement point. In comparison to other segments, the palm-to-digit V segments were associated with the lowest measures of variance at baseline and subsequently. Lamp warming was associated with significantly lower post-warming variance compared to baseline in all segments except for the palm-to-digit V (ulnar) segment. Exercise warming was associated with significantly lower post-warming variance compared to baseline in all segments except for the wrist-to-digit V (ulnar) segment.

In general, temperature variance increased again from post-warming to final (post-testing) temperature measurements. With regards to lamp warming, the final variance increases observed in all segments only reached significance for the palm-to-digit IIll segment. Nevertheless, the final temperature variance associated with lamp warming was similar to the baseline variation.
Final temperature variance was also higher than post-warming variance in the exercise group. There was an observed increase in variance from post-warming to post-testing (final) temperature measurements, which was significant for the palm-to-digit III and palm-to-digit V segments, but not for the wrist-to-digit III segment. The variation in temperature measurements for the wrist-to-digit V segment continued to decrease, although not significantly. Unlike what was observed following lamp warming, the variation in final temperature measurements following exercise did not approach the baseline variations. This suggests that the reduction in temperature variation may have been somewhat more sustained for exercise warming compared to lamp warming. The variance in the palm-to-digit V segment was an exception. The temperature variance for the lamp warming session was lowest in the palm-to-digit V segment and remained unchanged at the subsequent points of measurement. Figures 21-24 represent graphs plotting sequential temperature variance amongst subjects. Zero on the scale represents a reference point and correlates with a standard deviation of 1. Negative values on the scale correlate with a standard deviation less than one. Positive numbers represent higher variance.
Figure 23: Temperature Variance in Wrist-to-Digit V segment

![Graph showing temperature variance in Ulnar Wrist-Digit V over Baseline, Postwarming, and Final stages for Lamp and Exercise conditions.]

Figure 24: Temperature Variance in the Palm-to-Digit V Segment

![Graph showing temperature variance in Ulnar Palm-Digit V over Baseline, Postwarming, and Final stages for Lamp and Exercise conditions.]

There was less variance at baseline in the ulnar palm-to-digit V segment and correspondingly less change in variance after lamp warming. Note that the variance in temperatures in the palm-to-digit V segment was not significantly reduced by the lamp warming method. Also, post-testing variation in temperature measurements returned to baseline in the palm-to-digit V segment for the exercise group. The warming effect upon variation in temperature measurements was not sustained in the ulnar palm-to-digit V segment, but, in general variance was quite low in this segment.

*Does warming method affect nerve conduction velocity?*

**Mean conduction Velocity by Warming Method: Lamp vs Exercise**

There was no significant difference in mean segmental conduction velocity as a function of warming method. However, it should be noted that exercise warming trended towards slightly faster median nerve conduction. Post-warming temperatures were better sustained in the exercise groups compared to the lamp warming groups and this may account for this trend. Table 14 compares mean conduction velocity associated with lamp warming versus exercise warming.
**Table 14**: Least Square Mean Conduction Velocity by Warming Method:

<table>
<thead>
<tr>
<th>Nerve Segment</th>
<th>Conduction Velocity m/s (SEM)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lamp</td>
<td>Exercise</td>
</tr>
<tr>
<td>Median Nerve Wrist to Digit III</td>
<td>45.53 (1.644)</td>
<td>46.43 (1.669)</td>
</tr>
<tr>
<td>Median Nerve Palm to Digit III</td>
<td>51.60 (1.019)</td>
<td>51.98 (0.978)</td>
</tr>
<tr>
<td>Ulnar Nerve Wrist to Digit V</td>
<td>51.65 (0.976)</td>
<td>52.42 (0.985)</td>
</tr>
<tr>
<td>Ulnar Nerve Palm to Digit V</td>
<td>52.41 (1.560)</td>
<td>53.72 (1.684)</td>
</tr>
</tbody>
</table>

Table 14: m/s=meters per second; NS=nonsignificant; SEM=standard error of the mean

Sample size ranged from 72 to 76 observations for each segment and warming method combination. One subject had incomplete temperature data and was not included in all the analyses.
Does stimulation point affect nerve conduction velocity results?

Mean Conduction Velocity by Technique: Kimura vs Sakakibara

The Sakakibara technique consisted of stimulation at the wrists only. The Kimura technique consisted of stimulation at the wrists and at the palms. Table 15 compares overall mean segmental conduction velocity for the modified Kimura versus the modified Sakakibara techniques. The applied modified nerve conduction techniques resulted in non-significant differences in segmental nerve conduction except for the palm-to-digit V segment.

Table 15: Least Square Means Nerve Conduction Velocity by Technique:

<table>
<thead>
<tr>
<th>Nerve Segment</th>
<th>Conduction Velocity (m/s) (SEM)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Kimura</td>
<td>Sakakibara</td>
</tr>
<tr>
<td>Median Nerve</td>
<td>45.92 (1.621)</td>
<td>46.04 (1.690)</td>
</tr>
<tr>
<td>Wrist to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median Nerve</td>
<td>51.46 (0.925)</td>
<td>52.12 (1.074)</td>
</tr>
<tr>
<td>Palm to Digit III</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>52.04 (0.949)</td>
<td>52.03 (1.013)</td>
</tr>
<tr>
<td>Wrist to Digit V</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ulnar Nerve</td>
<td>50.52 (1.677)</td>
<td>55.60 (1.566)</td>
</tr>
<tr>
<td>Palm to Digit V</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

m/s = meters per second; SEM = standard error of the mean; NS = nonsignificant
Table 16 compares mean segmental nerve conduction velocity results via the Kimura technique versus the Sakakibara technique in cases and controls. The techniques result in significantly different mean conduction velocity for the palm to digit III segment controls, and the palm to digit V segment in cases and controls.

**Table 16: Mean conduction Velocity Comparing Techniques in Cases and Controls**

<table>
<thead>
<tr>
<th>Status</th>
<th>Technique</th>
<th>WD3</th>
<th>P-value</th>
<th>PD3</th>
<th>P-value</th>
<th>WD5</th>
<th>P-value</th>
<th>PD5</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>Kimura</td>
<td>41.60</td>
<td>NS</td>
<td>51.00</td>
<td>NS</td>
<td>52.16</td>
<td>NS</td>
<td>50.03</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Sakakibara</td>
<td>41.54</td>
<td>49.77</td>
<td></td>
<td></td>
<td>52.36</td>
<td></td>
<td>56.38</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Kimura</td>
<td>50.23</td>
<td>NS</td>
<td>51.92</td>
<td>0.048</td>
<td>51.91</td>
<td>NS</td>
<td>51.02</td>
<td>0.0028</td>
</tr>
<tr>
<td></td>
<td>Sakakibara</td>
<td>50.53</td>
<td>54.47</td>
<td></td>
<td></td>
<td>51.69</td>
<td></td>
<td>54.81</td>
<td></td>
</tr>
</tbody>
</table>

Table 16: WD3=wrist to digit III; PD3=palm to digit III; WD5=wrist to digit V; PD5=palm to digit V; NS=nonsignificant; Means=LeastSquare Means

Figure 25 illustrates these findings. Differences in mean nerve conduction velocity are significant for the palm to digit III segment in controls and the palm to digit V segment in cases and controls.
Figure 25: Mean conduction Velocity Comparing Techniques

![Mean Nerve Conduction Velocity graph]

**Figure 25:** WD3=wrists to digits III segment; PD3=palms to digit V segment; WD5=Wrist to digit V segment; PD5=palms to digit V segment; Mean=least square means

Mean conduction velocity was subsequently re-analyzed by excluding the four participants that were tested under warm ambient conditions. The data from fifteen subjects was re-analyzed. Generally, least square means were slower. However, it is unknown if this is a subject effect, an effect of cooler ambient temperatures, a modeling effect, or chance. Table 17 examines the relationship between the Kimura and Sakakibara techniques limited to the subjects under similar (cooler) ambient room temperatures.
Table 17: Mean Conduction Velocity Comparing Techniques
Limited to a Subset of Subjects Tested under Uniform Ambient Room Temperatures

<table>
<thead>
<tr>
<th>Status</th>
<th>Technique</th>
<th>WD3 Value</th>
<th>P-value</th>
<th>PD3 Value</th>
<th>P-value</th>
<th>WD5 Value</th>
<th>P-value</th>
<th>PD5 Value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case</td>
<td>Kimura</td>
<td>39.10</td>
<td>NS</td>
<td>50.96</td>
<td>NS</td>
<td>50.57</td>
<td>NS</td>
<td>50.29</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>Sakakibara</td>
<td>39.96</td>
<td></td>
<td>49.95</td>
<td></td>
<td>50.45</td>
<td></td>
<td>56.52</td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>Kimura</td>
<td>48.79</td>
<td>NS</td>
<td>53.01</td>
<td>0.058</td>
<td>51.74</td>
<td>NS</td>
<td>52.54</td>
<td>0.0063</td>
</tr>
<tr>
<td></td>
<td>Sakakibara</td>
<td>48.86</td>
<td></td>
<td>55.74</td>
<td></td>
<td>51.19</td>
<td></td>
<td>56.44</td>
<td></td>
</tr>
</tbody>
</table>

Table 17: WD3 = wrist to digit III; PD3 = palm to digit III; WD5 = wrist to digit V; PD5 = palm to digit V; NS = nonsignificant; Means = Least Square Means

Reanalyzing the data by excluding the four subjects who were tested under higher ambient room temperatures still resulted in significant differences in nerve conduction velocity between the Sakakibara and Kimura techniques along the palm-to-digit V segment.

Mean nerve conduction velocity along the palm-to-digit V segment was analyzed further. The palm-to-digit V segment was subdivided into quartiles as a function of distance (segment length). Quartile 1 represented the shortest distance length ascending to Quartile 4 which represented the longest distances. Mean conduction velocities obtained via Kimura versus Sakakibara were then compared within each quartile. The quartile analysis did not provide an explanation for differences in mean conduction velocity observed between the Kimura and Sakakibara techniques along the palm-to-digit V segment. Differences in mean conduction velocity between the Kimura and Sakakibara techniques did not vary as a function of distance (segment length). See Table 18 for details.
Table 18: Distance Length Quartile Analysis for Technique Comparison in NCV within Palm to Digit V Segment

<table>
<thead>
<tr>
<th>Quartile</th>
<th>Method</th>
<th>NCV m/s</th>
<th>SD</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Kimura</td>
<td>46.79</td>
<td>1.23</td>
<td>0.0022</td>
</tr>
<tr>
<td>n=38</td>
<td>Sakakibara</td>
<td>52.43</td>
<td>1.36</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Kimura</td>
<td>47.67</td>
<td>1.57</td>
<td>0.5082</td>
</tr>
<tr>
<td>n=38</td>
<td>Sakakibara</td>
<td>49.05</td>
<td>1.38</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Kimura</td>
<td>48.64</td>
<td>1.33</td>
<td>0.0004</td>
</tr>
<tr>
<td>n=38</td>
<td>Sakakibara</td>
<td>55.47</td>
<td>1.38</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Kimura</td>
<td>47.11</td>
<td>1.58</td>
<td>0.0010</td>
</tr>
<tr>
<td>n=38</td>
<td>Sakakibara</td>
<td>54.21</td>
<td>1.47</td>
<td></td>
</tr>
</tbody>
</table>

Table 18: n=number; m/s=meters per second; SD=standard deviation

The relationship between the Kimura and Sakakibara techniques does not differ as a function of length. Figure 26 illustrates this point further.

Figure 26: Quartile Analysis of Palm to Digit V by Distance
Discussion

There are no universally accepted diagnostic criteria for carpal tunnel syndrome. Case definition in epidemiological studies is commonly predicated upon nerve conduction test criteria. However, nerve conduction test results are not specific for carpal tunnel syndrome. Over reliance upon electrodiagnostic criteria runs the risk of misclassification of disease. The predictive value of nerve conduction tests depend, in part, upon the methodology used, and the case-mix under study. Case-mix is difficult to qualify because there are no definitive markers of severity. Descriptions of nerve conduction test methodologies within the epidemiological studies are often incomplete. As a result, it is difficult to accurately assess and compare findings within the medical literature. Thus, it often becomes difficult to distinguish findings such as treatment outcomes from natural history.

The median nerve is a mixed nerve, both anatomically and functionally. It contains a range of small unmyelinated nerve fibers as well as large myelinated fibers. Nerve conduction studies reflect the fastest conducting myelinated fibers. Historically, attempts at increasing the sensitivity of electrodiagnostic criteria have resulted in an increased statistical overlap with normal healthy populations. Of note, in this regard, is evidence that early symptoms of carpal syndrome may result from ectopic discharges of the median nerve, and not actual slowing of nerve conduction. However, further refinement of methodologies designed to improve the
sensitivity and specificity of nerve conduction tests remain an active area of research.

Temperature is recognized as an important source of error in nerve conduction tests. However, the regional anatomical distribution of temperature among various nerve segments and its differential effects on nerve conduction are not well appreciated. Neither is the control of regional temperature as a test variable well understood. Our study examined the impact of regional temperature on segmental nerve conduction in cases of carpal tunnel syndrome compared to healthy controls. Our study also examined the effect of two warming methods, and two methods of temperature measurement. Finally, our study examined the influence of stimulation point on distal nerve conduction.

In general, we found that lamp warming and exercise warming methods were each effective in raising surface skin temperatures. Differences in mean lamp compared to mean exercise post-warming segmental skin temperatures were not significant. Importantly, temperature was dynamic at each stage of testing. As such, the point at which measurements were obtained impacted the results. However, due to the small number of sequential measurements, the level of this impact was not fully quantifiable via our study design.

Ideally, each warming method should result in significant warming from baseline to post-warming that is maintained throughout the testing
period. Therefore, under ideal circumstances one would expect significant increases in temperatures from the baseline to post-warming sequence, but insignificant drops in temperature from the post-warming to final sequence. Mean temperatures differences from the baseline-to-warming sequence were significant for each warming method within all subgroups. However, warming was better sustained following exercise warming compared to lamp warming.

As stated, temperature is an important variable affecting nerve conduction results. Laboratory normative values are determined within a narrow temperature range, typically within a mean temperature range of 31°C to 33°C. However, normative values can be established within any applicable temperature range. For instance, Kimura established his normative values at a minimum range of 34°C. Another laboratory could equally choose to establish normative values at 30°C. Perhaps a more important consideration is the dispersion of temperature within the sample population under study. Effective warming methods must reduce the dispersion of temperature within its sample in order to enable testing under like conditions, both anatomically and from subject to subject. In this study, the subject to subject distribution of temperature dispersion was analyzed using the natural log of the variance for each corresponding nerve segment. The log transformation changes the scale of the data, but preserves their relative ordering. The resulting distribution of the log-transformed variable
approximates normality which facilitates comparisons between samples. In contrast, standard deviation, a commonly used measure of dispersion, is a square root transformation and is positively skewed. As such, it deviates from a normal distribution which complicates comparisons between samples.

The subject to subject dispersion of temperatures from baseline to post-warming was reduced via each warming method. However, exercise seemed to reduce temperature variance in a more sustained fashion, thereby, resulting in more stable testing conditions as well as more consistent subject to subject temperature measures across the testing period. This observation may have significance for establishing normative values in populations under study and help distinguish disease states from normal.

A potential confounder in this study was the uncontrolled ambient room temperatures. However, the biostatistical model found that the effect of room temperature was the same across levels of warming method, point temperature measurement method, and subject classification. Furthermore, there were no significant differences in ambient temperatures between cases and controls. The mean ambient room temperature for cases was 21.90°C (Minimum 20.2°C, Maximum 27.6°C); the mean ambient room temperature for controls was 22.65°C (Minimum 20.3°C, Maximum 27.2°C). Interestingly, skin temperatures were generally warmer for cases compared to controls at most measurement points, despite slightly cooler ambient room temperatures for cases. This finding may reflect autonomic function differences between
cases and controls. Skin temperatures were also better sustained in the exercise warming groups compared to lamp warming groups. It remains uncertain if this latter finding represented a true physiologic difference, a response to different ambient temperature conditions, or random findings. Repeating this study under controlled ambient temperatures may help clarify this question and reduce the likelihood of a Type 1 Error.

Importantly, data points on the graphs depicting temperature trends broken down by the smallest subgroups (e.g., segmental cases/control-lamp/exercise subgroups) were generated from small sample sizes. Specifically, at this level of analysis, each data point represented a number as small as seventeen to twenty observations thus raising concerns about random error due to a small sample size. These graphs should be viewed with caution in order to avoid misinterpretation. Nevertheless, when viewing the graphs in total, there appeared to be consistent trends. Skin temperatures in cases seemed warmer than controls. Skin temperature in cases seemed to be associated with less variance compared to controls.

The discordant findings between the Kimura and Sakakibara techniques along the palm-to-digit V segment are difficult to explain. Reproducibility of nerve conduction tests across short segments is a well recognized problem. As previously stated, Landau projects a twenty percent error rate for segments shorter than six centimeters. In our study, the palm-to-digit V segment of the ulnar nerve represented the shortest segments that
were tested. Notably, nerve conduction velocity differed significantly between the Sakakibara and the Kimura techniques along this segment. For this reason, we subdivided the palm-to-digit V segment into ascending quartiles by distance. Quartile 1 represented the shortest distances whereas Quartile 4 represented the longest. Quartile analysis did not reveal a pattern that would implicate distance as an explanation for the differences between the Sakakibara and Kibara technique. Another possible explanation includes differences in nerve recruitment based upon a more distal stimulation point in the Kimura technique. However, this explanation also seems unlikely because nerve conduction reflects only the fastest myelinated fibers. A third possible explanation relates to the temperature instability during the testing period. However, temperature related explanations seem unlikely given the positive responses to warming techniques along palm-to-digit V segment and the relatively low subject-to-subject temperature variance observed in this segment throughout the testing period. Perhaps the explanation lies in differences in latency onset between proximal and distal stimulation points. However, any such difference was not evident along the palm-to-digit III segment where the Kimura and Sakakibara techniques compared more closely. Other unknown reasons, including chance, are possible.

Although mean nerve conduction velocity did not differ significantly as a function of warming method, this study had low power to reject the null hypothesis due to the small sample size. Detailed analysis of the data
revealed interesting trends. For instance, it appears that mean nerve conduction velocity was slightly faster, albeit insignificantly so, for the exercise group even though mean post-warming surface skin temperatures appeared somewhat cooler. Conceivably this finding could have resulted from physiological differences at the level of the nerve that were not measured. It has been noted that the temperature effects from exercise seemed more sustained than those from lamp warming. Again, repeating this study under warmer controlled ambient room conditions might reduce the variability in temperature measures and lead to different findings. Continuous temperature monitoring would also serve to better quantify temperature relationships to nerve conduction.

The capacity to distinguish disease within the digital segments of the median and ulnar nerves as distinct from focal disease confined to carpal nerve segments is limited. This differentiation is especially important in the setting of vibration exposure where, for reasons already described, carpal tunnel release has resulted in mixed outcomes. The technique developed by Sakakibara, et. al., was intended to identify and differentiate disease within each segment. Our findings shed doubt in this approach. None of our subjects had a history of significant vibration exposure. Yet, nerve conduction velocity was significantly slower in the palm-to-digit segments of the median nerve in our subjects with presumed isolated carpal tunnel syndrome.
Electrodiagnostic studies often compare segmental conduction within similar nerves in order to identify disease. In this regard, segmental conduction of the median nerve is often compared to that of the ulnar nerve. Therefore, one could propose that conduction along the palm-to-digit segments of the median and ulnar nerves could likewise be compared. However, the poor correlation between the Sakakibara and the Kimura techniques within the palm-to-digit V segment of the ulnar nerve raises concerns about the suitability of this comparison. Given the instability of the palm-to-digit V findings in our study, comparing the median palm-to-digit segmental results to the ulnar palm-to-digit segmental results does not seem feasible. Further refinement and control of testing conditions may mitigate this concern. Controlling ambient room temperature has already been discussed. Another modification that could be considered is the addition of arm exercises as a warming technique. Finally, given the dynamic nature of temperature, future studies should implement continuous temperature monitoring.
References


Anbar, M. Quantitative Dynamic Telethermometry in Medical Diagnosis and Management. Boca Raton, Florida: CRC Press. 1994


