Original article

Quantification of heat threshold and tolerance to evaluate small fiber neuropathy- an indigenously developed thermal model of pain

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ABSTRACT

Introduction: A wide variety of diseases alter the perceptions of different sensations, often evaluated in a subjective manner. Assessment of temperature perception and tolerance is a useful screening tool to evaluate the Degenerative and neuropathic changes of an individual. Therefore the current study was intended to design and develop an inexpensive device to quantify the heat threshold and tolerance in healthy participants.

Materials and methods: The study was carried out in 30 apparent healthy participants for heat threshold, and tolerance was recorded on both hands' thenar and dorsal sites on two occasions. The minimum temperature when the subject was perceived is threshold and maximum until the subject withstood tolerance. The data was collected using the electronically controlled device for these two extremes. The entire study was carried out at a controlled room temperature precisely.

Results: The heat threshold was 39.84 ± 2.33 °C, and the tolerance was perceived at 46.84 ± 3.36 °C. There were no intraindividual differences ($p > 0.05$) in the heat threshold measured on two different periods as well as between the two hands ($p > 0.05$). As expected, there were significantly higher threshold values on the palm's thenar aspect than dorsum ($p < 0.05$). The tolerance was significantly higher in the thenar aspect than the dorsum of both hands. ($p < 0.01$, $p < 0.03$). There were no significant inter-hand differences of both surfaces of the hand.

Conclusion: Our study showed that the results of threshold and tolerance using the indigenously built device were consistent and reproducible proves the robustness of the methodology. It is a cost-effective and user-friendly device that provides quantitative results of temperature extremes.

1. Introduction

The peripheral nerve fibers convey various sensations from peripheral organs to cortical sensory areas. These fibers are classified into A, B & C fibers based on their diameter, myelination, and conduction velocity. C fibers are responsible for controlling autonomic balance, slow pain & temperature conduction.¹ They are unmyelinated, less in conduction velocity (<2 m/s). The degenerative changes in these fibers due to various reasons cause small fiber neuropathy.^{2,3} The primary etiological elements for small fiber neuropathy are Diabetes, hypothyroidism, endocrine disorders, hereditary diseases, and other potentially infectious diseases.⁴ The symptoms of small fiber neuropathy are highly

variable includes burning, tingling, prickling, and the common is short bursts of pain.⁵ These symptoms often extend in limbs as "stocking-glove distribution." It also cultivates autonomic derangement, which primes disturbance in visceral organs.⁶

Small fiber neuropathy often diagnosed using various electrophysiological procedures like nerve conduction studies, electromyography (EMG) in addition to imaging techniques. However, these fibers having small diameters and cannot implement these tests to evaluate functional impairment.⁷ The classic test to assess the small fiber injury is temperature and pain perception. Quantification of experimental pain depends on the type of noxious stimuli used, their application, and the assessment method where the stimuli are often applied in fixed or ascending

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Fig. 1. Thermal model of Pain Device with components

1) temperature organizing box, 2) heat-producing metal plate (LM-35 thermal sensor), 3) temperature control button for participant safety, 4) PC for real time thermometry with oscilloscope (DAQ smart).

magnitudes.⁸ They can be assessed using threshold and tolerance measurements and subjectively characterized by pain scores.⁹ The temperature perception has two extremes, minimal heat threshold (MHT) and maximum temperature tolerance (MTT). Hence these quantitative objective variables of temperature perception provide potential information about small fiber function.^{10,11} We designed and developed a household device to quantify temperature threshold and tolerance, reflecting small fiber activity. Therefore, we focused on the psychophysics of heat stimuli when applied to the thenar and dorsum of the hand and digitized the data of two extremes of perception and tolerance. Thus, The present study aimed to characterize the device and established methodology for MHT and MTT in healthy participants.

2. Materials & methods

2.1. Instrument design

The computer-based electronically controlled heat-producing device is an in-house built tool using a USB DAQ –Oscilloscope for data acquisition. It has four components A) temperature organizing box, B) heat-producing metal plate, C) temperature control button for participant safety, and D) PC for real time thermometry. The temperature sensor used in the system was a fast response pre-calibrated IC-LM35 with a response time of less than 2 s. The heating device was a solid-state semiconductor-based heater with a cross-sectional area of 1 sq. cm and is controlled electronically. The data was displayed on the oscilloscope of the DAQ application as shown in [figure - 1](#).

2.2. Study population

The study protocol was reviewed and approved by the Institutional ethic committee, Narayana Medical College and Hospital, Nellore. The study was carried out in the 30 participants who are medical students and other technical staff of the hospital premises acquainted with the investigator using non – random sampling technique (Convenient sampling). Apparent healthy participants aged between 18 and 25 years were recruited into the current study. The subjects with a history of known acute or chronic medical illness, chronic smokers, alcoholics, and intake of centrally-acting drug patients were excluded from the study. The entire procedure was explained to each participant and their right to withdraw from the study at any time. According to the Declaration of Helsinki (1975) and later amendments, written informed consent was obtained from all participants. There were 13 males and 17 females

Table 1

Shows heat threshold and Tolerance.

Threshold	Mean		39.84
	95% Confidence Interval for Mean	Lower Upper	39.32 40.36
	Median		39.90
	Std. Deviation		2.33
	Minimum		34.7
	Maximum		46.2
	Range		11.5
Tolerance	Mean		46.84
	95% Confidence Interval for Mean	Lower Upper	46.09 47.59
	Median		46.40
	Std. Deviation		3.36
	Minimum		40.60
	Maximum		58.60
	Range		18.00

among the participants recruited for the study. The room temperature at which this protocol was executed was 32–35 °C to avoid confounding results on the outcome. The data acquisition was executed in the participants to record threshold and tolerance after explaining the procedure and demonstrated one trial to each participant. Later, the two extremes of temperature perception were measured two times in the thenar and dorsum aspect of the hand and two successive days to find out the reproducibility.

2.3. Outcome measurement

The outcome was measured in terms of two extremes of temperature.

2.3.1. Minimum heat threshold (MHT)

The minimum temperature at which the subject is perceived the warmth in the device. The dorsum of the hand is placed over the heated metal, and the device was heated up until the subject is felt the warmth. The subject also receives a safety control button to let us know the perception point of temperature. The same procedure is repeated on another side (thenar aspect) of the hand, and twice the data is recorded at each location with an interval of 20 min.

2.3.2. Maximum temperature tolerance (MTT)

It is the maximum temperature at which the subject cannot tolerate further heat. The subject can press the standard control button to let us know the threshold and tolerance recorded on the computer screen. This procedure was also repeated on both sides as well as in both hands of each participant.

2.4. Statistical analysis

The data analysis was carried out using 'R' software. The data sets were represented as Mean $\pm$ SD. The normality of data was tested using the Kolmogorov-Smirnov test. Descriptive statistics were analyzed and expressed for each variable of temperature. As the data sets were skewed from a normal distribution, non-parametric tests were implemented to determine differences between the thenar and dorsum of the hand.

3. Results

The mean age of the participants was 18 ± 1.5 years. The mean threshold temperature (MHT) was 39.84 ± 2.33 °C, whereas the tolerance was experienced at 46.84 ± 3.36 °C, as shown in [Table - 1](#). There were no intraindividual differences ($p > 0.05$) in pain threshold as measured on two different periods. Similarly, the threshold values were statistically similar between the two hands ($p > 0.05$). As expected, there

Table 2

Effect of Period, dexterity and site on heat Threshold (MHT).

Recordings	Dexterity	Site	Mean	SD	Median	Min	Max	p-value
Primary	Left	Dorsum	39.2	2.4	39.6	34.7	43.5	$p < 0.05$
	Left	Thenar	40.8	1.9	41.1	37.6	44	
	Right	Dorsum	39	2	39.1	35.7	42	$p > 0.05$
	Right	Thenar	40.4	2.6	41.1	36.1	46.2	
Secondary	Left	Dorsum	39.8	2.1	40.6	36.2	42.5	$p < 0.05$
	Left	Thenar	41.1	1.8	41.5	36.2	43.5	
	Right	Dorsum	39.8	2.1	40.6	35.2	42.5	$p > 0.05$
	Right	Thenar	40.7	2.6	40.9	36.1	46.4	

Table 3

Effect dexterity and site on heat tolerance (MTT).

Dexterity	Site	Mean	SD	Median	Min	Max	p-value
Left	Dorsum	45.54	2.27	45.05	42.5	49.3	$p < 0.01$
	Thenar	48.29	3.78	47.40	43.9	58.6	
Right	Dorsum	45.45	2.53	45.10	40.6	50.5	$p = 0.03$
	Thenar	48.12	3.67	47.65	43.5	53.5	

All the numerical values are expressed in Celsius.

were significantly higher threshold values on the thenar aspect of the palm than dorsum ($p < 0.05$), as shown in Table – 2. The tolerance of temperature (MTT) was significantly higher in the thenar aspect of the palm than the dorsum surface of both hands ($p < 0.01$, $p = 0.03$), as displayed in Table – 3. However, there were no significant differences between both hands ($p > 0.05$ – Results were not displayed).

4. Discussion

The current study was intended to evaluate the characterization and robustness of an indigenously developed & in-house built device for heat threshold and heat tolerance in healthy participants.

The non invasive and quantitative assessment of any variable would be more informative in order to screen and diagnose subclinical conditions. There is enormous transition in the electronics and it has been even encroached in medicine for various purposes. The authors of current study has been working on inexpensive and non invasive evaluation of autonomic neuropathy using heart rate variability, dynamic pupillometry.^{12,16} In addition we are also working on utility of sensory perception interms of heat threshold and tolerance provide us the broad range of peripheral nerve conduction especially small fiber activity.

The lab - based assessment of individual changes in pain sensitivity can predict differences in acute, chronic pain, and prognosis. Jensen TS et al. (1991) concluded that the clinical applications of their findings are broad and quite important. However, performing sophisticated quantitative sensory testing requires time, expertise, and equipment not readily available in many clinical settings. It would be helpful to know whether simply enquiring participants about their pain sensitivity provides information similar to that obtained from experimental pain testing.¹³ The experimental and clinical studies on acute pain have shown that women are more sensitive to pain. Schaffner N et al. (2008) showed that men have a higher pain tolerance than women for induced heat pain. The still reduced number of subjects prevent from computing normative estimates. Nevertheless, in assessing the basic psychophysical properties of pain threshold and tolerance, their data may contribute to a more conclusive interpretation of brain imaging studies aiming to assess laterality effects.¹⁴ However in our study, we did not concentrate on gender discrimination in perception of heat threshold and tolerance. But we found there was a significant change in both surfaces of hand due to thickness of the skins. It can be attributed to anatomical variation temperature perception. But there is difference was found out between two hands indicate symmetrical sensory perception. However, some studies have postulated cerebral dominance can discriminate the threshold and tolerance of heat.¹⁵ A familiar feature in diabetic

neuropathies is emerging painless ulcers, which remain unnoticed in quite a few patients. We, therefore, introduced a warm-sensitivity index in which heat is perceived but not reported as painful.¹⁷ We believe that this measure may be a screening tool in witnessing deterioration of small nerve fiber service in neuropathies.¹⁸ Further studies are necessary to establish the reproducibility and validity of this measure. However, we would note that the reproducibility of the thermal threshold measures has been demonstrated in several previous studies as mentioned earlier. There is paucity in literature and few studies were performed in his domain. Revealing of early and subclinical neuropathy is an important task in the treatment and handling of diabetic patients. The neuropathies are clinically and electrophysiological heterogeneous, and there is no simple relationship between peripheral nerve function and glycemic control.

5. Limitations

The present study has some limitations. This study was only established in healthy volunteers who are acquainted with the investigator. The results can not generalize and the study was intended to prove the concept rather to provide results. The sample size was less, and relationships with other dependent variables were not established. This protocol will be extrapolated in different neuropathic patients to characterize the study results for accuracy and reliability.

6. Future steps

The device utility will be revealed by extending the study in multiple suspected population and implementing appropriate study designs. The robustness of methodology and execution will be further unveiled during data collection. The data analysis will be done by developing the platform to produce automated results.

7. Conclusion

The current study reports suggest consistent and reproducible values in heat threshold and heat tolerance to the thermal model of pain with little variations. It is cost-effective, a portable, user-friendly device that provides reliable readings to evaluate small fiber neuropathy and response to treatment quantitatively.

Ethical considerations

The study design was reviewed and approved by the host institution's Institutional Ethics committee.

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Declaration of competing interest

On behalf of all the authors, the corresponding author states no

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