Current Perception Threshold Testing in Chronic Ankle Instability

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Research article

Keywords: Chronic ankle instability, Current perception threshold, Sensory nerve function

Posted Date: October 23rd, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-48846/v1>

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Abstract

Background: Damage to sensory input is one of the pathologies underlying chronic ankle instability (CAI). Therefore, it is necessary to evaluate the sensory function of patients with CAI. This study aims to quantitatively evaluate sensory nerve function in patients with CAI and healthy controls using current perception threshold (CPT) measurements.

Methods: Fifty-nine subjects with CAI and 30 healthy control individuals participated in this study. CPT values at the anterior talofibular ligament region were tested on the injured and uninjured sides in CAI patients and on a random side in the healthy control group.

Results: There were no significant differences in age, gender, height, weight or BMI between the CAI and healthy control groups. The CPT values did not show significant gender differences. The CPT values were not significantly correlated with age or BMI. Compared to the control group (250 Hz: 24.32 ± 9.28 , 5 Hz: 6.87 ± 1.56), the CAI group had significantly higher CPT values on the injured (250 Hz: 42.83 ± 28.49 , 5 Hz: 23.43 ± 18.53) and uninjured sides (250 Hz: 38.62 ± 19.98 , 5 Hz: 18.84 ± 14.21) under 250 Hz and 5 Hz electrical stimuli ($p < 0.01$). No significant difference was observed under 2000 Hz stimuli. There were correlations among CPT values at different frequencies ($p < 0.01$).

Conclusion: This study revealed increased sensory thresholds in injured and uninjured ankles of 250 Hz- and 5 Hz-related sensory nerve fibers among patients with CAI. The bilateral change in sensory threshold may indicate a central sensory modulation process.

Level of Evidence: Level III, case-control study.

Background

Ankle sprain is one of the most common injuries in daily life and sports. Up to 70% of individuals who sustain an acute ankle sprain may develop residual physical disability [1]. Perceived instability and repetitive ankle sprains are known as chronic ankle instability (CAI) [2]. The underlying neurophysiological mechanism of CAI remains unclear. CAI is divided into mechanical CAI and functional CAI [3]. Mechanical CAI is due to laxity of the ankle stabilizing structures (ligaments, joint capsule, and tendons) [2, 4]. Functional CAI is attributed to deficient proprioceptors in the soft tissue. Although no mechanical instability is detected, there is a sensory function disorder that impacts sensory input and results in recurrent ankle sprains [5]. The two types of instability can exist independently of one another but often occur together [6].

Postural control is dependent on integrated sensory input, central information processing in the central nervous system, and motor output [7]. Errors in the joint repositioning test have been used in assessing CAI-associated deficits in joint proprioception. An increase in errors in ankle joint repositioning was reported [5]. Cho et al [8] used an isokinetic test and showed decreased joint position sense in CAI participants.

Sensory function can be evaluated subjectively and objectively [9]. Subjective evaluation is performed by physical examinations. For example, the pinprick test and vibration sensory test. However, it is difficult to standardize and quantify these subjective tests. Objective measurements, which are quantitative measurements, are compatible. The two-point discrimination test, thermal pain threshold test, filament-prick pain threshold test, pressure pain threshold test, and joint position sensory test could be measured quantitatively. In this regard, current perception threshold (CPT) testing can selectively evaluate the A-beta, A-delta, and C fibers for sensory nerves. A-beta fibers are large myelinated fibers that can be activated by 2000 Hz electrical stimuli, which transmit pressure and tactile messages; A-delta fibers are thinly myelinated fibers that can be activated by 250 Hz electrical stimuli, which transmit fast pain; and C fibers are unmyelinated fibers that can be activated by 5 Hz electrical stimuli, which transmit slow pain [10, 11]. The Neurometer® CPT/C is a transcutaneous electrical stimulator that delivers sinusoidal electrical stimuli via surface electrodes [12]. CPT testing can be performed on any skin/mucosa area of the body and has been used in the evaluation of diabetic neuropathy [13, 14], diabetic foot problems [15], carpal tunnel syndrome [16], fracture [9], peripheral nerve injury [17], pain [18], restless legs syndrome [19] and other clinical disorders. To the best of our knowledge, there is no report describing CPT in CAI patients.

Therefore, the aim of this study was to quantitatively evaluate sensory nerve function at the anterior talofibular ligament region using CPT measurements.

Methods

This was designed as a case-control study.

Patients

Fifty-nine subjects with CAI (male: 10, female: 49) and 30 healthy controls (male: 8, female: 22) recruited from a regional hospital from April 2017 to November 2018 participated in this study. Healthy controls were staff and medical students in the hospital. The inclusion and exclusion criteria for patients with CAI were selected according to criteria from the International Ankle Consortium [20]. The inclusion criteria for the CAI group were (1) at least 1 significant lateral ankle sprain, resulting in inflammatory symptoms and 1 or more days of activity time loss. The initial sprain occurred at least 12 months prior to the study. The most recent injury occurred at least 3 months prior to the study. (2) A continuing feeling of “giving way” and/or recurrent sprain and/or “instability”. Individuals in the healthy control group had never experienced an ankle sprain or episode of instability. The exclusion criteria for both groups were (1) previous lower limb surgery, fracture or acute injuries to the musculoskeletal structures, and (2) neurologic disorders or other systemic diseases such as diabetes mellitus that impact foot and ankle sensation and/or function.

This study was conducted in accordance with the Declaration of Helsinki. Participants read and signed an informed consent form approved by the ethics committee of our hospital prior to the study.

Current Perception Threshold (CPT) Measurement

CPT measurements were performed using a neurometer (Neurotron, Baltimore, MD, USA). A CPT value of 1 is equal to an output intensity of 0.01 mA with an available maximum of 9.99 mA. The stimuli were applied to the skin of the anterior talofibular ligament region (superficial peroneal nerve, L5 dermatome) of the injured and uninjured ankle in participants with CAI by a well-trained doctor. The order of the test side was randomly assigned. The electrical stimuli were delivered through two 10 mm diameter gold-plated electrodes at frequencies of 2000 Hz, 250 Hz and 5 Hz to the tested site. The electrical stimuli were increased slowly until the participants reported a sensation of stimulation. The current then rapidly decreased and increased until the same threshold measure was obtained on at least three consecutive trials [10]. The CPT was defined as the minimum electrical stimulus sensed by the participants [14]. To prevent guessing, “no” stimulation was randomly delivered. The testing ankles of healthy controls were randomly assigned by random number software. The experiment was conducted in a quiet room in the hospital.

Statistical Analysis

Statistical analyses were performed using SPSS 26.0 (IMB Co., Inc., Chicago, USA). The normality of the variable distribution was evaluated using the Kolmogorov-Smirnov test. Continuous data were expressed as the meanstandard deviation (SD). Group comparisons of all variables were performed using independent t-tests for two groups and ANOVA for three groups with normally distributed data. Nonparametric Mann-Whitney tests for groups with nonnormally distributed data. The chi-square test was used for categorical data. Multiple linear regression analysis was used for correlation of impact factors. Statistical significance was defined as $p<0.05$.

Results

Demographic Data

No significant between-group differences were present for age, gender, height, weight or body mass index (BMI) (Table 1).

Table 1 Participant Demographics

	CAI	Healthy	p
	(n=59)	(n=30)	
Age, y	31.6810.36	29.709.11	0.378
Sex	Male: 10♀Female: 49	Male: 8♀Female: 22	0.403
Height, m	1.640.08	1.670.08	0.060
Weight, kg	60.9113.34	66.9317.95	0.252
BMI, kg/m ²	22.433.54	23.594.81	0.199
Time since last ankle sprain, m	12.7516.31		

CAI/Chronic ankle instability, BMI/body mass index

Comparisons of the CPT Values Between Groups

CPT values are reported in Table 2. Significant group differences existed for CPT values at 250 Hz and 5 Hz. In the between-group comparison, both the injured and uninjured sides of the CAI group showed higher CPT values than healthy controls ($p<0.001$). No significant differences were found between the injured and uninjured sides of the CAI patients. (Figure 1).

Table 2 Comparison of CPT (mA*100) of the anterior talofibular ligament region

	Injured side	Uninjured side	Control	p
	(n=59)	♂n=59♀	(n=30)	
2000 Hz	194.8064.58	217.8192.19	222.40	0.144
250 Hz	42.8328.49	38.6219.98	24.329.28	<0.01
5 Hz	23.4318.53	18.8414.21	6.871.56	<0.01

CPT/Current perception threshold

Comparison of CPT values in different genders with CAI

No significant differences were found between the male and female groups with CAI. (Table 3)

Table 3 Comparison of CPT (mA*100) in different genders

	Male	Female	p
	(n=10)	(n=49)	
2000 Hz	221.7082.47	189.3159.85	0.150
250 Hz	38.1025.38	43.8029.23	0.569
5 Hz	24.6321.60	23.1918.08	0.825

CPT Current perception threshold

Correlations among age, BMI and CPT values

There was no significant correlation between CPT value and age. No significant correlation between CPT value and BMI was observed either. (Table 4)

Table 4 Table 4 Multiple correlation analysis of influencing factors

	2000 Hz		250 Hz		5 Hz	
	r	p	r	p	r	p
Age	0.216	0.101	0.194	0.142	0.192	0.146
BMI	-0.198	0.133	-0.200	0.129	-0.153	0.248

BMI body mass index

Correlation among CPT values at different frequencies

There were significant correlations among CPT values at different frequencies. The CPT values at each frequency were significantly correlated with the CPT values at the other two frequencies. (Table 5)

Table 5 Multiple correlation analysis of CPT at different frequencies

	r	p
2000 Hz-250 Hz	0.419	<0.01
2000 Hz-5 Hz	0.459	<0.01
250 Hz-5 Hz	0.834	<0.01

Discussion

The pathogenesis of CAI is very complicated. Most ankle sprains influenced the anterior talofibular ligament. Therefore, we tested the CPT values in this area of the injured and uninjured ankle. The results showed that compared to healthy controls, patients with CAI had higher CPT values at 250 Hz and 5 Hz

electrical stimuli, which were related to fast-pain related myelinated A-delta and slow-pain related C fibers of the sensory nerve, respectively.

Sensory disorder is one of the pathophysiologic changes in CAI. Due to injury to the receptors in the ligaments, capsule, and tendons of the ankle, sensory function becomes impaired [2]. Receptors include mechanoreceptors and nociceptors. Mechanoreceptors received tactile, pressure, and motor information. Nociceptors received thermal and pinprick information.

Using the CPT tests, the different subgroups of sensory nerve fibers could be directly stimulated and tested. The Neurometer® CPT/C can stimulate 3 types of sensory nerve fibers. Thus, the quantitative evaluation of different sensory nerves is available. Griffioen et al [21] showed higher CPT under 2000 Hz and 250 Hz stimuli in patients with chronic pain following lower extremity fracture. Liao et al [22] measured CPT in trigeminal neuralgia patients and found that CPT under 5 Hz stimulus decreased in the acute stage but increased in the chronic stage. In our study, CAI patients showed increased CPT values under 250 Hz and 5 Hz stimuli.

Previous studies have reported postural control deficits of the bilateral limb after unilateral ankle sprain and CAI, suggesting central organization altered after ankle sprain [7, 23]. Terada et al [24] used transcranial magnetic stimulation to evaluate corticospinal excitability and reported a potential increase in corticospinal inhibition in CAI. Rosen et al [25] used functional near-infrared spectroscopy to study cortical activation and found larger cortical activation variability in CAI. A systematic review reported decreased neural excitability of the soleus and the fibularis longus in CAI patients using the H-reflex, a spinal reflex [26]. Consistently, in our study, both the injured and uninjured sides showed increased CPT values under 250 Hz and 5 Hz stimuli, and these changes suggested central sensory adaption in CAI.

In consideration of gender, age and BMI effects, previous studies showed inconsistent results. Uddin et al [18] reported that age and gender were not correlated with CPT scores. Nakatani-Enomoto et al [27] reported higher CPT in men than in women and in older individuals than in young subjects. In this study, there was no correlation between gender, age and BMI factors and CPT values at any frequency. The inconsistency may be due to the different sample sizes and objectives of the studies.

Correlations among CPT values at different frequencies were found in our study. Participants with higher CPT values under one frequency showed trends of higher CPT values under other frequencies. This may be caused by individual variability. The correlations may reflect the consistency of the sensory threshold test using CPT measurements.

However, there are some disadvantages in CPT tests. These testing procedures require participant reaction and feedback, similar to the hearing test. Thus, they are not entirely objective methods. Nerve conduction velocity measured by electromyography is an objective measurement, but until now, there have been reports of lower motor nerve conduction velocity [28] rather than sensory nerve studies. The conduction velocity can reflect the function of large myelinated fibers [29].

There are some limitations in this study. First, this was a case-control study conducted in a tertiary referral center, and unknown selection bias might have affected the study results. Second, only CPT values at the anterior talofibular ligament region were measured, and future studies are needed to investigate the CPT values at more sites of the lower extremities in CAI subjects. Studies of the relations between CPT and other sensory tests are also needed.

Conclusion

This study revealed increased sensory thresholds in injured and uninjured limbs of 250 Hz- and 5 Hz-related sensory nerve fibers among patients with CAI. The bilateral change in sensory threshold may indicate a central sensory modulation process.

Abbreviations

CAI: chronic ankle instability; CPT:current perception threshold; BMI:body mass index.

Declarations

Acknowledgements

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

The datasets during and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Authors' contributions

RZ participated in the data collection/analysis and writing of the manuscript; XZ participated in the data collection and data analysis; YC and WS provided experimental guidance during this study and revised this paper critically for important intellectual content. All authors read and approved the final manuscript.

Ethics approval and consent to participate

This case-control study involving human participants was conducted in accordance with the ethical standards of the ethics committee in Beijing Tongren Hospital Capital Medical University and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Written consent to participate was provided by participants included in the study.

Competing interest

The authors declare that they have no competing interests.

Funding

The authors received no financial support for this research.

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Figures

Figure 1

CPT values in different test sites under 3 frequencies