American Pain Society
RESEARCH
EDUCATION
TREATMENT
ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 16, No 3 (March), 2015: pp 207-213
Available online at www.jpain.org and www.sciencedirect.com

Original Reports

Diurnal and Nocturnal Skin Temperature Regulation in Chronic Complex Regional Pain Syndrome

Johanna C. M. Schilder,* Sjoerd P. Niehof,† Johan Marinus,* and Jacobus J. van Hilten*

**Department of Neurology, Leiden University Medical Center, Leiden, The Netherlands.*
†Department of Experimental Anesthesiology, Erasmus Medical Center, University Medical Center, Rotterdam, The Netherlands.

Abstract: **Skin temperature changes due to vasomotor disturbances are important features of complex regional pain syndrome (CRPS). Because this phenomenon has only been studied under controlled conditions, information on daily circadian variability is lacking. Also, studies in chronic CRPS patients with abnormal posturing, in which coldness of the affected extremity is more common, do not exist. We examined the response to external heating as well as circadian temperature changes over several days in the affected legs of 14 chronic CRPS patients with abnormal posturing and 17 controls. Skin temperatures were recorded hourly for 14 days using wireless sensors. Although the patients' affected extremities were significantly colder before external heating, the vasodilatory response was similar in the 2 groups. Additionally, median skin temperature differences between both legs and their variability was larger in patients than in controls during the day, but not during the night. These findings indicate that the mechanisms underlying impaired skin circulation in CRPS during daytime are reversible under certain circumstances. The large variation in skin temperature differences during the day questions the validity of using a single measurement in the diagnosis of CRPS, and our results indicate that only temperature differences >1.0°C should be considered to reflect vasomotor disturbances.**

***Perspective:** This article shows that chronic CRPS patients have a normal vasodilatory response to external heating and that skin temperature differences between the affected and unaffected lower limbs, which were highly variable during daytime, disappeared during sleep. This indicates that part of the vasomotor regulation in these patients is still functional.*

Key words: *Complex regional pain syndrome, skin temperature, thermoregulation, vasomotor disturbances.*

Skin temperature changes of the affected limb are an important characteristic of complex regional pain syndrome (CRPS).[28] In the acute phase of the syndrome the skin temperature of the affected side is commonly perceived as warmer than the nonaffected limb, whereas in the chronic phase (>6 months) the clinical presentation may reverse.[28] However, about 20 to 30% of patients have a cold extremity from onset,[3,15] and in some cases the skin temperature of the affected extremity continuously varies between cold and warm.[13,30]

Skin temperature disturbances, addressed from both the patient's and clinician's perspectives, play a prominent role in the Budapest diagnostic criteria of CRPS.[9] Little is known, however, about skin temperature variability under normal daily circumstances. Because variability of skin temperature may affect the validity and reliability of information obtained for the diagnostic criteria, knowledge of its daily behavior may contribute to improvement of the diagnostic process and eventually improve classification of patient subtypes in this heterogeneous syndrome. Additionally, little is known about nocturnal skin temperature regulation in CRPS. Because dermal

Received August 11, 2014; Revised October 29, 2014; Accepted November 22, 2014.
This study is part of TREND (Trauma RElated Neuronal Dysfunction), a Dutch Consortium that integrates research on epidemiology, assessment technology, pharmacotherapeutics, biomarkers, and genetics on CRPS type 1. The consortium aims to develop concepts on disease mechanisms that occur in response to tissue injury, its assessment, and treatment. TREND is supported by a grant of the Dutch Ministry of Economic Affairs (BSIK03016). The authors declare that there are no conflicts of interest.
Address reprint requests to Johanna C. M. Schilder, MD, Department of Neurology, Leiden University Medical Center, P.O. Box 9600, 2300 RC Leiden, the Netherlands. E-mail: j.c.m.schilder@lumc.nl
1526-5900/$36.00

http://dx.doi.org/10.1016/j.jpain.2014.11.012

vasomotor changes are important in the circadian regulation of body heat loss and are associated with sleepiness and sleep induction,[10] information on skin temperature behavior before and during sleep in the affected extremity may aid to further clarify the pathophysiology of blood flow disturbances in CRPS.

There are some indications that abnormal posturing in CRPS is related to coldness.[5] Though this may suggest a more prominently impaired thermoregulation in this subtype of the condition, proper studies on skin temperatures in these patients have not been conducted. Therefore, we examined the response to external heat perturbation as well as diurnal and nocturnal temperature variability over several days in chronic CRPS patients with an affected limb that was also characterized by abnormal posturing.

Methods

Participants

Fourteen patients with CRPS type 1 of 1 lower extremity and a disease duration of at least 6 months and 17 healthy controls were included in the study. All patients fulfilled the Budapest clinical criteria for CRPS[9] and suffered from abnormal posturing—most commonly a fixed plantar flexion/inversion position of the ankle in combination with restrictions in range of motion,[20] because data in the present paper were collected as part of a wider study on abnormal posturing in CRPS.[23] Patients were recruited from the outpatient clinic of the neurology department of the Leiden University Medical Center. Control subjects were excluded if they suffered from peripheral vascular disease or other conditions that impaired lower limb function, based on their medical history. The study was approved by the local medical ethics committee, and informed consent was obtained from all participants.

Measurements

Two approaches were used to investigate thermoregulation of the lower limbs in patients and controls: 1) external heat perturbation and 2) long-term skin temperature registration during normal daily circumstances.

External Heat Perturbation and Effect on Skin Temperature

Skin temperatures were measured in both feet with a surface thermometer (Testo quicktemp 825-T4; Testo, Lenzkirch, Germany) while participants were sitting upright in a chair with both bare feet on the floor, after a 15-minute acclimatization period in a room of 22 to 23°C (baseline measurement [BM]). A template was used to ensure exact (re)localization of the thermometer in each participant, that is, medially at 5 locations at the dorsum of the foot, which data were averaged afterwards. Both feet were then heated in a water bath at 37 to 39°C for 5 minutes, and skin temperature was measured directly after drying (ie, after heating [AH]), as well as 15 minutes later (15mAH) in the same way. This protocol was repeated at 7, 14, and 35 days after the first measurement. Skin temperatures of each participant were averaged over these 4 time points. We also registered whether patients perceived the skin temperature of the affected side as warmer, cooler, or equal as compared to the unaffected side at the first measurement. Mean numerical rating scale (NRS) score of pain prior to baseline temperature measurement was registered in CRPS patients.

Long-Term Registration

Skin temperature data were collected for 2 weeks with thermoregistration buttons (TBs) (iButton type DS1922L; Maxim, San Jose, CA), which have been shown to be a convenient and reliable tool for this purpose.[25] The TBs were directly placed on the skin above the extensor digitorum brevis muscle belly on both feet and fixed with Fixomul tape (Beiersdorf, Hamburg, Germany). This location was marked with a water-resistant marker. Skin temperature was recorded hourly with a thermal sensitivity of ±.5°C during 14 days. Participants recorded the exact time they went to bed for the night and the time they got out of bed—the time in between is referred to as "night." All remaining temperature data are referred to as "day." Participants also documented the periods that the TBs were removed (eg, during showering), and measurements from 15 minutes before to 15 minutes after these intervals were excluded. As no information was available on ambient temperature during the measurements, the absolute differences in skin temperatures between right and left legs (absΔRL) were calculated at all time points, and their absolute mean differences (MabsΔRL) and standard deviations (SDabsΔRL) for day (/D) and night (/N) per subject were used for comparisons between groups.

Statistical Analysis

External Heat Perturbation

Differences in skin temperatures between both groups and sides at all time points were subjected to a mixed analysis of variance, with time (BM, AH, 15mAH) and side (affected [patients]/right [controls] vs unaffected [patients]/left [controls]) as within-subject factors and with group (CRPS patients vs healthy controls) as between-subjects factor. The degrees of freedom were adjusted using the Greenhouse-Geisser estimates for the tests of within-subjects effects as the sphericity assumption was violated.[6]

Long-Term Registration

As data were not normally distributed, not even after commonly used transformations, differences in MabsΔRL and SDabsΔRL between groups during day and night were analyzed with Mann-Whitney U tests. To determine the optimal MabsΔRL value to discriminate between patients and controls, receiver operating characteristic curve analysis was used, where the highest sum of sensitivity and specificity (ie, Youden index) was used as the optimal cut-off point.

All statistical analyses were performed with IBM SPSS Statistics, version 20.0 (IBM Corp, Armonk, NY). *P* values <.05 were considered significant.