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Long-term skin temperature measurements – A practical diagnostic tool in complex regional pain syndrome

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Abstract

Despite the development of the IASP criteria, diagnosing complex regional pain syndrome (CRPS) remains a challenge because all symptoms vary interindividually, including the vascular abnormalities. Previous studies showed that skin temperature asymmetries between the affected and contralateral extremity around 2 °C are useful for diagnosing CRPS. However, they were either assessed only at one single point in time or during specific investigations including controlled thermoregulatory modulation of sympathetic activity which limits their practicability. The present study evaluated long-term skin temperature changes under everyday circumstances in 22 patients with CRPS, 18 patients with limb pain of other origin and 23 healthy controls. The asymmetries in skin temperature and oscillation number (Q_{Oscill}), the percentage of assessed time with a-synchron temperature changes on both body sides and the determination coefficient of the individual regression (r^2_{id}) were compared between the groups. Patients with CRPS differed significantly from healthy controls in nearly all parameters. Minor differences between both patient groups were found regarding the percentage of assessed time with side difference >2 °C ($\Delta T2$). However, both patient groups differed significantly in parameters characterizing the skin temperature dynamics. A sum score ($2*Q_{Oscill} + r^2_{id} + \Delta T2$) allowed diagnosing CRPS with a specificity of 67% vs. patients with other painful diseases and 79% vs. healthy controls (sensitivity: 73%, respectively, 94%) and reflected the severity of the dysfunction in CRPS better than the mean skin temperature side differences alone. The applied skin temperature analysis can be easily applied in the clinical settings and serves as a further facet in the difficult diagnosis of CRPS.

Keywords: Complex regional pain syndrome; Skin temperature; Sympathetic nervous system; Thermoregulation; Diagnostic criteria

1. Introduction

Complex regional pain syndrome (CRPS) is currently still a clinical diagnosis. Several studies have determined the validity of the IASP diagnostic criteria for CRPS showing a high sensitivity and low specificity, which may lead to an overdiagnosis of CRPS [9,15,18]. Despite the further development of the diagnostic criteria by Harden and Bruehl [17], diagnosing CRPS remains a challenge due to considerable interindividual variability in symptomatology including vascular abnormalities. During a controlled thermoregulatory cycle three vascular regulation patterns ('warm', 'intermediate' and 'cold' type) have been identified [37]. Furthermore, intraindividual shifts are common for CRPS and hence, with skin

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temperature recording only at one single point in time it would be almost random whether the affected limb is warmer or cooler than the unaffected one [21,32].

In addition to temperature recordings at rest, it is essential to test the reaction of the autonomic nervous system through "challenges" [32]. There is a good correlation between skin-surface temperature and fingertip blood flow and changes in the acral temperature reflecting sympathetically induced changes in the microcirculation [20,27]. Controlled alterations of sympathetic vasoconstrictor activity can be induced by whole-body warming and cooling, eliciting blood flow and temperature changes in the palmar finger pads [5]. Recently, Wasner et al. [36] showed that a maximal skin temperature side difference of more than 2.2 °C during changes of the environmental temperature using a thermal suit is highly sensitive and specific for distinguishing CRPS from other extremity pain syndromes. However, the methodological complexity of these investigations limits its clinical practicability.

Several other studies examined the function of the sympathetic nervous system in CRPS [3,4,6,7,10,11,16,19,25,26,28–31], but unfortunately only a few of them included a control group of limb pain of other origin [6,10,11,16,30,31]. It has already been shown that side differences in the skin temperature and color could be produced and maintained even in healthy subjects by a combination of short-term immobility and dependency of the hand [33] and may also occur in other chronic pain states [11].

The present study had two aims: firstly, to assess the vascular abnormalities in CRPS by comparing long-term period skin temperature changes under everyday circumstances of patients with definitive CRPS to patients with limb pain of other origin and to healthy controls. Secondly, to develop a practical approach for differentiation of CRPS from other painful states using a complex analysis of skin temperature changes.

2. Methods

2.1. Patients and healthy controls

After approval by the local Ethics Committee of the Ruhr University Bochum (Germany) 40 patients were recruited from the Pain Clinic of the University Hospital Bergmannsheil in Bochum from March 2006 to April 2007. Twenty-two patients with unilateral CRPS of the upper limb (CRPS) were compared to 18 patients with unilateral painful states of other origin (non-CRPS) and 23 healthy control subjects. In all patients one of the upper extremities was affected. The relevant clinical history and findings of the patient groups are summarized in Table 1. Exclusion criteria for both patient groups were generalized vascular diseases, rheumatoid arthritis and other bilateral painful states like osteoarthritis on both hands.

All patients with CRPS except one (CRPS II, female, 48 years old – scintigraphy not performed) had an enhanced bone metabolism in the late phase of a 99-m technetium-triple-phase-skeleton-scintigraphy and the diagnosis was based on the criteria defined by Bruehl et al. [9]. All patients with CRPS complained about pain and dysfunction, which were disproportional to the inciting event and could not be explained by the existence of other conditions that could account for them. In accordance with Bruehl et al. [9], all but two patients reported at least one symptom in three of the following four categories: hyperalgesia and/or allodynia, temperature and/or skin color asymmetries, sudomotor changes and/or edema and decreased range of motion and/or motor dysfunction and/or trophic changes. However, those two patients who reported symptoms in less than three of the four symptom categories developed more symptoms in the course of the disease some weeks after the investigations and were therefore assessed as CRPS in the early stages. At the time of the evaluation, all except for two patients presented at least one sign in three of the above-mentioned four categories (Table 1). The classification of the patients as CRPS type I ($n = 19$) or type II (injury of the brachiocervical plexus: $n = 1$, injury of the ulnar nerve: $n = 1$, injury of the median nerve: $n = 1$) was based on the absence or presence of electromyography and/or nerve conduction abnormalities, respectively.

The control group consisted of patients with neuropathic pain after nerve injury ($n = 3$: median nerve ($n = 1$), superficial branch of the radial nerve ($n = 1$), ulnar nerve ($n = 1$)) and patients with joint and soft tissue pain ($n = 15$: posttraumatic arthrosis ($n = 7$), soft tissue injury ($n = 5$), no somatic pain correlate ($n = 3$)). One patient with posttraumatic arthrosis as well as one patient with nerve injury reported at least one symptom of three of the above-mentioned four categories and presented at least one sign in three of the above-mentioned four categories. However, the current diseases of the patients with limb pain of other origin accounted for such a degree of pain and dysfunction. A triple-phase-skeleton-scintigraphy was performed in 13 cases and showed in none of the control patients any CRPS-typical enhanced bone metabolism.

Most of the patients ($n = 32$) underwent an individualized psychological evaluation by an experienced psychotherapist (J.F.). Those patients with a psychological diagnosis according to ICD-10 ($n = 26$) were divided into two groups depending on the severity of their psychological pathology (Table 1). Low grade of psychopathology was defined as psychopathology that contributes to a limited amount to the pain, e.g. dysfunctional coping strategies. Patients with a high grade of psychopathology that contributes to pain in a greater amount either fulfilled the criteria for severe psychiatric diseases, such as personality disorder, bipolar disorder,

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Table 1
Clinical data

Variable	CRPS ($n = 22$)	Non-CRPS limb pain ($n = 18$)	p
Gender (female, n (%))	16 (73%)	9 (50%)	0.072●
Age (years), mean ± SD (range)	53 ± 14 (21…74)	41 ± 11 (19…57)	0.007+
Affected side (right, n (%))	17 (77%)	8 (44%)	0.033●
Precipitating event, n* (%)			
Fracture	14 (64%)	8 (44%)	
Crush injury	6 (27%)	11 (61%)	
Operation	14 (64%)	10 (56%)	
Cast	5 (23%)	4 (22%)	
Other	3 (14%)	1 (6%)	
Not known	2 (9%)	1 (6%)	
Pain duration (months), mean ± SD (median; range)	7 ± 8 (5; 1…34)	18 ± 20 (12; 2…75)	0.006+
Average pain intensity (examination day, NRS 0–10), mean ± SD (range)	5 ± 2 (2…8)§1	6 ± 2 (1…9)	0.117+
Maximal pain intensity (examination day, NRS 0–10), mean ± SD (range)	6 ± 2 (3…9)§2	7 ± 3 (1…10)	0.330+
Supplied areas with clinical hypoesthesia or dysesthesia, n (%)	10 (45%)	10 (55%)	
Branches of the median nerve*	4 (18%)	4 (22%)	
Branches of the radial nerve*	6 (27%)	3 (17%)	
Branches of the ulnar nerve*	3 (14%)	4 (22%)	
Brachial plexus*	1 (5%)	0 (0%)	
Patients with positive symptom categories*, #, n (%)			
Sensory symptoms	18 (82%)	5 (29%)	
Vasomotor symptoms	17 (77%)	9 (53%)	
Sudomotor/edema symptoms	20 (91%)	8 (47%)	
Motor/tropthic symptoms	21 (95%)	10 (59%)	
Sum of positive symptom categories, n (%)			
0	1 (5%)	2 (12%)	
1	1 (5%)	5 (29%)	
2	0 (0%)	4 (24%)	
3	5 (23%)	5 (29%)	
4	15 (68%)	1 (6%)	
Patients with positive sign categories*, #, n (%)			
Sensory signs	17 (77%)	8 (47%)	
Vasomotor signs	16 (73%)	6 (35%)	
Sudomotor/edema signs	17 (77%)	4 (24%)	
Motor/tropthic signs	21 (95%)	12 (55%)	
Sum of positive sign categories, n (%)			
0	1 (5%)	3 (18%)	
1	1 (5%)	2 (12%)	
2	0 (0%)	8 (47%)	
3	10 (45%)	4 (24%)	
4	10 (45%)	0 (0%)	
Patients with ⩾3 positive symptom categories and ⩾3 positive sign categories◇, n (%)	20 (91%)	2 (12%)	
Signs of disuse (e.g. reduced callosity and/or circumference), n (%)	11 (50%)	5 (29%)	
Hints of self-injurious behavior, n (%)	3 (14%)	4 (24%)	
Current psychological diagnosis, n (%)			
No psychopathology	***4 (18%)***	***2 (11%)***	
Low degree of psychopathology*	***7 (32%)***	***4 (22%)***	
ICD-10 F40-49	1 (5%)	0 (0%)	
ICD-10 F60-69	7 (32%)	4 (22%)	
High degree of psychopathology*	***6 (27%)***	***9 (50%)***	
ICD-10 F30-39	1 (5%)	1 (6%)	
ICD-10 F40-49	1 (5%)	2 (11%)	
ICD-10 F60-69	5 (23%)	5 (28%)	
No information available	***5 (23%)***	***3 (17%)***	

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Table (*continued*)

Variable	CRPS ($n = 22$)	Non-CRPS limb pain ($n = 18$)	p
Current medication, n (%)[*]			
No medication	3 (14%)	2 (11%)	
Moderate-acting opioids	2 (9%)	4 (22%)	
Strong-acting opioids	3 (14%)	2 (11%)	
Tricyclic antidepressants	10 (45%)	7 (39%)	
Serrotonin reuptake inhibitors	2 (9%)	0 (0%)	
Anticonvulsives	9 (41%)	6 (33%)	
Traditional non-steroidal antirheumatics	0 (0%)	2 (11%)	
Coxibs	9 (41%)	2 (11%)	
Other non-opioid pain medication	6 (27%)	6 (33%)	
Antihypertensive medication[Δ]	6 (27%)	1 (6%)	

● $p < 0.05$ (Pearson χ^2-test).
+ $p < 0.05$ (Mann–Whitney U-test).
[*] Multiple answers possible.
[§1] Patients who rated the average pain intensity as 0 (NRS (0–10) were excluded from the calculations ($n = 4$)).
[§2] Patients who rated the maximal pain intensity as 0 (NRS (0–10) were excluded from the calculations ($n = 3$).
[#] According to Bruehl et al. [9].
[◇] Sensitivity of 70% and specificity of 83% for the diagnosis of CRPS [9]. *NRS*: numeric rating scale; *CRPS*: complex regional pain syndrome; *non-CRPS*: limb pain of other origin.
[Δ] Under antihypertensive medication was summarized any medication for treatment of essential arterial hypertension (monotherapy or a combination therapy including ACE inhibitors, angiotensin II receptor antagonists, beta blockers, calcium channel blockers and/or diuretics).

major depression, fear and anxiety disorder or strongly exaggerated the physical symptoms for psychological reasons (ICD-10 F68.0) and displayed a distinct conflict of goals, e.g. financial or social compensations, which was additionally exacerbating their condition.

Twenty-four healthy subjects (15 (63%) females, 33 ± 12 (21...69) years old) without history of trauma, neurological or vascular diseases were recruited from March 2006 to March 2007 from among students, members of the hospital staff or their relatives. None of them was on any medication.

2.2. Investigations and measurements

Skin temperature of both extremities and ambient air temperature were measured with a temperature data logger svea® TDL (Medicommerz GmbH, Kirchzarten, Germany). TDL is a temperature monitoring device (250 g, $80 \times 153 \times 30$ mm) with a thermal sensitivity of 0.1 °C at 0–50 °C. The device monitored and stored data at a 1-min interval over a course of 5 to 8 hours under everyday circumstances (recording times for: CRPS, 459 ± 36 (362...480) min, for non-CRPS: 447 ± 65 (267...480) min and for healthy controls 466 ± 31 (392...480) min). The measuring probes were fixed by a sticking plaster on the palmar pad of the index finger of both hands. The air ambient temperature was measured by a sensor fixed on the dorsum of the hand. 1.5-m long cables connected the temperature sensors to the data logger that was carried either in the pocket or in a small bag.

In order to accomplish a standardization of the measurement and to be able to compare the dynamics of the sympathetic vasoconstrictor activity, all subjects were instructed to perform certain standard procedures to change the environmental temperature. After a resting phase of 45 min in a warm room, they were asked to go out of the room, for example, onto a balcony where the environmental temperature was lower, and stay there for 5–10 min to achieve a cutaneous vasoconstriction. Afterwards, they were instructed to return to the warm room and repeatedly go out for further 5–10 min after a resting phase of 30 min, respectively. For the rest of the measurement period subjects were allowed to carry out their daily activities. They were asked to keep a diary about these daily activities, for example, meal times, physical exercises, walking, resting phases, etc.

During the measurement preparations, patients were informed about any potential source of error such as wetness near the sensors and thermal insulation of the examined areas by blankets or clothes. They were instructed to avoid these situations with the greatest possible care.

2.3. Calculations

All data were transferred to a personal computer via an integrated port in a HyperTerminal program of Microsoft® Windows XP and were saved as a csv-file. Subsequently, the data of each subject were analyzed, partly macro-assisted, in a file by the Microsoft® Excel program where the curves of the temperature changes over the assessed time were created and the different parameters were calculated. In patients, the affected hand was defined as test side, the unaffected hand, as control side. In healthy subjects the test side was the

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non-dominant body side – in most of the cases it was the left side, only in two cases (1 m, 1 f) it was the right side.

The following parameters were calculated in order to estimate the side differences of skin temperature and curve progression between the control and test side.

2.3.1. Mean and maximal side differences in skin temperature

The mean side difference in skin temperature (ΔT) as well as the absolute mean ($abs\Delta T$) and maximal ($absT_{max}$) side differences in skin temperature between both extremities during the investigation period was determined by the following formula:

ΔT = mean (skin temperature on the test side − skin temperature on the control side)
$abs\Delta T$ = |mean (skin temperature on the test side − skin temperature on the control side)|
$absT_{max}$ = maximum |skin temperature on the test side − skin temperature on the control side|

Furthermore, the minimal and maximal skin temperatures on the test (minTt, maxTt) and on the control side (minTc, maxTc) as well as the difference between the minimal and maximal temperature during skin temperature on the test (diffTt) and on the control side (diffTc) were assessed.

The percentage of assessed time with an absolute skin temperature side difference was calculated for different cut-offs from 0 °C up to 14 °C (0, 0.2, 0.4, etc. up to 14). Furthermore, the percentage of assessed time with a skin temperature side difference of more than 2 °C ($\Delta T2 = \Delta T2c + \Delta T2w$) was calculated separately for the percentage of assessed time when the test side was more than 2 °C colder ($\Delta T2c$) and warmer ($\Delta T2w$).

2.3.2. Side differences in the skin temperature curves on both tested sides

Time of a-synchronicity (*Asynchr*, Fig. 1A) was defined as the time during which the skin temperature of both hands changed in different directions (e.g. the temperature of the test side decreased, while the temperature of the control side increased and vice versa). A-synchronicity was calculated as percentage of the assessed time when the angle between the temperature curve and the tangent graphs had opposite algebraic signs on both sides.

Another parameter that was used to describe the a-synchronicity of the curve progression was the coefficient of determination (r^2_{id}) of the individual regression equation, f(*T°C control hand*) = *T°C test hand*.

2.3.3. Side differences in the skin temperature changes of more than 2 °C

The oscillation number of more than 2 °C was determined separately for each hand by a macro-assisted counting of the number of ascents and descents of the graphs of more than 2 °C (Fig. 1B). The side differences in the frequency of oscillations that occurred during the measurement period were assessed by building a ratio:

Q_{Oscill} = number of oscillations of more than 2 °C on the test side/number of oscillations of more than 2 °C on the control side.

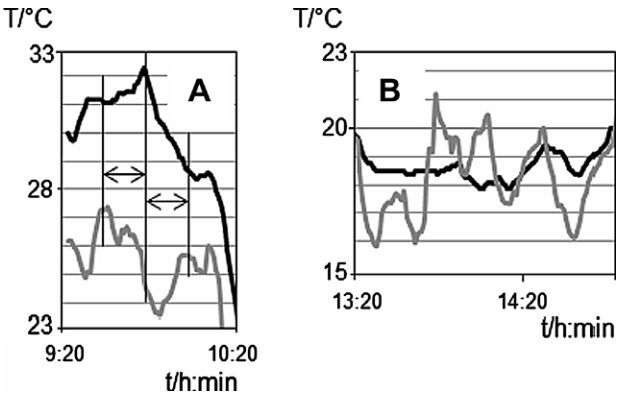

Fig. 1. (A) Example of an a-synchronic curve progression in a patient with CRPS: the affected hand (black) gets warmer while the contralateral one (gray) gets colder and vice versa. (B) Example of decreased oscillation number on the affected hand in a patient with CRPS: the skin temperature of affected hand (black) is remarkably stable, while the skin temperature on the contralateral hand (gray) oscillates several times.

2.4. Statistical analysis

The variables comprising age, gender, affected side, duration of disease, mean and maximal pain intensity (numeral rating scale 0 = 'no pain' up to 10 = 'strongest pain') served for sample description as well as for control parameters. Group differences regarding nominal variables (e.g. gender, affected side and number of pathological values) were analyzed by χ^2-tests using the Yate's continuity correction when in one of the cells the expected count was <5. Mann–Whitney *U*-test was conducted for comparison of metric variables (e.g. age, duration of disease, pain intensity and temperature data) between the groups. Levene's test was used to assess the equality of variance between the different samples. Pearson's correlation was calculated for the comparison of the mean and maximal side differences (not absolute values) and the duration of the disease (months). A linear regression was calculated to test whether the measured variables (ΔT, $abs\Delta T$, $\Delta T2w$, $\Delta T2c$, $\Delta T2$, Q_{oscill}, *Asynchr*, r^2_{id}) were influenced by the probands' age. In order to determine reference values and to compare the temperature regulation patterns of the patients with the group of healthy controls, the 95%-confidence interval for healthy controls

(mean + 1.96 * SD) was calculated for all relevant parameters, after confirming that the parameters were normally distributed in the group of healthy controls in the one-sample Kolmogorov–Smirnov test. p-values of <0.05 were regarded as statistically significant, and p-values of <0.01, as highly significant.

Four regulation patterns were defined, depending on whether essential skin temperature side differences of more than 2 °C were present. An 'indifferent' type was postulated when the percentage of side differences did not exceed the 95%-confidence values for healthy controls (≅13.2% of the assessed time). In patients with 'warm' type of regulation the skin temperature on the affected side was more than 2 °C warmer than contralateral during most of the investigation time, and in patients with 'cold' type of regulation the temperature was more than 2 °C colder. An 'intermediate' type of regulation was defined when the direction of the skin temperature side difference changed during the measurement time and the affected hand was alternately either 2 °C warmer or colder than contralateral. Additionally, all probands were split into two further samples based on whether their results exceeded the lower 95%-confidence value of healthy controls for r^2_{id} and Q_{Oscill} or the higher 95%-confidence value of healthy controls for *Asynchr*.

A discriminant function analysis was performed in order to distinguish more exactly between patients with CRPS and patients with limb pain of other origin. Based on that, a sum score was calculated, including the following parameters: the percentage of time with a side difference of more than 2 °C ($\Delta T2$), the coefficient of determination of the individual regression equation (r^2_{id}) and the quotient of the frequency of oscillations of more than 2 °C (Q_{Oscill}). Each of the parameters could attain four possible values: 0 – value within the standard deviation of the group of healthy controls, 1 – value greater than the standard deviation of the group of healthy control and smaller than the twofold of it, 2 – value between the twofold and the threefold of it, 3 – value greater than the threefold of it. The sum score was built by the following equation: $2 * Q_{Oscill} + r^2_{id} + \Delta T2$. Hence, a proband could achieve from 0 to 12 points with 12 points indicating the highest degree of thermoregulatory dysfunction. Furthermore, the sensitivity, specificity, positive and negative predictive values were calculated to estimate the discrimination power of Q_{Oscill}, r^2_{id}, $\Delta T2$ and of the sum score as a diagnostic tool.

3. Results

3.1. Clinical data

The gender proportion did not differ significantly between the three groups. Healthy controls had a significantly lower mean age than both patient groups ($p < 0.001$ vs. CRPS, $p = 0.03$ vs. non-CRPS). Compared to patients with limb pain of other origin, the group of CRPS patients had a significantly higher mean age, a slightly higher percentage of women, significantly shorter duration of disease and the right side was significantly more often affected. The reported average and maximal pain intensity on the examination day did not differ between the two patient groups (Table 1). Three of the patients with CRPS had no pain during the investigations; one patient had no resting pain but reported pain related to movement of the extremity. All of these four patients had suffered from ongoing spontaneous pain prior to treatment.

All patients received individually adjusted physical and occupational therapies. Nineteen patients with CRPS (86%) and sixteen patients with limb pain of other origin (88%) took pain medication (Table 1). During or prior to the investigations, none of the patients was treated by interventions such as sympathetic blocks, sympathectomy, spinal cord stimulations or epidural pumps that might have affected limb blood flow.

The minimal and maximal skin temperatures in the unaffected limb as well as the difference between the minimal and maximal skin temperatures that were measured during the investigations did not differ significantly among the three groups (Table 2).

3.2. Average skin temperature side differences and vascular regulation patterns

3.2.1. Healthy controls

Healthy controls demonstrated only minimal side differences between both hands in the skin temperature, in the number of oscillations (Q_{Oscill}), in the direction of curve progression (*Asynchr*) and had also the highest r^2_{id}. In the one-sample Kolmogorov–Smirnov test, the distribution of all parameters did not differ significantly from the empirical normal distribution, although $\Delta T2w$ and $\Delta T2c$ presented a positive skew >1 and r^2_{id} had a negative skew <1 (Table 2). All skin temperature curves were similar (Fig. 2A).

3.2.2. CRPS vs. healthy controls

Patients with CRPS differed significantly from healthy controls in almost all parameters (Fig. 2B and C), i.e. skin temperature measurements showed a significantly increased *Asynchr* and a significantly decreased r^2_{id}. Moreover, in CRPS Q_{Oscill} was on average decreased and its variance was significantly higher.

3.2.3. Non-CRPS vs. healthy controls

Patients with limb pain of other origin also demonstrated considerable side differences, especially in $\Delta T2$ (Fig. 2E). Q_{Oscill} was on average similar having equal variance in both groups, although *Asynchr* was significantly increased and r^2_{id} was significantly decreased in the non-CRPS.

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Table 2
Descriptive statistics for the temperature data

	Healthy controls ($n = 23$)	Patients with CRPS ($n = 22$)	Patients with non-CRPS ($n = 18$)	Mann–Whitney U-test			Levene's test			Healthy controls				
										Kolmogorov–Smirnov test	Skewness	Kurtosis	Lower CI value	Upper CI value
ΔT (°C)	−0.1 ± 0.6 (−1…0.9)	0.9 ± 2.0 (−2.5…5.6)	1.1 ± 0.1 (−2.5…2)	*			**			$p = 0.94$	0.289	−0.96	–	1.0
absΔT (°C)	0.5 ± 0.3 (0.1…1)	1.5 ± 1.6 (0…5.6)	0.8 ± 0.7 (0…2.5)	*			**	§§	#	$p = 0.68$	0.143	−1.189	–	1.1
absT_{max} (°C)	3.9 ± 2.5 (0.5…9.4)	6.2 ± 3.5 (1.1…13.7)	4.1 ± 2.4 (1.1…10.4)	*		#				$p = 0.98$	0.092	−0.412	–	8.8
minTt	18.0 ± 4.6 (9.6…24.5)	22.2 ± 5.2 (15.0…31.9)	19.4 ± 5.6 (9.3…30.0)	*						$p = 0.57$	−0.220	−1.184	–	–
minTc	17.7 ± 4.6 (9.8…25.4)	20.9 ± 4.5 (14.7…30.2)	19.7 ± 5.4 (10.1…28.7)							$p = 0.92$	−0.092	−0.966	–	–
maxTt	34.9 ± 0.8 (33.3…36.2)	34.9 ± 1.2 (30.0…36.5)	34.3 ± 2.7 (24.3…36.2)							$p = 0.98$	−0.130	−0.585	–	–
maxTc	34.9 ± 0.7 (33.6…36.1)	35.0 ± 1.0 (32.2…36.6)	34.4 ± 2.3 (26.2…37.4)							$p = 0.88$	−0.326	−0.629	–	–
diffTt	16.9 ± 4.7 (9.5…25.7)	12.6 ± 5.4 (0.4…20.3)	15.0 ± 4.6 (5.3…22.9)	*						$p = 0.68$	0.202	−1.146	–	–
diffTc	17.2 ± 4.6 (9.3…25.8)	14.1 ± 3.9 (5.7…20.6)	14.7 ± 4.7 (6.5 …24.7)							$p = 0.53$	0.164	−0.855	–	–
ΔT2w (% of assessed time)	3.1 ± 4.4 (0…12.6)	25.5 ± 28.8 (0…96.0)	10.1 ± 13.1 (0…42.3)	**		#	**	§§	#	$p = 0.10$	1.302	0.085	–	11.8
ΔT2c (% of assessed time)	4.8 ± 5.0 (0…17.4)	6.8 ± 11.3 (0…43.5)	9.3 ± 14.5 (0…57.0)				*	§		$p = 0.40$	1.139	0.642	–	14.6
ΔT2 (% of assessed time)	8.0 ± 5.4 (0…18.1)	32.3 ± 26.9 (0…96.0)	19.4 ± 16.6 (0…57.0)	**	§		**	§§		$p = 0.91$	0.233	−0.929	–	18.6
Q_{oscill}	1.01 ± 0.20 (0.76…1.47)	0.87 ± 0.42 (0.2…1.73)	1.01 ± 0.18 (0.7…1.36)				**		##	$p = 0.79$	0.837	−0.002	0.62	–
Asynchr (% of assessed time)	8.8 ± 3.1 (3.8…14.8)	13 ± 4.9 (7.7…29.8)	12.5 ± 4 (2.9…19.6)	**	§§					$p = 0.95$	0.249	−0.526	–	14.7
r^2_{id}	0.93 ± 0.04 (0.79…0.97)	0.74 ± 0.20 (0.18…0.95)	0.84 ± 0.13 (0.44…0.96)	**	§§	#	**	§§		$p = 0.55$	−2.162	7.134	0.85	–

Data are shown as means ± SD (range). CRPS vs. healthy controls: $^{*}p < 0.05$. $^{**}p < 0.01$; non-CRPS vs. healthy controls: $^{\S}p < 0.05$. $^{\S\S}p < 0.01$; CRPS vs. non-CRPS: $^{\#}p < 0.05$. $^{\#\#}p < 0.01$. *CRPS*: complex regional pain syndrome; *non-CRPS*: limb pain of other origin; *CI*: 95%-confidential interval; ΔT: mean side difference in skin temperature; *abs*ΔT: absolute mean side differences; *abs*T_{max}: absolute maximal side differences; *minTt:* minimal skin temperature on the test side; *maxTt*: maximal skin temperature on the test side; *minTc*: minimal skin temperature on the control side; *maxTc* maximal skin temperature on the control side; *diffTt*: difference between the maximal and minimal skin temperature on the test side; *diffTc*: difference between the maximal and minimal skin temperature on the control side; *ΔT2w:* percentage of assessed time when the test side was more than 2 °C warmer; *ΔT2c:* percentage of assessed time when the test side was more than 2 °C colder; *ΔT2:* percentage of assessed time with a skin temperature side difference of more than 2 °C; Q_{Oscill}: ratio between the frequency of oscillations that occurred during the measurement period on the test side and the control side; *Asynchr:* percentage of assessed time during which the skin temperature of both hands changes in different directions; r^2_{id}: the coefficient of determination of the individual regression equation (*f (T°C control hand) = T°C test hand*).

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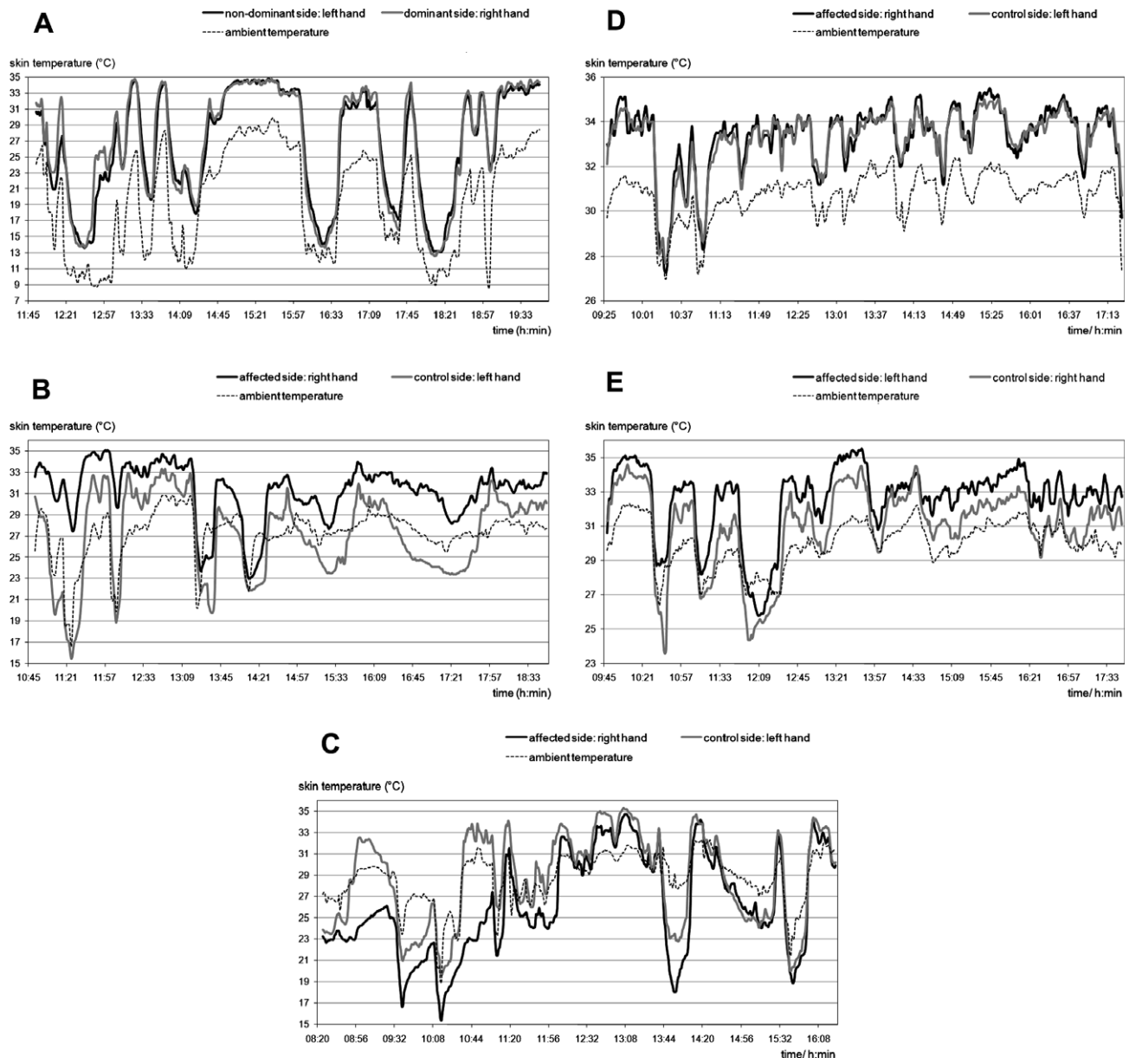

Fig. 2. Skin temperature curves indicating cutaneous sympathetic vasoconstrictor activity in the finger of both hands in a healthy control (A), patients with CRPS (B–D) and a patient with limb pain of other origin (E) during long-term measurements under everyday circumstances. A patient with CRPS (B) presents a 'warm' regulation type (affected extremity more than 2 °C warmer in 83% of the assessed time) and a more complex regulatory dysfunction with additionally decreased oscillation number on the affected side ($Q_{Oscill} = 0.68$) and a low intraindividual correlation between the skin temperature on the affected and unaffected hand ($r^2_{id} = 0.53$), thus achieving a sum score of 8 points. Another patient with CRPS (C) revealed a 'cold' regulation type (affected extremity more than 2 °C colder in 44% of the assessed time); the number of oscillations of more than 2 °C was similar on both hands ($Q_{Oscill} = 0.88$), but the intraindividual correlation between the skin temperature on the affected and unaffected hands was low ($r^2_{id} = 0.4$), thus achieving a sum score of 6 points. In some single patients no regulatory dysfunction was found during the long-term measurements under everyday circumstances (D) – in this example the affected hand was not more than 2 °C warmer or colder at any time during the assessment ($Q_{Oscill} = 1.29$, $r^2_{id} = 0.93$, sum score = 0 points.). Surprisingly, some patients with limb pain of other origin had also a disturbed skin temperature regulation, e.g. a patient with CRPS-like disorder and posttraumatic arthrosis 9 months after trauma (E), who revealed a 'warm' type of regulation with a skin temperature side differences >2 °C in 20% of the measured time; however, the quotient of oscillations >2 °C was within the normal range ($Q_{Oscill} = 1.17$, $r^2_{id} = 0.65$) and, achieving a sum score of only 3 points, this patient was not falsely classified as a CRPS. Q_{Oscill}: ratio between the frequency of oscillations that occurred during the measurement period on the test side and the control side; r^2_{id}: the coefficient of determination of the individual regression equation (f (*T°C control hand*) = *T°C test hand*).

3.2.4. Differences between both patient groups

Patients with CRPS revealed on average a considerably decreased Q_{Oscill} with significantly higher variance. In the group of patients with CRPS r^2_{id} was significantly lower and $absT_{max}$ was significantly higher, although the patient groups

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did not differ on average in *ΔT*, *absΔT*, *ΔT2* and in *Asynchr*.

3.2.5. Effects of age

In the group of the healthy controls the coefficients of the estimated regression model ranged between −0.025 and 0.101. None of the parameters were significantly influenced by the independent variable 'age'. In the other two groups the coefficients of the estimated regression model were not significant either.

3.2.6. Distribution of the different regulation types (Table 3)

Sixteen of all 40 patients (50% of the CRPS group and 28% of the non-CRPS group) but none of the healthy controls presented a pathologically long-lasting side difference with a >2 °C warmer test hand and fulfilled therefore the criteria of a 'warm' regulation type. The other two dysfunctional regulation types occurred in both patient groups less frequently (CRPS: 14% 'cold' type, 9% 'intermediate' type; non-CRPS: 17% 'cold' type, 5% intermediate' type).

In summary, the highest prevalence (73%) of a dysfunctional regulation type ('warm', 'cold' or 'intermediate') was found in the CRPS group (CRPS vs. healthy controls: χ^2-value = 19.209, $p < 0.001$). However, 50% of the non-CPRS patients revealed one of the pathological regulation types (non-CRPS vs. healthy controls: χ^2-value = 8.775, $p = 0.003$) as well. Thus, when comparing both patient groups with each other, no significant difference (χ^2-value = 2.182, $p = 0.14$) was found between the observed frequencies.

3.2.7. Percentage of time with a skin temperature side difference

The three groups differed in their mean values regarding the percentage of the measured time (ordinate) which the subjects presented an absolute side difference greater than a defined cut-off (abscissa) (Fig. 3A). In comparison to healthy controls (Fig. 3B), side differences of CRPS patients were more pronounced and furthermore, those side differences were observed more frequently and for a longer period of time during measurements. However, considerable side differences could also be observed in some patients with limb pain of other origin (Fig. 3D). A cut-off of more than 2 °C side difference during more than 13.2% of the measured time would allow the diagnosis of CRPS with a higher specificity, but at the cost of the sensitivity. For example, a maximal specificity of 100% could be achieved when a side difference of more than 2 °C was present in more than 60% of the measured time, or when a side difference of more than 5.6 °C was present in more than 10% of the measured time.

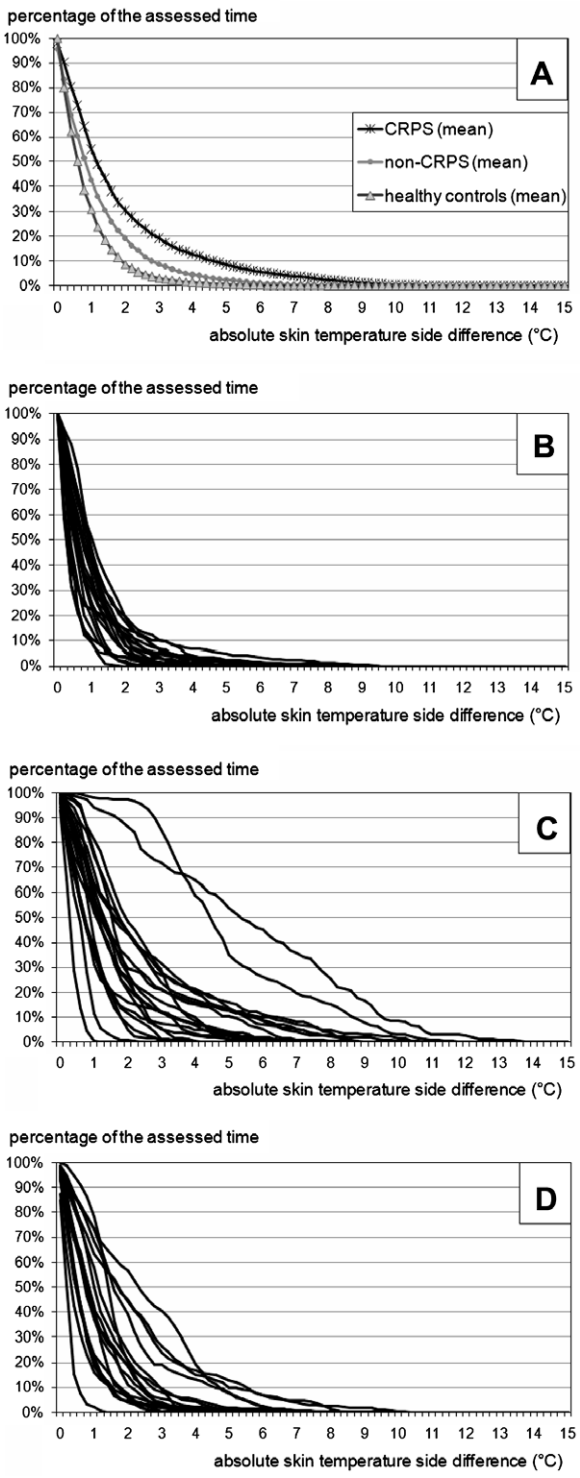

Fig. 3. Percentage of the measured time (ordinate) with an absolute side difference greater than a certain cut-off (abscissa), presented as group means (A) and separately for each of the healthy controls (B), patients with CRPS (C) and patients with limb pain of other origin (D). Although the three groups differ in their means (A), there are also some patients with limb pain of other origin (D) who presented considerable side differences during the long-term skin temperature measurements under everyday circumstances and even a cut-off of more than 2 °C side difference and more than 13.2% of the measured time would not allow the diagnosis of CRPS with a high specificity and a satisfactory sensitivity. *CRPS*: complex regional pain syndrome; *non-CRPS*: limb pain of other origin.

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3.2.8. Relationship between regulation type and duration of the disease

In the CRPS group the duration of the disease (in months) showed a significant negative correlation ($r = -0.51$, $p = 0.015$) with the maximal side difference between the affected and the contralateral hand (not absolute values), indicating that the more acute the disease, the warmer the affected extremity and vice versa. In the non-CRPS group no clear correlation was found. The duration of the disease in the group of patients with CRPS and a 'warm' regulation pattern was on average 4 months ($n = 11$, range: 1–15 months) in contrast to an

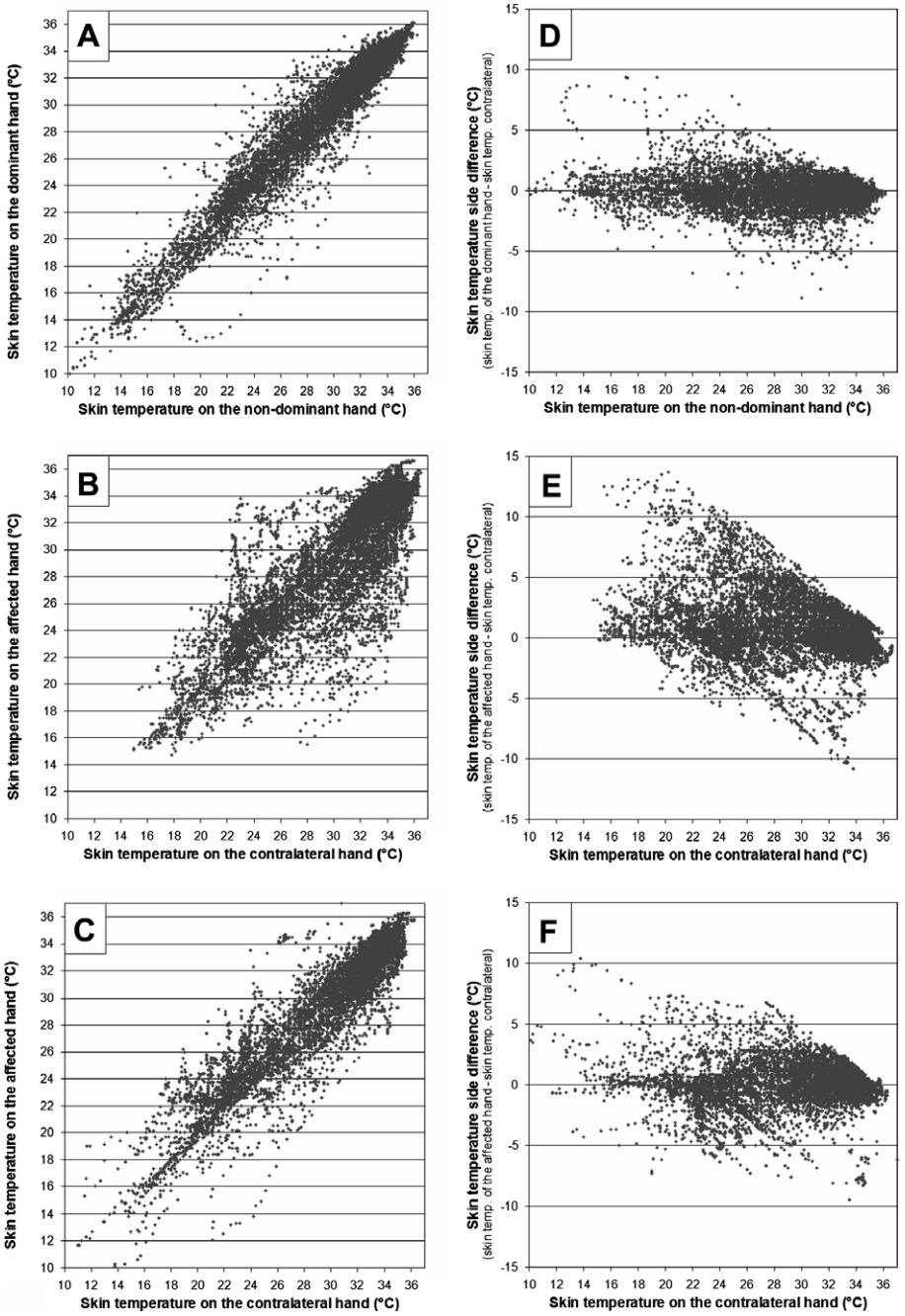

Fig. 4. Correlation between the skin temperature on both hands (A–C) and relationship between the skin temperature of the control side and the skin temperature side differences (D–F) in the total sample of probands. In the group of healthy controls the skin temperature on both hands correlates highly within one individual (A) and only minimal side differences (D) were found over the whole range of skin temperature of the control hand (except for only a few outliers: single measuring points during the long-term skin temperature recording). In the group of patients with CRPS the correlation between the skin temperature on the affected and the unaffected hands was lower (B) and the largest side differences in skin temperature were found when the skin temperature of the contralateral hand was between 20 and 34 °C indicating a high to intermediate level of sympathetic activity (E). Also in the group of patients with limb pain of other origin some thermoregulatory dysfunction was present, but to a lesser extent (C and F).

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average disease duration of 18 months ($n = 3$, range: 6–34 months) in patients with 'cold' regulation pattern.

On the other side, when the patients were divided into two groups according to the duration of the disease, the following proportion was found: nearly the half of the patients with CRPS of up to 6 months duration ($n = 8$; ≅47%) revealed another regulation type than 'warm' – 5 patients demonstrated an 'indifferent' type of regulation and one patient presented a 'cold' type of regulation. In the other patient group without CRPS most of the patients had a disease history longer than 6 months ($n = 13$; ≅72%) and three of them displayed a 'warm' regulation type.

3.3. Dynamic changes of the temperature side differences

Presenting the skin temperature values of all probands belonging to a group, some group differences were found in the correlation between the skin temperatures of both hands (Fig. 4A–C) and in the relationship between the skin temperature of the control side and the skin temperature side differences in the total sample of probands (Fig. 4D–F). In the group of healthy controls there was a very high intraindividual correlation between the skin temperature of both hands ($r^2_{id} = 0.93 \pm 0.04$ (0.79...0.97)) (Fig. 4A). Only minimal side differences were found over the whole range of skin temperature of the control hand (10–36 °C) except for only a few outliers (single measuring points during the long-term skin temperature recording, Fig. 4D). The intraindividual correlation in the CRPS group was on average significantly lower ($r^2_{id} + 0.74 \pm 0.20$ (0.18...0.95)) than in the two control groups and the variance was much higher (Fig. 4B). In patients with CRPS the largest side differences in skin temperature were found when the skin temperature of the contralateral hand was between 20 and 34 °C (corresponding to a high to intermediate level of sympathetic activity) (Fig. 4E). Similar effects, but to a lesser extent, were observed in the group of patents with limb pain of other origin, as well (Fig. 4C and F).

Based on the 95%-confidence values of the healthy controls, the number of patients with a decreased r^2_{id} was significantly higher in both patient groups (CRPS vs. healthy controls: χ^2-value = 17.787, $p < 0.001$, non-CRPS vs. healthy controls: χ^2-value = 7.671, $p = 0.006$) in comparison to the group of healthy controls ($n = 1$, ≅5%). A decreased r^2_{id} was found in 14 (64%) of the patients with CRPS, but in only 7 (39%) of the patients with limb pain of other origin (χ^2-value = 2.431, $p = 0.119$). 27% ($n = 6$) of the CRPS group and 33% ($n = 6$) of the non-CRPS group presented an increased time with a-synchron curve progression (CRPS vs. non-CRPS: χ^2-value = 0.173, $p = 0.677$; CRPS vs. healthy controls: χ^2-value = 2.923, $p = 0.087$; non-CRPS vs. healthy controls: χ^2-value = 4.120, $p = 0.042$).

According to the reference values of the healthy controls, a decreased number of oscillations on the affected side was present only in 6 (27%) of the patients with CRPS but in none of the other probands (CRPS vs. non-CRPS: χ^2-value = 3.834, $p = 0.05$; CRPS vs. healthy controls: χ^2-value = 5.070, $p = 0.024$).

3.3.1. Skin temperature regulation patterns including dynamic changes

Several regulation patterns were defined, depending on whether the affected hand presented a side difference of more than 2 °C and/or a decreased number of oscillations of more than 2 °C, based on the 95%-confidence values for healthy controls (Table 3). A complex regulatory dysfunction with side differences in the skin temperature and the oscillation number was found in 6 of the patients with CRPS (27%), but in none of the patients with other painful states. Twelve (55%) patients with CRPS and 9 (50%) patients with limb pain of other origin demonstrated a regulatory dysfunction with side differences only in the skin temperature, but not in the oscillation number. Nine of the patients with limb pain of other origin (50%) and 4 (18%) patients with CRPS presented a regulation pattern without any pathological findings.

Table 3
Distribution of the different regulation patterns in patients with CRPS, with limb pain of other origin and in healthy controls: *n* (%)

	Oscillation frequency on the affected side	Side difference > 2 °C				
		Indifferent type	Intermediate type	Warm type	Cold type	Sum
Healthy controls	normal	21 (91%)	–	–	2 (9%)	23 (100%)
	decreased	–	–	–	–	–
	sum	21 (91%)	–	–	2 (9%)	23 (100%)
CRPS	normal	4 (18%)	1 (4,5%)	9 (41%)	2 (9%)	16 (73%)
	decreased	2 (9%)	1 (4,5%)	2 (9%)	1 (4,5%)	6 (27%)
	sum	6 (27%)	2 (9%)	11 (50%)	3 (14%)	22 (100%)
Non-CRPS	normal	9 (50%)	1 (5%)	5 (28%)	3 (17%)	18 (100%)
	decreased	–	–	–	–	–
	sum	9 (50%)	1 (5%)	5 (28%)	3 (17%)	18 (100%)

CRPS: complex regional pain syndrome; *non-CRPS*: limb pain of other origin.

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3.4. Sensitivity and specificity of the skin temperature asymmetries

A comparatively good sensitivity for distinguishing CRPS from other painful states was achieved by analyzing the percentage of time with side differences of more than 2 °C. However, the highest specificity of 100% for diagnosing CRPS was obtained by analyzing the decreased number of oscillations on the affected side (Table 4).

In order to enhance the diagnostic power of skin temperature asymmetries for identifying CRPS a sum score was calculated based on a discriminant function analysis including Q_{Oscill}, r^2_{id} and $\Delta T2$. The patients with CRPS achieved on average significantly higher values (mean ± SD: 6 ± 3, range: 0…12) in comparison to patients with limb pain of other origin (mean ± SD: 3 ± 3, range: 0…8, $p = 0.005$) and healthy controls (mean ± SD: 1 ± 1, range: 0…5, $p < 0.001$). However, patients with limb pain of other origin also had significantly higher scores than healthy controls ($p = 0.001$, Fig. 5). Using a cut-off value of 4 points, 6 patients with CRPS were false negative and 6 of the control patients were false positive. Thus, CRPS could be diagnosed with a specificity of 67% vs. non-CRPS and 79% vs. healthy controls; the sensitivity was 73% and 94%, respectively.

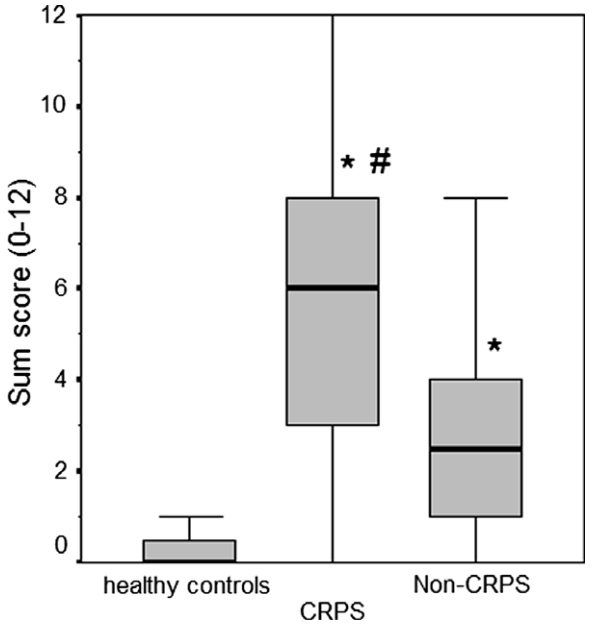

Fig. 5. Sum score ($2 * Q_{Oscill} + r^2_{id} + \Delta T2$) based on reference values and a discriminant function analysis for description of the skin temperature dysregulation in patients with CRPS on the upper extremity ($^*p < 0.01$ vs. healthy controls; $^{\#}p < 0.01$ vs. limb pain of other origin). Using a cut-off of 4 points, CRPS can be diagnosed with a specificity of 73% vs. non-CRPS and 94% vs. healthy controls (sensitivity: 67%, respectively, 79%). *CRPS*: complex regional pain syndrome; *non-CRPS*: limb pain of other origin; Q_{Oscill}: ratio between the frequency of oscillations that occurred during the measurement period on the test side and the control side; r^2_{id}: the coefficient of determination of the individual regression equation (f (*T°C control hand*) = *T°C test hand*); $\Delta T2$: percentage of assessed time with a skin temperature side difference of more than 2 °C.

4. Discussion

In recent complex experimental investigations including controlled thermoregulatory modulation of the sympathetic activity [36,37], skin temperature side differences between the affected and contralateral extremity around 2 °C were shown to be a useful criterion for diagnosing CRPS, consistent with recently proposed modifications of the IASP criteria for CRPS [17,22]. In the face of the limited practicability of these experimental test procedures in clinical settings, the skin temperature changes in CRPS were evaluated during daily conditions with altering ambient temperature and physical factors, in one-minute intervals during on average 7.5 h and were compared to a group of patients with limb pain of other origin and healthy probands. In summary: (1) patients with CRPS differed significantly from healthy controls in all parameters proving skin temperature asymmetries. The maximal skin temperature side differences during different thermoregulatory states correlated with the duration of the CRPS, i.e. the more acute the disease, the more often the affected extremity

Table 4
Sensitivity and specificity of the skin temperature asymmetries for diagnosing CRPS

	CRPS vs. non-CRPS				CRPS vs. healthy controls	
	False negative	False positive	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
Pathologically increased* $\Delta T2$ (% of assessed time)	6	9	73	50	73	91
Pathologically decreased* Q_{Oscill}	16	0	27	100	27	100
Pathologically decreased* r^2_{id}	8	7	64	61	96	64
Pathologically increased* *Asynchr* (% of assessed time)	16	6	27	67	27	96

CRPS: complex regional pain syndrome; non-CRPS: limb pain of other origin; $\Delta T2$: percentage of assessed time with a skin temperature side difference of more than 2 °C; Q_{Oscill}: ratio between the frequency of oscillations that occurred during the measurement period on the test side and the control side; r^2_{id}: the coefficient of determination of the individual regression equation (f (*T°C control hand*) = *T°C test hand*); *Asynchr:* percentage of assessed time during which the skin temperature of both hands changes in different directions.

* Beyond the 95%-confidence interval for healthy controls.

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was warmer and vice versa. (2) More than 2 °C increased or decreased temperature on the affected upper limb compared to the unaffected side was frequently observed in CRPS but also in other painful states, indicating a low specificity. (3) However, a more complex dysregulation pattern with additionally decreased oscillation frequency on the affected side compared to contralateral areas was found only in CRPS, resulting in the highest specificity for distinguishing between CRPS and non-CRPS. (4) The calculation of a sum score including several parameters, describing the dynamic changes during daily activities, allowed the diagnosis of CRPS vs. non-CRPS with a specificity of 67% and sensitivity of 73% (vs. healthy controls: 79%, respectively, 94%).

Our results, that a side difference >2 °C occurred more often and for a longer period of time in CRPS but also in other painful states like neuropathic pain after nerve injury, soft tissue injury, posttraumatic arthrosis or psychosomatic pain disorder (Fig. 3A–C), are in accordance with previous human [6,11,31,36] and animal studies [34]. In patients with carpal tunnel syndrome and a conceivable affection of the autonomic nerve fibers due to median nerve lesion, the blood flow and skin temperature regulation were impaired in the innervation territory of the median nerve [1,14,23,24,39]. On the other hand, the dorsum of the affected leg was mostly colder in patient with severe residual pain after prolapsed disc surgery and a correlation between the temperature and the pain sensations was found [13]. Furthermore, a temperature side difference could be maintained by short-term immobility of one limb in healthy subjects [33]. Inflammation is another possible mechanism for skin temperature abnormalities [8]. Thus, not only neuropathic pain after nerve lesions causing vasomotor dysfunction, but also unilateral limb disuse or inflammatory processes may result in a skin temperature side difference which considerably complicates the diagnostic procedures.

In two cases in the control patient group the measuring probes on the palmar pad of the index finger were located outside the affected territory after nerve injury of the superficial branch of the radial or ulnar nerve. Disturbed sympathetic regulation after nerve injury without CRPS occurs due to the impairment of the postganglionic fibers but is not expected to spread beyond the supply area of the affected nerve [2,35]. Therefore, only skin temperature side differences outside the supply area of the affected nerve are relevant for diagnosing CRPS. The patient with neuropathic pain after median nerve lesion presented an 'indifferent' regulation type. Thus, although the skin temperature was assessed in the area of the affected nerve, this did not induce false positive results of the present analysis.

Under experimental settings the individual vascular abnormalities in CRPS depended on the sympathetic vasoconstrictor ability [24,36]. A vasoconstriction impairment, measured in the blood flow, was found only in CRPS after provocation of the autonomic nervous system by different clinical tests (mental arithmetic, cold pressor test, inspiratory gasp and Valsalva maneuver), all of them acting through both peripheral and central pathways and, therefore, suggesting a supraspinal dysfunction of the sympathetical regulation [4,6,7,31]. However, in all of these studies CRPS patients were compared either to patients with limb pain of other origin or to healthy controls, except in one study which included both control groups [31].

The long-term temperature assessment allowed the analysis of the skin temperature changes during environmental alterations like a-synchronicity and asymmetries in the oscillation number. We found a more complex dysregulation pattern with additionally decreased oscillation frequency on the affected side compared to the contralateral side only in CRPS but in none of the other probands, resulting in the highest specificity for distinguishing between CRPS and non-CRPS. In a former case report about a patient with CRPS, sympathetic activation, induced by deep inspirations, resulted only in small blood-flow oscillations on the affected side, which were passively induced by blood pressure and venous tone changes, whereas marked short-lasting blood flow drops were seen on the unaffected side [38]. In eight CRPS patients, a remarkably stable instantaneous flow during baseline measurements was found in either limb, in contrast to healthy controls, therefore suggesting a possible bilateral dysfunction [4]. However, in some of these patients the contralateral control extremity was also affected. In the present study, we included only patients with unilateral complaints. Some of the patients with CRPS (Fig. 2D) showed almost no oscillation number side differences and, interestingly, a few patients presented even a considerably greater number of oscillations on the affected side.

A 'warm' regulation type is assumed to be typical for the early stages of CRPS I and a 'cold' regulation type for the chronic stages. In accordance with previous studies, the duration of the disease and the maximal temperature side difference during the thermoregulatory cycle correlated inversely [25,37]. However, statistical analysis of the correlation between the regulation type and the duration of the disease needs to be interpreted with caution because only five patients suffered from CRPS for longer than 6 months, two of them presenting a 'warm' regulation type. Moreover, nearly half of the patients suffering from CRPS no longer than 6 months revealed another regulation type than 'warm'. Thus, it is very important for future studies to investigate the shift in the skin temperature side differences during the course of the disease.

The medication of the patients, e.g. tricyclic antidepressants (TCA), might have influenced the autonomic

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function. But only one of the five patients without any medication during the investigation presented an indifferent regulation type. And only two of the 12 patients with CRPS, not receiving TCA, presented a type of regulation similar to that of healthy controls. On the other hand, six of the patients with limb pain of other origin, not receiving TCA, presented a warm or cold regulation type. Furthermore, three patients with CRPS receiving antihypertensives presented a type of regulation similar to healthy controls; the other four patients taking antihypertensives (CRPS: $n = 3$; non-CRPS: $n = 1$) presented a warm type of regulation. Therefore, we assume that patients' medication was not primarily responsible for false positive results in the present investigation. This assumption is supported by the results of one of a few former studies which included only patients without vasoactive medication showing significant differences between patients and healthy controls, but not between both patient groups [12]. The present results differ slightly from two studies that included only patients without vasoactive medication [36,37]. However, this can be at least party ascribed to the different testing procedures.

Asymmetries in the skin temperature changes (e.g. oscillation number) over a long-term period during daily activities with alternating ambient temperature can be helpful for discriminating CRPS from other painful states whereas the skin temperature side difference alone is not sufficient for the diagnosis of CRPS. Although there are some limitations like the semi-standardization of the test and potential artifacts, e.g. induced by limb movement and posture influences or a position near a heat or cold source, this can be considered in the evaluation of the patients' activities diary. Furthermore, it is important that the environmental temperature changes are great enough to induce sympathetically mediated skin blood-flow changes in the intact limb to avoid overlooking sympathetic deficits in the affected limb, e.g. by going inside a cold room on a warm day. In the present study, the difference between minimal and maximal skin temperature in the control side during measurements was on average 15 °C, indicating significant skin temperature changes due to sympathetic activity. The applied technique of skin temperature measurement and analysis can be easily implemented in clinical settings as the only technical investment is a portable temperature data logger and the analysis of the obtained data is effortless using a precast evaluation file in Microsoft® Excel (can be provided). The time needed for instruction of the patients and fixing the measuring probes amounts to less than 15 min and the data transfer and calculations last another 10–15 min. Thus, it can be a useful bedside test that may serve as a further facet in the difficult diagnosis of CRPS.

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