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Repeatability of dermatomal warm and cold sensory thresholds in patients with sciatica

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Abstract Quantification of thermal thresholds is a useful method to assess and follow up the function of afferent small A- δ and C-fibres in patients with nerve dysfunctions. The object of this study was to estimate thermal test-retest repeatability in 19 patients with unilateral sciatica (14 L5 and 5 S1) in affected and non-affected dermatomes on the symptomatic (S) and non-symptomatic (NS) sides. Detection thresholds were measured at six sites, two within each of the L4, L5 and S1 dermatomes. The test was repeated after 1–2 h and the coefficient of repeatability (CR=2SD of test-retest differences) was calculated. Warm threshold repeatability did not differ between S and NS sides, but cold threshold CR was higher in the affected dermatome on the foot as compared to the contralateral dermatome ($P=0.04$). Warm thresholds

were more variable (CR=5°C and 4.7°C on S and NS sides) than cold thresholds (CR=2.2°C and 2.1°C on the S and NS sides). The expected range of variation for the second measurement was between 51% and 200% for warm and between 45% and 230% for cold thresholds. The sensitivity was better on the foot than the lateral calf (5 of 14 vs 1 of 14 abnormal thresholds) in the subgroup with L5 sciatica. We conclude that dermatomal thermotesting has acceptable repeatability, particularly at proximal lower extremity sites. The test may be useful in longitudinal investigations of patients with sciatica, e.g. in treatment follow-up studies.

Keywords Thermotest · Repeatability · Sensory thresholds · Low-back pain · Sciatica

Introduction

Quantification of thermal thresholds [11, 16, 23, 43, 44] is a simple method to assess the function of afferent thin myelinated A- δ fibres and unmyelinated C-fibres [1, 21] and abnormalities have been found in several types of neurological disorders [6, 22, 24, 27, 28, 31, 37, 39]. The test has recently been applied in patients with sciatica [34, 41, 46], but a systematic evaluation of thresholds in the L4, L5 and S1 dermatomes has not been performed previously.

Thermotest repeatability has been studied in healthy volunteers using various testing algorithms [3, 4, 5, 6, 8,

12, 15, 17, 20, 25, 26, 30, 32, 33, 41, 42, 45], but many previous studies fail to give actual estimates of repeatability [4, 15, 20, 25, 26, 32, 41] or they used inappropriate measures of agreement [12, 20, 33, 41]. Repeatability has been studied in the hand and the foot [12, 20, 33, 41], but data regarding more proximal sites are lacking. Information about repeatability in the calf and the thigh may be of particular interest, because warm thresholds recently have been found to be abnormal in patients with sciatica [34, 42, 46].

Quantitative sensory testing is used increasingly in clinical trials [2, 15, 35, 36], and the normal test-retest variation must be known in order to interpret the test re-

sults during follow-up. It is also useful to know whether test-retest repeatability is influenced by disease or by symptoms like pain [38], but knowledge about the latter subject is limited. Only a few studies have assessed repeatability in patients with diabetic neuropathy [6, 8, 15, 17, 20, 30, 32] or complex regional pain syndrome type I (CRPS I) [27]. A few authors have found lower repeatability in patients as compared to controls [6, 8, 17], but others have not [32, 33].

The main purpose of the present study was to estimate lower extremity test-retest repeatability [7] and intraclass correlation [18] of thermal thresholds in dermatomes of the foot, the calf, and the thigh in patients with unilateral sciatica. We also intended to compare the repeatability in the affected dermatome versus the non-affected contralateral dermatome. Another objective was to provide preliminary estimates of test sensitivity and the regional distribution of abnormal thresholds.

Materials and methods

Nineteen patients with lumbosacral radiculopathy (11 men and 8 women, mean age 44.8 years, range 19–74 years; 14 L5, 5 S1) were recruited consecutively from patients under evaluation for disc surgery. This number is usually adequate for a reliability study [18]. Twelve patients had a history of less than 6 months duration of symptoms. Patients with other neurological disorders, diabetes or vascular claudication were excluded. The affected root level was diagnosed on the basis of clinical and radiological findings by attending physicians who were unaware of thermal test results. The local ethics committee approved the protocol.

The investigator (J.A.Z.) was unaware of clinical and radiological data at the time of thermotest. Later, pain perception (pin-prick test) was scored as abnormal or normal from the hospital records. Touch sensation was scored abnormal if asymmetrical von-Frey hair thresholds were found in the affected dermatomes on the day of thermal testing. Patients rated their leg pain intensity at the time of investigation on visual analogue scales with a range of 0 to 100. Nine patients were pain free at the time of investigation and ten had pain levels of between 5 and 75% (mean 37%). Patients were without analgesic medication at the time of investigation.

Somedit thermotest with a computer interface and software (method of limits) and a 25×50-mm thermode was used. Skin temperature was used as baseline, and the rate of change was 1°C/s. The patients were supine and they pressed a button as soon as they perceived the first sensation of warmth or cold (sensory detection threshold). Seven warm followed by seven cold stimuli were applied at each skin site. The highest and the lowest threshold values were deleted, and the mean of the remaining five values was used in further calculations.

Six points on both symptomatic (S) and non-symptomatic (NS) sides were investigated, and the test was repeated after 1–2 h. Stimulation points were centrally located within the dermatomes. Point 1 was just above the patella (L4), points 2, 3 and 4 were 15 cm distal to the knee joint on the medial part (point 2, L4), lateral part (point 3, L5) and the dorsal part (point 4, S1) of the calf respectively. Point 5 was on the foot, just below the lateral malleolus, and point 6 was on the foot between the first and third metatarsal bones, with the distal part of the thermode approximately 4 cm proximal to the MTP joints (L5).

Statistical analysis

To estimate the magnitude of variability, the individual test 2–test 1 differences were calculated for each point. The coefficient of repeatability is two times the standard deviation of these differences ($CR=2SD_{diff}$) [7]. Approximately 95% of retest-test differences is expected to be in the (–CR, +CR) range. CR was also computed after logarithmic transformation, allowing the expected range for the retest/test ratio to be calculated (as a percentage).

The intraclass correlation coefficients (ICC) were computed as described by Fleiss [18]. ICC is the fraction of total variance (between subjects + within subjects) which is caused by variation between subjects.

To assess a possible systematic difference between test 1 and test 2, two repeated measures ANOVAs (one for cold and one for warmth) were performed. Tests, points, and sides (S vs NS) were used as within-subject repetition factors. Two additional repeated measures ANOVAs were performed on the absolute (positive) threshold differences, in order to test whether repeatability differed between sites and between sides.

In order to investigate whether repeatability was larger in the symptomatic dermatome (L5 in 14 subjects, S1 in 5 subjects) as compared to the contralateral dermatome, we compared the absolute test 1–test 2 differences with paired Wilcoxon signed-rank tests. The statistical power to detect „large effects“ (100% of SD) and „medium effects“ (80% of SD) was 92% and 55% respectively [13, 29]. To explore the association between repeatability and age, we performed two linear regression analyses, one for cold and one for warmth, on across-site mean absolute threshold differences.

Patient control limits (95% two-sided limits with 80% confidence probability) were calculated as NS side mean thresholds +2.5 between-subjects SD [40]. The abnormality rates were calculated in the 14 patients with L5 symptoms.

Results

Significant test 2–test 1 mean threshold differences were not found (ANOVA). Repeatability varied significantly across sites (ANOVA, warm $P=0.05$, cold $P=0.03$), and the highest CR values were found on the foot (S1 and L5) and on the lateral calf (L5) (Table 1). We observed a few large „outlying“ warm threshold test-retest differences ($>6^{\circ}\text{C}$) in the distal (foot) S1 (5/38 sites) and L5 (1/38 sites) areas as well as in the lateral (L5) calf area (2/38 sites) both on S and NS sides. The lowest warm threshold repeatability was found in the oldest subjects ($P=0.03$). Repeatability did not correlate with pain intensity.

Bland-Altman plots revealed that test 2–test 1 differences increased with the magnitude of thresholds. A logarithmic transformation removed this association. When we used the logarithmic transformation before calculating CR (as a ratio in %), we found similar CR values between sites and sides (Table 1). A second cold (warm)-threshold measurement could be expected to lie between 45 and 230% (51 and 200%) of the first measurement (averaged across the 12 sites). When CR was expressed in degrees centigrade we found a smaller CR for cold thresholds than for warm thresholds (Table 1). Most cold thresholds had, according to Fleiss [18], good ($ICC>0.4$) or excellent ($ICC>0.75$) repeatability (Table 1). Warm threshold ICC values were lower (good repeatability).

Table 1 Thermal thresholds and repeatability [*CR* coefficient of repeatability (2SD of test 1–test 2 differences), *ICC* intraclass correlation coefficient (fraction of total variance caused by variation between subjects)]

	Symptomatic side			Non-symptomatic side		
	Detection threshold ^a (°C) Mean (SD)	CR (ratio ^b) (°C)	ICC	Detection threshold ^a (°C) Mean (SD)	CR (ratio ^b) (°C)	ICC
Cold thresholds						
Suprapatellar (L4)	1.5 (1.0)	1.3 (47%)	0.80	1.3 (0.7)	1.2 (52%)	0.62
Medial calf (L4)	2.0 (1.2)	1.8 (51%)	0.69	1.9 (1.1)	2.0 (40%)	0.56
Lateral calf (L5)	2.3 (1.4)	2.6 (42%)	0.61	2.2 (1.3)	2.6 (34%)	0.49
Dorsal calf (S1)	2.1 (1.3)	1.5 (52%)	0.83	2.2 (1.8)	2.1 (43%)	0.79
Dorsum foot (L5)	3.2 (3.0)	3.4 (49%)	0.82	2.2 (1.6)	1.7 (46%)	0.86
Lateral foot (S1)	1.6 (0.9)	1.9 (42%)	0.40	1.5 (1.1)	2.7 (42%)	0.27
Warm thresholds						
Suprapatellar (L4)	4.3 (1.5)	3.5 (48%)	0.35	4.1 (1.4)	2.8 (55%)	0.47
Medial calf (L4)	6.1 (2.0)	3.6 (55%)	0.61	6.1 (2.6)	5.1 (52%)	0.52
Lateral calf (L5)	8.2 (2.9)	5.4 (53%)	0.57	7.4 (3.0)	6.2 (40%)	0.43
Dorsal calf (S1)	6.4 (2.6)	4.1 (57%)	0.67	6.3 (2.6)	3.1 (62%)	0.82
Dorsum foot (L5)	9.1 (3.0)	5.5 (50%)	0.59	7.3 (2.3)	3.5 (65%)	0.73
Lateral foot (S1)	7.2 (3.6)	7.0 (39%)	0.52	7.4 (3.9)	6.2 (38%)	0.68

^aMean test 1 and test 2 values, with pooled standard deviation for test 1 and test 2 given in parentheses

^bLower CR limit for test 2/test 1 ratio (the upper limit is the inverse of the tabulated fraction)

Table 2 Absolute thermal test 2–test 1 differences (°C) in affected versus contralateral non-affected dermatomes

	Affected dermatome ^a Mean (SD)	Non-affected dermatome Mean (SD)	<i>P</i> -value ^b
Cold threshold calf	0.8 (0.9)	0.9 (0.8)	0.43
Cold threshold foot	1.2 (1.5)	0.6 (0.5)	0.04
Warm threshold calf	2.0 (2.0)	2.1 (2.4)	0.89
Warm threshold foot	1.9 (1.6)	1.5 (1.1)	0.20

^aL5 (*n*=14) or S1 (*n*=5)

^bWilcoxon signed-rank test

Table 3 Distribution of abnormal thresholds in the symptomatic lower extremity of 14 patients with unilateral L5 sciatica

Point	Abnormal thresholds (<i>n</i>)			Control limits (°C) ^a	
	Cold	Warm	Cold or warm	Cold	Warm
Suprapatellar (L4)	1	1	1	2.9	7.0
Medial calf (L4)	1	0	1	4.2	11.7
Lateral calf (L5)	1	0	1	4.8	13.7
Dorsal calf (S1)	0	0	0	6.4	12.4
Dorsum foot (L5)	3	3	5	6.0	12.6
Lateral foot (S1)	0	0	0	3.7	16.3

^aControl limits were defined as NS side average+2.5 SD

The repeatability was of the same magnitude on the S and the NS sides (ANOVA, warm thresholds *P*=0.53, cold thresholds *P*=0.93) (Table 1). For cold thresholds in the affected dermatome at the foot, the mean absolute test 2–test 1 difference was higher for cold thresholds on the S than on the NS side (*P*=0.04, Table 2).

Abnormality rates based on NS side control limits for the subgroup with L5 symptoms are shown in Table 3. The sensitivity was low with this method; 5 of 14 patients (36%) had abnormal warm or cold thresholds on the dorsal foot, while only one patient had a definite abnormality in the lateral calf L5 dermatome.

In this subgroup, post-hoc paired Wilcoxon signed-rank tests revealed that cold and warm thresholds were significantly higher in the dorsal foot on the symptomatic side compared to the non-symptomatic side [mean S vs NS = 3.8°C vs 2.5°C, *P*=0.02 (cold) and 9.5°C vs 7.9°C, *P*=0.02 (warm)]. Lateral calf threshold differences were insignificant for cold (*P*=0.73) and warm (*P*=0.16).

Discussion

Fagius and Wahren [17] found a CR range (calculated from log-transformed thermal detection thresholds) in the foot of 40–190% in controls and 37–265% in diabetics. Claus et al. [11] published test-retest histograms from healthy subjects, which indicated that the retest threshold varied from about 25% to about 200%. Yarnitsky and Sprecher [45] calculated the CR in the foot to be 3.8°C for warm and 4.3°C for cold thresholds. Kemler et al. [27] reported the CR on the S (and NS) side on the dorsal foot to be 2.9°C (4.4°C) for warm and 5.3°C (3.4°C) for cold detection thresholds in CRPS I patients. The results from these four studies are in general accordance with our own estimates. Although patients with sciatica in general seem to have repeatability of the same magnitude as healthy sub-

jects and other patient groups, our results suggest that cold thresholds in an abnormal dermatome may be slightly more variable than thresholds at a non-symptomatic site.

Warmth-insensitive areas in the forearm (e.g. areas of at least 4.84 cm² with thresholds larger than 41°C) have recently been demonstrated in healthy volunteers, and the authors suggested that this is probably caused by a very low warmth receptor density in some normal skin areas [19]. This may contribute to the large test-retest differences in individual areas in some of our patients. It is not known whether other skin properties, e.g. the curved anatomy of the foot, contribute to reduce repeatability. To the authors' knowledge, no reports have been published of similar insensitive fields in the legs of healthy humans, at least not fields as large as our thermode area (12.5 cm²); however, insensitivity was never observed in two adjacent skin areas of healthy arms [19]. Caution must therefore be exercised before an increased warm threshold in a sciatica patient can be interpreted as a sign of C-fibre dysfunction. We propose to investigate whether thresholds are more repeatable (without loss of test sensitivity) when warm thresholds are measured in two adjacent skin areas.

Levy et al. [30] found larger variation for cold than for warm thresholds. Dyck et al. [15], on the other hand, emphasised that cold thresholds were more reliable than warm thresholds [8]. In the present study, repeatability was lower for warm than for cold thresholds when results were expressed in degrees centigrade. When test-retest variation was normalised and expressed as a log-transformed ratio, repeatability was almost equal for warm and cold thresholds, because warm thresholds in general are of greater magnitude than cold thresholds [11, 27]. We conclude that a logarithmic transformation of thermal threshold ratios may be preferable [17, 33]. In diabetic patients [8], as well as in the present study, elevated thresholds seem to predict low repeatability, but this confounding is lost when the ratio scale is applied.

Pearson's correlation coefficient does not measure repeatability [7], and ICC [18] is a better measure of agreement [15]. ICC estimates suggested that thermotest repeatability was acceptable both for cold and warm thresholds. ICC values were higher for cold as compared to warm thresholds for the majority of the 12 points, probably due to the presence of warmth threshold outliers. It should be noted that high ICC values can occur in two different situations:

1. When the within-subject variation is small
2. When the between-subject variation is large

The time interval between the two test sessions was shorter in the present than in previous studies. We chose to study short-time repeatability to avoid the effects of

disease progression or regression. Others have mainly focused on repeatability over days or weeks (or "reproducibility"; see British Standards Institution definitions [9]). In general, an estimate of short-time repeatability can be considered as a lower-limit estimate of across-weeks reproducibility.

Sample sizes can be calculated from the present variability estimates. In order to detect a mean cold threshold difference equal to 0.5°C in a paired (unpaired) follow-up study, we need approximately 41 (148) subjects. We need about 54 (197) subjects in a paired (unpaired) study to detect a population mean warm threshold difference equal to 1°C. Both thermal thresholds in themselves [10, 14, 46] and test-retest differences (present study) seem to increase with age. Warm threshold repeatability did not differ between sides, although C-fibres seem to be more severely affected in sciatica than A- δ fibres [46]. Cold threshold repeatability, on the other hand, was slightly worse on the symptomatic compared to the non-symptomatic side. Thus, a slightly larger sample may be needed in follow-up studies of older as compared to younger subjects, and a study on patients may require more subjects than a study performed on symptom-free volunteers.

The estimates in Table 3 suggest that thermal testing has a rather low sensitivity in unilateral L5 sciatica, especially in the lateral calf; however, these preliminary data should be regarded with some caution. First, the putative presence of subclinical contralateral nerve root dysfunction [34] may have reduced sensitivity in the present design. Second, the future use of individual S-NS differences may improve sensitivity. Third, the possible presence of warmth-insensitive areas in the legs may necessitate routine testing in at least two adjacent skin areas. Fourth, because thermal testing has the potential ability to detect a subclinical dysfunction, a prospective study is needed in order to determine the possible prognostic significance of abnormal thresholds in adjacent or contralateral dermatomes.

Conclusion

We conclude that dermatomal thermotesting has acceptable repeatability, at least in the setting of a scientific follow-up study of patient groups. Our results suggest that the distal test sites may be most sensitive in diagnosis, while proximal sites, due to the partially better repeatability, may prove to be useful in longitudinal follow-up studies. The cause of the particularly large test-retest differences in some subjects, including on the non-symptomatic side, is unknown, and this matter needs further study.

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