Temperature Sensation in Parkinson's Disease Measured by Quantitative Sensory Testing

Michaela Kaiserova (michaela.kaiserova@fnol.cz)
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
https://orcid.org/0000-0003-4776-9055
Zuzana Grambalova
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
Pavel Otruba
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
Anetta Janova
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
Jana Zapletalova
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
Katerina Mensikova
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta
Petr Kanovsky
Palacky University Olomouc Faculty of Medicine and Dentistry: Univerzita Palackeho v Olomouci Lekarska fakulta

Research

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Abstract

Background

The pathophysiology of abnormal temperature sensation in Parkinson's disease (PD) remains unclear. Abnormal thermal detection does not seem to depend on the dopaminergic deficit, suggesting that other systems play a role in these changes, probably both central and peripheral.

Methods

We measured thermal detection thresholds (TDT) using quantitative sensory testing (QST) in 28 patients with PD and compared them with 15 healthy controls.

Results

Of 28 patients, 21 % had increased TDT according to the normative data. TDT were higher on the dominant side. No correlation between TDT and disease duration, severity of motor impairment, and dopaminergic therapy was observed. 50 % of the patients had difficulty differentiating between warm and cold stimuli, as TDT were within the normal range in most of these patients.

Conclusions

These results suggest that abnormal thermal detection may be present from early stages of the disease and is more pronounced on the dominant side. Abnormal differentiation between the thermal stimuli suggest impaired central processing of thermal information.

Introduction

Apart from motor symptoms, Parkinson's disease (PD) is characterized by a number of non-motor features, such as autonomic dysfunction, sleep disturbances, sensory, neuropsychiatric, and gastrointestinal symptoms. Sensory symptoms are common in PD, usually manifested as pain, numbness, paresthesias, or dysesthesias. Patients often describe coldness and tingling or tightening of the muscles without objective evidence of sensory loss [1–3]. There have been several studies concerning peripheral nerve pathology in PD, such as polyneuropathy [4, 5], small fibre neuropathy [6, 7] or motor neuron disease [8, 9]; some sensory symptoms are supposed to be caused by central pathology [10].

Only a limited number of studies have investigated thermal abnormalities in PD [11–19] and the underlying pathophysiology still remains unclear. Most of the published studies found increased thermal detection thresholds but no responsiveness to levodopa, suggesting that thermal abnormalities do not depend on dopaminergic deficit. Some studies found reduced thermal detection thresholds after STN-DBS (Deep Bran Stimulation of the Subthalamic Nucleus) [3, 11, 14, 16, 20, 21], suggesting that central pathology plays a role in abnormal thermal sensation. Peripheral deafferentation probably also plays a role [15, 17], as small fiber neuropathy has been confirmed on skin biopsies in PD patients [6, 7].

The aim of our study was to describe the characteristics of temperature detection in PD. We measured thermal detection thresholds in PD using quantitative sensory testing (QST) and correlated the results with the disease duration, severity of motor impairment, and dosage of dopaminergic medication. We also assessed the side-to-side difference in thermal detection thresholds.

Material And Methods

The study protocol, was approved by the Ethics Committee of Palacky University in Olomouc; all participants gave their informed consent prior to their recruitment into the study. All procedures were performed in accordance with relevant guidelines and regulations.

Patients and Controls

The study included 28 patients with PD (11 male, 17 female; mean age 57.5 years, SD = 7.8) (Table 1) and 15 healthy age-matched controls (mean age 58.2, SD = 10.2). The diagnosis of PD was established according to the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria [22]. None of the patients had dementia (25 patients underwent complete neuropsychological testing; 3 patients were administered the Mini-Mental State Examination (MMSE) with results within the normal range. All patients and controls underwent QST and a nerve conduction study (NSC). Of the 28 examined patients, 17 patients were treated with levodopa, dopamine agonist, or both; the other 11 were dopa naïve.

Table 1
Patients´characteristics

Patient	Sex	Age (years)	Dominant side	Duration of PD (years)	H&Y	Abnormal absolute QST values (1)	Discrimination abnoramlities	Antiparkinsonian drugs	Levodopa equivalent (mg) (2)
1	M	54	L	1	2,5				
2	F	52	L	6	3	cold dominant		LD, rop	880
3	M	72	L	3	3			LD, pram	360
4	F	61	L	1	1				
5	M	63	L	1	2	cold dominant	bilateral		
6	M	59	L	5	2		bilateral	LD, pram	1010
7	F	61	L	7	2			LD, rop	980
8	F	62	L	2	1				
9	F	59	L	11	2			LD, rop	720
10	F	47	L	1	1		bilateral		
11	F	56	L	3	1		bilateral	rop	320
12	F	59	L	1	1	warm dominant	Dominant side		
13	F	64	L	2	2				
14	M	54	L	2	1		bilateral		
15	M	58	R	3	2		bilateral	LD, rot	880
16	Z	55	R	3	1			LD, rop	660
17	M	56	R	2	2			LD	1000
18	Z	61	R	1	2		bilateral		
19	M	56	R	1	1			pram	210
20	Z	50	R	1	1		Dominant side		
21	Z	46	R	0,5	1				
22	Z	72	R	11	3			LD, rop	1230
23	Z	52	R	6	2		bilateral	LD	1000
24	M	37	R	10	2		Dominant side	LD, rop	880

1) Absolute QST values according to the normative data (Rolke et al., 2006)

2) Levodopa equivalent (Moller et al., 2005)

Moller, J.C., et al., 2005. Pharmacotherapy of Parkinson's disease in Germany. J Neurol. 252, 926 – 35.

Rolke, R., et al., 2006. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): standardized protocol and reference values. Pain. 123, 231 – 43.

Patient	Sex	Age (years)	Dominant side	Duration of PD (years)	H&Y	Abnormal absolute QST values (1)	Discrimination abnoramlities	Antiparkinsonian drugs	Levodopa equivalent (mg) (2)
25	M	60	R	1	1	warm non-dominant		rop	320
26	Z	55	R	9	2	cold dominant, warm bilateraly	bilateral	pram	210
27	Z	73	R	11	4	warm bilateraly	bilateral	LD	400
28	M	57	R	8	3		non-dominant side	LD, rop	720

1) Absolute QST values according to the normative data (Rolke et al., 2006)

2) Levodopa equivalent (Moller et al., 2005)

Moller, J.C., et al., 2005. Pharmacotherapy of Parkinson's disease in Germany. J Neurol. 252, 926 – 35.

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Quantitative sensory testing

Thermal thresholds (cold detection threshold, CDT, and warm detection threshold, WDT) were tested using Medoc,TSA 2001, Israel. Testing was performed on the dorsum of both feet using the methods of limits [23]. Five stimuli of each modality were delivered. In the next step, 10 thermal stimuli were applied in random order and the patient was asked to identify the type of the stimulus (warm vs. cold).

Nerve conduction study

NCS was performed using the Keypoint IV® system (Medtronic, Tonstakken, Denmark) under standardized conditions [24]. The motor conduction of the deep peroneal and tibial nerves and sensory conduction of the sural and superficial peroneal nerves were measured.

Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics for Windows, Version 22.0 (Armonk, NY: IBM Corp.). The Wilcoxon signed-ranks test was used to evaluate paired measurements (side-to side differences in thermal detection thresholds in patients and controls, comparison of thermal detection thresholds on dominant vs. non-dominant side). The Mann-Whitney U test was used to compare differences between patients and controls. The relationships between thermal detection thresholds and selected quantitative parameters (disease duration, Hoehn & Yahr score) were assessed using the Spearman’s correlation. Tests were performed at the significance level of 0.05.

Results

Subjects

Patients´ characteristics are listed in Table 1. The mean disease duration of PD patients was 4.1 years (minimum 0.5 years, maximum 11 years), SD 3.6. Disease duration was measured from the time when the first motor symptoms occurred. Hoehn & Yahr score ranged from I to III.

Nerve conduction studies and Quantitative sensory testing

Conduction studies excluded polyneuropathy in all subjects, both patients and controls. WDT and CDT in PD and controls are listed in Tables 2 and 3. In the control group, the mean temperature was obtained from the average values of both feet; the mean CDT was 28.9 °C (median 29.1 °C), the mean WDT was 38.3 (median 37.6 °C). Six PD patients (21%) had increased thermal detection thresholds (CDT or WDT or both) according to the normative data given by Rolke et al. (2006) [25]. All control subjects had thermal thresholds within the normal range. PD patients showed significantly higher thermal detection thresholds on the more affected side than on the non-dominant side (cold P = 0.015, warm P = 0.045) (Table 2, Figs. 1 and 2). In the control group, there was no side-to-side difference in the thermal detection thresholds (cold P = 0.099, warm P = 0.615) (Table 3). Fourteen patients (50%) had difficulties with differentiating between warm and cold stimuli. No significant correlation between thermal detection thresholds and disease duration, Hoehn & Yahr score, or dopaminergic drug intake was observed.

Table 2
Cold and warm detection thresholds in Parkinson's disease patients

	Mean (ºC)	SD	Median (ºC)	Minimum (ºC)	Maximum (ºC)	Wilcoxon signed-ranks test (P)
dominant CDT	27,3	2,6	27,9	18,2	30,2	0,015
non-dominant CDT	28,0	2,5	28,8	19,0	31,0	
dominant WDT	39,9	3,5	38,9	34,6	47,4	0,045
non-dominant WDT	39,2	3,7	38,6	35,0	48,9	

CDT, cold detection threshold; WDT, warm detection threshold; dominant, more affected side; non-dominant, less affected side

Table 3
Cold and warm detection thresholds in control group

	Mean (ºC)	SD	Median (ºC)	Minimum (ºC)	Maximum (ºC)	Wilcoxon signed-ranks test (P)
Left foot - CDT	29,1	2,0	29,6	23,2	31,0	0,099
Right foot - CDT	28,6	2,3	28,9	21,2	31,1	
Left foot - WDT	38,4	2,9	37,6	34,3	43,0	0,615
Right foot - WDT	38,1	2,9	37,6	34,4	45,2	

CDT, cold detection threshold; WDT, warm detection threshold; dominant, more affected side; non-dominant, less affected side

Discussion

Little is known about the abnormal temperature sensation in PD, although the impaired temperature sensation may negatively affect the quality of life in PD. Using QST as a diagnostic method, several studies found an increased temperature threshold in PD [14, 16–18]; other studies did not find any difference between the patients and the control group [13, 26]. In our study, only 21% of the patients had increased thermal detection thresholds (CDT or WDT or both) according to the normative data given by Rolke et al [25]. With regard to these findings, abnormal thermal thresholds measured by QST are present in the minority of patients and do not seem to be a typical finding in PD. The study of Lin et al. found similar results [15]. In their cohort of PD patients, 32.1% had abnormal thermal thresholds.

On the other hand, 50% of the patients had difficulty differentiating between warm and cold stimuli; increased thermal detection thresholds, however, were present only in 4 of those patients (28%). This means that patients may have preserved ability to detect a thermal stimulus per se, demonstrated as a normal thermal threshold in QST, but they have difficulty differentiating the type of the applied stimulus. This suggests a deficit in the central processing of the thermal information.

Previous studies [14, 17] found no difference in somatosensory thresholds between the dominant and non-dominant side. Our observation was different. PD patients in our cohort showed higher thermal thresholds on the more affected side compared to the non-dominant side, both for cold and warm stimuli.

Next, we focused on the disease duration, severity of the disease, and antiparkinsonian drug intake as possible modifying parameters of temperature detection thresholds. There was no correlation of CDT or WDT with the disease duration, suggesting that abnormal thermal sensation may be present from the early stages of PD. This finding is consistent with the reports by Nolano et al. [17, 18] and supported by the study of Strobel et al., who found abnormal thermal thresholds in idiopathic REM sleep behavior disorder [27], which is considered a frequent and important premotor symptom of PD [18].

The severity of motor impairment, as measured by Hoehn & Yahr scores, did not correlate with the thermal thresholds, suggesting no association between abnormal thermal detection thresholds and dopaminergic deficit. This is also supported by the finding of no significant difference in WDT or CDT in PD patients who take levodopa and who are dopa naïve. Our findings are consistent with other studies that showed no effect of dopamine treatment on thermal sensation [13, 14].

Conclusions

Abnormal thermal detection may be present from the early stages of PD and is more pronounced on the more affected side. But only a minority of patients have increased thermal detection thresholds as measured by QST. More commonly observed is difficulty differentiating between warm and cold stimuli, which suggests an impaired central processing of thermal information.

List Of Abbreviations

PD Parkinson’s disease

STN-DBS Deep Bran Stimulation of the Subthalamic Nucleus

QST Quantitative sensory testing

NCS Nerve conduction study

CDT Cold detection threshold

WDT Warm detection threshold

MMSE Mini-Mental State Examination

Declarations

Ethics approval and consent to participate

The study protocol, was approved by the Ethics Committee of Palacky University in Olomouc; all participants gave their informed consent prior to their recruitment into the study. All procedures were performed in accordance with relevant guidelines and regulations.

Consent for publication

All contributing authors have given their consent for the publication of this study.

Availability of data and material

The data that support the findings of this study are available from the corresponding author, upon reasonable request.

Competing interests

The authors declare that they have no conflicts of interest.

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Author contributions

M.K. study design, patient examination, data collection and analysis, drafting the initial manuscript. Z.G., P.O., A.J. patient examination, data collection. J.Z. statistical analysis. PK study design, study supervision, review of the final version of the manuskript

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Not applicable.

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Figures

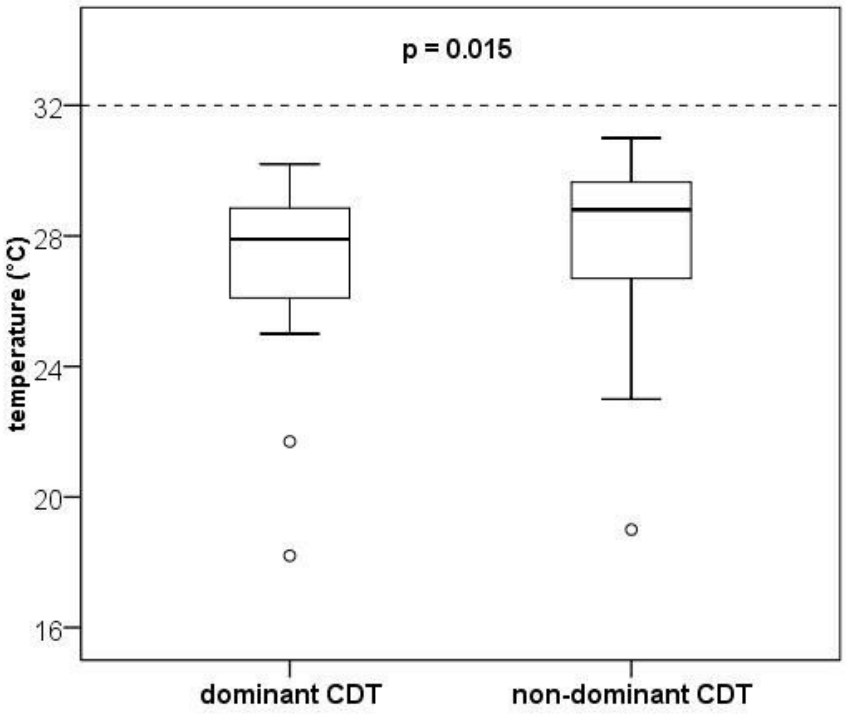

Figure 1

Cold detection threshold in Parkinson's disease patients. CDT, cold detection threshold; dominant, more affected side; non-dominant, less affected side

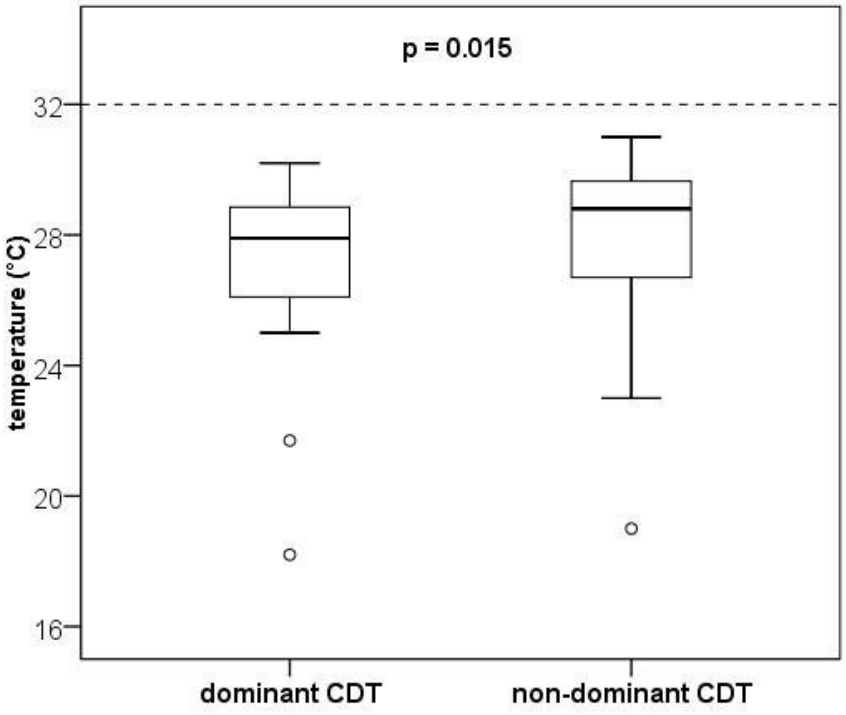

Figure 1

Cold detection threshold in Parkinson's disease patients. CDT, cold detection threshold; dominant, more affected side; non-dominant, less affected side

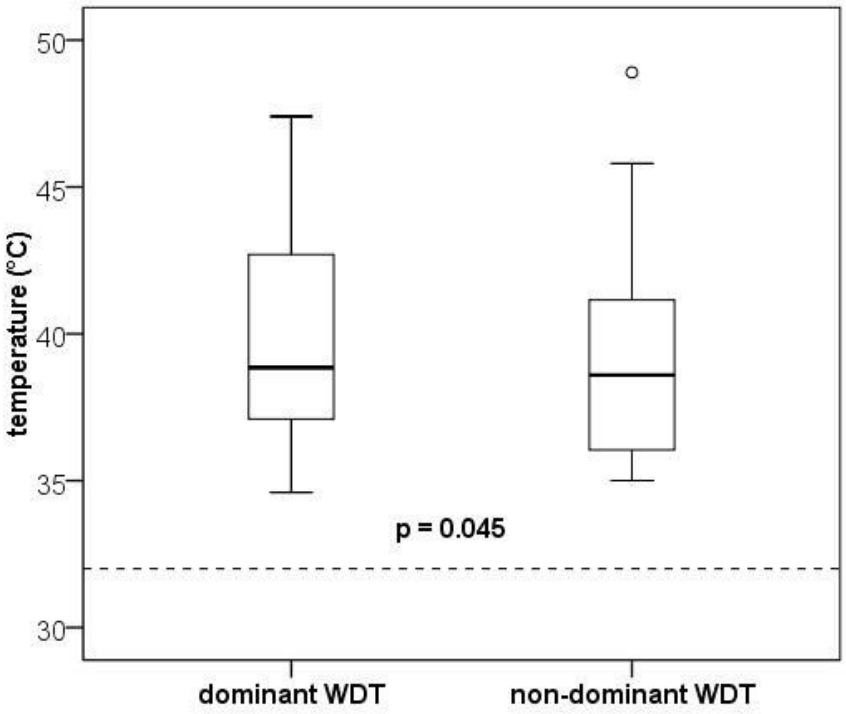

Figure 2

Warm detection threshold in Parkinson's disease patients. WDT, warm detection threshold; dominant, more affected side; non-dominant, less affected side

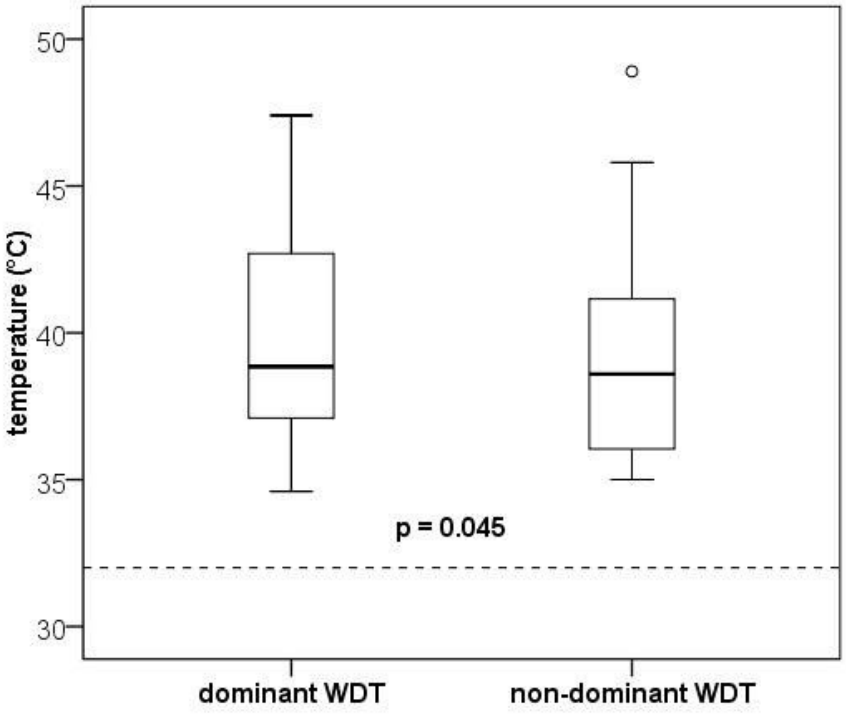

Figure 2

Warm detection threshold in Parkinson's disease patients. WDT, warm detection threshold; dominant, more affected side; non-dominant, less affected side