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# Quantification of Pain Threshold in Parkinson's Disease

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## Abstract

**Background** Parkinson's disease (PD) is the second most common degenerative neurologic disorder after Alzheimer's disease. Pain is one of the major clinical symptoms of Parkinson's disease, occurring in 50-83% of patients. Pathways mediating pain are complex and include basal ganglia and thalamocortical-basalganglia circuits.

**Objective** To quantitatively assess pain perception in Parkinson disease patients, by determining pain threshold in patients with and without pain through using electrical stimulation.

**Methods** A cross sectional observational study recruiting 18 patients with a clinical diagnosis of Parkinson disease and healthy controls from the neurologic unit in Al-Kadhimiya teaching hospital in Baghdad; between May 2010 to Jan 2011. There were 13 men and 5 women with a mean age of (66.5 ± 10.2 years). The control group includes 18 healthy subjects, [12 males/ 8 females] with a mean age of 56.6±6.74 years. Quantitative sensory testing was carried at the neurophysiology laboratory in Al-Kadhimiya hospital; using bipolar stimulating electrodes on the forearm, index finger, mid leg, and big toe.

**Results** Fourteen Out of 18 patients (77.7%) reported pain, while 4 (22.3%) had no pain. There was a highly significant statistical difference in electrical perception between the affected and unaffected side, and between Parkinson disease patients and the controls. There was no statistically significant difference between males and females [p =0.8248], and between patients with and those without pain [p =0.3279]. And between upper and lower limbs on the affected side [p =0.1412], and body side involvement whether right or left in both the patients and controls.

**Conclusion** Chronic pain is present in 77.7% of Parkinson disease. Patients with Parkinson disease had lower pain threshold compared to controls. The affected side had lower pain threshold. The left or right body side and gender had no effect on pain threshold.

**Key worlds** Parkinson disease, Pain

## Introduction

Parkinson's disease (PD) is the second most common neurologic degenerative disorder after Alzheimer's disease. Pathophysiologically there is neuronal loss within the substantia nigra of the midbrain and the neocortex. Pain was reported in (50-83%) of Parkinson's disease [1-3]. Pain is a complex symptom involves sensory pathways within the basal ganglia and the thalamocortical-basal ganglia circuits. Although standard sensory assessments have proved that conduction along peripheral and central pain

pathways is normal in patients with Parkinson disease. Studies assessing more delicate sensory functions, such as spatial, proprioceptive, and tactile-discrimination sensations, showed abnormalities. There is also evidence of a dopaminergic modulation of the objective pain threshold in PD patients [3-5].

Patients with PD often have joint and muscles pains secondary to the rigidity and abnormal postures associated with the disease. Levodopa therapy as well as physiotherapy may alleviate these pains to some extent. Other causes of pain in PD include compression of nerve roots or dystonia-related muscle spasms. In rare cases, people with PD may develop unexplained burning or stabbing sensations, this type of pain, called "central pain," originates in the brain. Dopaminergic drugs, opiates, antidepressants, and other types of drugs may all be used to treat this type of pain [4-6].

The objectives of this study were to quantitatively assess pain perception in patients with PD, with or without pain using electrical stimulation to assess pain threshold.

## Methods

A cross sectional observational study recruiting eighteen patients with a clinical diagnosis of PD and controls from the neurologic unit in Al-Kadhimiya teaching hospital in Baghdad; between May 2010 to Jan 2011. There were 13 men and 5 women with a mean age of 66.5 years (± 10.2, range: 54 to 79). Eighteen healthy subjects were studied as a control group [12 males/ 8 females] with a mean age of 56.6 ± 6.74 years. Patients were included if they fulfilled the UK Parkinson's Disease Society Brain Bank clinical diagnostic criteria [1]. Patients and controls were excluded from the study if they had peripheral neuropathy, joint problems and diabetes mellitus, or patients on antidepressants or antiepileptic medications. Patients consent to participate in the study was taken verbally from the patient and his or her companion; and the study was approved by ethical committee of Al-Nahrain College of Medicine. A full detailed history of the neurologic symptoms was obtained from the patient by filling a structured questionnaire form. Patients underwent a full general and neurological examination in the morning before intake of medication in the neurology unit Al-Kadhimiya teaching hospital. All patients received their last anti parkinsonian medication on the evening before examination.

Quantitative sensory testing of the patient and controls were performed at the neurophysiology laboratory in Al-Kadhimiya hospital; using bipolar stimulating electrodes on the forearm and index finger in the upper limbs and the mid leg and big toe in the lower limbs bilaterally. The electrical sensory threshold was determined by progressive increasing of intensity of stimulation starting at an intensity of zero mill amperes at a frequency of 1 hertz [HZ].

The patients indicated verbally the point at which a first sensation of pain was perceived, considered to be minimum pain thresholds and when the pain became severe, considered to be the maximum pain thresholds.

Statistical analysis: Statistical analysis was done using graph pad software. Quick calculation for scientist to analyze the difference between continuous variables. Level of significance was set at P value equal to or less than 0.05 (7).

## Results

Out of 18 patients 14 (77.7%) reported pain while 4 (22.3%) had no pain. There was no statistically significant difference in pain perception from the affected side between males and females [p =0.8248] (Table 1). There was a statistically significant difference in pain thresholds between affected and unaffected sides in patients with PD [p =0.0427], and between patients with PD and controls [P< 0.0001] (Table 1). There was no statistically significant difference in pain thresholds between PD patients with and without pain [p =0.3279],

(Table 1) or upper and lower limbs on the affected side [p =0.1412] (Table 1).

**Table 1. Pain threshold testing in Parkinson disease patients**

| Character | | Minimum (mAamp) | Maximum (mAamp) | Mean (mAamp) | The two-tailed P value |
|---|---|---|---|---|---|
| **Gender** | Male[13]<br>Female[5] | 7<br>8 | 14<br>11 | 10±1.8<br>9.8 ± 1.3 | 0.8248 |
| **Body side** | Affected side<br>Normal side | 14<br>10 | 7<br>19 | 10.5 ± 4.9497<br>14.5 ±6.36 | 0.0427 |
| **Presence of Pain** | Yes<br>No | 9<br>8 | 14<br>18 | 10.5± 4.9497<br>13.5±6.36 | 0.3279 |
| **Limb affected** | Upper Limb<br>Lower Limb | 8<br>6 | 18<br>13 | 13±7.07<br>9.5± 4.9497 | 0.1412 |

Comparison in pain threshold measured showed highly significant difference between Parkinson disease patient and the control subjects but no significant difference of body side involvement whether right or left body side in both the patients and the control (Table2).

**Table 2. Pain threshold testing for different sides for the study sample**

| Tested Side | | Pain Threshold In mAmp | t test | P value |
|---|---|---|---|---|
| **Within Cases** | Right side<br>Left side | 10.7 ± 2.3<br>11.9 ± 3.8 | 1.15 | 0.26 |
| **Within Control** | Right side<br>Left side | 14 ± 1.8<br>14.4 ± 2.2 | 0.46 | 0.56 |
| **Between Cases and Control** | Right side (cases)<br>Right side (control)<br>Left side (cases)<br>Left side (control) | 10 ± 1.6<br>14 ± 1.8<br>10 ± 1.6<br>14.4 ± 2.2 | 6.3 | < 0.0001 |

## Discussion

Pain was reported in 77.7% of parkinsonian patients in the present study. This rate is similar to the one reported in the study by Nègre-Pagès *et al* [3], but higher than the rate seen in the Tinazzi *et al* study [5].

The present study showed a significantly lower electrical pain threshold in Parkinson disease patients compared to control subjects, in agreement with the studies by Tinazzi *et al*, Schestatsky *et al*, Mylius *et al*, and Lee *et al* [5,8-10]. The present study as well as the study of Tinazzi *et al* were used electrical stimulators to assess pain threshold while Mylius *et al* determined electrical pain thresholds during painful heat stimulation (conditioning stimulation) and during innocuous stimulation (control stimulation) [5,9].

The accuracy of psychophysical results that depend on subjective reaction may be hampered in patients with disorders like PD because of the slowness of reaction of Parkinson disease, which

can cause art factual threshold elevations. The change in pain perception in patients with PD is based on anatomophysiologic studies showing that the basal ganglia contain neurons with somatosensory function [11].

The present study showed lower pain thresholds for electrical stimulation on the affected side compared to the normal side reflecting the role of central dopaminergic pathways in the generation of pain. This is in agreement with the study of Schestatsky *et al* and the known fact that levodopa therapy alleviates pain in patients with Parkinson disease [8, 12,13].

There were no significant differences in electrical pain thresholds between male and female patients with Parkinson disease in the present study as well as in other studies [8-10].

We did not find prove any significant correlation between pain thresholds and body side involvements or upper versus lower limbs. The role of the basal ganglia in pain modulation was provided by studies showing that stimulation of the substantia nigra activates neurons in lamina V of the spinal cord, resulting in inhibition of the response to nociceptive stimuli. Furthermore, the descending pain-inhibition pathway originating in the midbrain is partially dopaminergic. Nigral neurons respond to low-intensity mechanical stimulation, and striatal neurons respond to noxious stimulation. In both cases, the cutaneous receptive fields are large and bilateral and may include the whole body and this may explain the approximately similar pain thresholds of upper and lower limbs [11].

## Conclusion

Chronic pain is present in 77.7% of Parkinson disease. Patients with Parkinson disease had lower pain threshold compared to controls. The body side involved and gender had no effect on pain threshold

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