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Beneficial effect of levodopa therapy on stooped posture in Parkinson's disease

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ABSTRACT

Objective: This study was designated to quantitatively evaluate the effect of levodopa on spinal posture in patients with PD using a computer-assisted handheld SpinalMouse device.
Methods: Prospective case-study involving 48 patients with definite PD. All patients were recruited between September 2011 and September 2013 and included 22 dopa-naïve, evaluated before and 3 months after initiation of treatment, and 26 patients with response fluctuations studied during the "off" and "on" states. The SpinalMouse instrument, a computer-assisted mechanical hand-held device, designed to noninvasively assess the curvature of the spine was guided along the midline of the vertebral column in upright, full flexion, and full extension positions to objectively assess spinal posture.
Results: In the dopa-naïve patients, spinal incline in the upright position was $12.4 \pm 1.2^{\circ}$ before and $7.6 \pm 1.3^{\circ}$ after treatment; $p = 0.002$. Corresponding area-under-the-curve (AUC) values were $131.7 \pm 8.0\ cm^2$ and $87.1 \pm 7.3\ cm^2$; $p < 0.0001$. In the response fluctuations patients, spinal incline was $13.3 \pm 1.3^{\circ}$ in the "off" and $9.3 \pm 1.2^{\circ}$ in the "on" period; $p = 0.015$. Corresponding AUC values were $144.6 \pm 9.2\ cm^2$ and $103.1 \pm 8.2\ cm^2$; $p < 0.0001$.
Conclusions: This is the first study that objectively measured and quantified abnormalities of spinal posture in patients with PD. Findings suggest that levodopa does have a beneficial effect on anterior flexion of the thoracolumbar spine, and thus indicate that the disorder of stooped posture in PD is mediated, at least in part, by dopamine deficiency.

1. Introduction

Posture abnormalities represent one of the main disabling features of Parkinson's disease (PD). They range from anterior flexion of the thoracolumbar spine (stooped posture) to extreme forward flexion of the trunk (camptocormia) or severe lateral flexion (Pisa syndrome) and dropped head. Besides the apparent disfigurement, these spinal deformities may interfere with daily activities, disrupt gait, increase falls, and produce pain and discomfort. Their occurrence correlate with genetic background, patients' age, disease duration, disease severity, skeletal and soft tissue changes, and cognitive alterations [1–3]. Possible mechanisms include dystonia, rigidity, muscle weakness, and proprioceptive disintegration [5–7]. It was generally believed that reduced central dopaminergic transmission is not involved in the pathogenesis of these postural abnormalities [1] and hence thought to be resistant to levodopa treatment [2,7]. Nevertheless, minor improvements in forward bending in the "on" vs. the "off" state have been noted [3,8], and isolated single cases of levodopa-induced alleviation of symptoms were reported [9,10].

Current assessments of posture abnormalities and their response to treatment are unsatisfactory. Most studies rely on subjective estimation, judgments based on video recordings or goniometric measurements. In order to address the question of the role of dopamine on stooped posture, we used a quantitative measure, the SpinalMouse (IDIAG AG, Switzerland), a computer-assisted mechanical hand-held device, designed to noninvasively assess the curvature of the vertebral column and the mobility in the sagittal and frontal planes and in flexion and extension, with a high inter-rater reproducibility [11,12]. In clinical practice the device was shown to be reliable as a research tool in spinal abnormalities without exposure of the examined subjects to imaging with radiation [13].

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Using this instrument, we studied patients with early PD before and after initiation of treatment with levodopa and patients with advanced disease and response fluctuations during the "on" and "off" states.

2. Patients and methods

Patients were recruited from the outpatient Movement Disorders Unit of the Rabin Medical Center, a tertiary medical facility in Israel, over a period of two years (September 2011 to September 2013). All patients fulfilled the diagnostic criteria for PD of the United Kingdom PD Society Brain Bank [14]. The institutional ethics committee approved the study, and all patients signed an informed consent form to participate.

Forty-eight patients with PD were included in the study: 22 who had not yet been exposed to levodopa and were about to initiate pharmacological treatment and 26 with motor fluctuations on long-term levodopa treatment. All completed the Roland-Morris Disability Questionnaire (RMDQ) on lower back pain [15]. The clinical evaluation was performed by the same neurologist (R.D.) in all patients using the motor subscale of the Unified Parkinson's Disease Rating Scale (UPDRS-III). The posture score was derived from UPDRS item 28, which specifically evaluates the degree of stooped posture on a 0–4 scale.

2.1. Posture

Spinal mobility, posture, and range of motion were evaluated with the SpinalMouse. The dopa-naïve patients were examined before and 3 months after stable treatment with levodopa (125 mg TID). The patients with response fluctuations were examined first in the "off" state and again during the "on" state, 45 min after taking their regular levodopa dose. "Off" period was defined as the state before intake of the first morning dose. Patients who had difficulty to arrive at the clinic without intake of the morning dose (6/26) were examined at least 5 h thereafter, long enough to confirm their "off" state.

The SpinalMouse was applied in accordance with the manufacturer's instructions. The two rolling wheels of the device follow the contour of the spine. The device is guided along the midline of the spine starting at the spinous process of C7 and terminating at the top of the anal crease (approximately S3). The angle measurements are communicated from the device to a personal computer. Data are sampled every 1.3 mm as the mouse is rolled along the spine, for a sampling frequency of approximately 150 Hz. This information is then used to calculate the relative positions of the sacrum and vertebral bodies of the underlying bony spinal column.

2.2. Clinical measurements

For each patient included in the study, the spine was assessed twice for three test positions: standing upright, maximal flexion, and maximal extension. "Standing upright" was defined as a comfortable, erect standing without special effort and without any outside help. The relevant parameters recorded by the SpinalMouse in each position were as follows: all individual motion segment angles (from T1–2 through to L5–S1), thoracic curvature (T1–2 to T11–12), lumbar curvature (T12–L1 to the sacrum),"hip" (sacral) angle, and trunk angle of inclination (angle between the vertical line from C7 and a line joining C7 to the sacrum, Fig. 1A). The results were used to calculate the ranges of flexion and

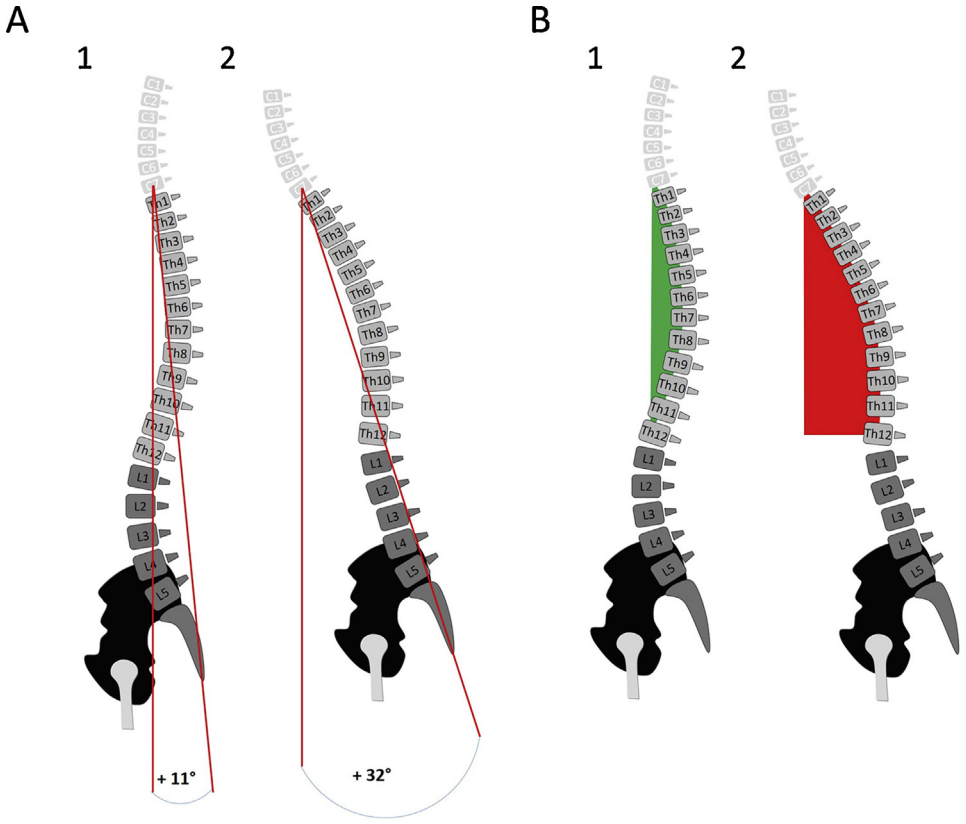

Fig. 1. *Angle of incline and the area under the curve (AUC).* (A) Example of the trunk angle of inclination in upright position. The angle between the vertical line from C7 and a line joining C7 to the sacrum was measured as the angle of inclination. Example of a patient with less (A_1) and stronger forward bending (A_2) in the upright position. (B) Example of the area confined by the thoracic curvature (area under the curve, AUC), defined by a virtual vertical line from C7 and a horizontal line from T12. Example of a patient with less (B_1) and stronger forward bending (B_2) in the upright position.