Dysfunction of the basal ganglia, but not the cerebellum, impairs kinaesthesia

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Summary
Precise knowledge about limb position and orientation is essential for the ability of the nervous system to plan and control voluntary movement. While it is well established that proprioceptive signals from peripheral receptors are necessary for sensing limb position and motion, it is less clear which supraspinal structures mediate the signals that ultimately lead to the conscious awareness of limb position (kinaesthesia). Recent functional imaging studies have revealed that the cerebellum, but not the basal ganglia, are involved in sensory processing of proprioceptive information induced by passive and active movements. Yet psychophysical studies have suggested a prominent role of the basal ganglia in kinaesthesia. This study addresses this apparent dichotomy by investigating the contributions of the cerebellum and the basal ganglia to the perception of limb position. Using a passive movement task, we examined the elbow position sense in patients with a dysfunction of the basal ganglia (Parkinson’s disease, \( n = 9 \)), patients with cerebellar degeneration [spinocerebellar ataxia (SCA) types 6 and 8, \( n = 6 \)] and age-matched healthy control subjects (\( n = 11 \)). In comparison with healthy control subjects, Parkinson’s disease patients, but not SCA patients, were significantly impaired in the ability to detect displacements correctly. A 1° forearm displacement was correctly recognized in >75% of trials by control subjects and SCA patients, but only in 55% of Parkinson’s disease patients. Only at 6° displacement did Parkinson’s disease patients exhibit a response rate similar to those of the two other groups. Thresholds for 75% correct responses were 1.03° for controls, 1.15° for cerebellar patients and 2.10° for Parkinson’s disease patients. This kinaesthetic impairment significantly correlated with the severity of disease in Parkinson’s disease patients, as determined by the Unified Parkinson’s Disease Rating Scale (\( r = -0.7, P = 0.03 \)) and duration of disease (\( r = -0.7, P = 0.05 \)). In contrast, there was no significant correlation between performance and the daily levodopa equivalent dose. These results imply that an intact cerebro-basal ganglia loop is essential for awareness of limb position and suggest a selective role of the basal ganglia but not the cerebellum in kinaesthesia.

Keywords: kinaesthesia; Parkinson’s disease; spinocerebellar ataxia; basal ganglia; cerebellum

Abbreviations: SCA = spinocerebellar ataxia; MMSE = Mini-Mental State Examination; UPDRS = Unified Parkinson’s Disease Rating Scale; WFN score = World Federation of Neurology Ataxia Score

Introduction
Since the excellent work of Goldscheider (1898), muscle sense has been divided into (i) passive motion sense, (ii) active motion sense, (iii) position sense, and (iv) gravito-inertial sense. Kinaesthesia is defined as the conscious perception of active or passive motion and direction of movements. It relies on the processing of proprioceptive information derived mainly from muscle spindles and joint and cutaneous receptors (Goodwin et al., 1972; Burgess et al., 1982; Hasan and Stuart, 1988; Bosco and Poppele, 2001). In contrast to the abundance of information about the neuroanatomical and neurophysiological characteristics of proprioceptive pathways (Bloedel and Courville, 1981; Burgess et al., 1982; Wiesendanger and Miles, 1982; Hasan, 1992; Bosco and Poppele, 2001), there is limited knowledge about which neural structures play a role in the advanced processing of proprioceptive information that ultimately lead to awareness of body position and motion.

Passive movements are one method of inducing proprioceptive stimulation for the investigation of human kinaesthesia. Several functional MRI and PET studies have revealed...
activations of the contralateral primary and secondary sensorimotor cortex, supplementary motor area and bilateral inferior parietal lobes during passive movements, identifying these areas as sites of central processing of proprioceptive information (Gao et al., 1996; Weiller et al., 1996; Jueptner et al., 1997). In addition, passive movements induced activations in the same parts of the cerebellar hemispheres and dentate nuclei as active movements (Gao et al., 1996; Jueptner et al., 1997). However, passive movements were not accompanied by activations in the basal ganglia, which led to the conclusion that the basal ganglia are not involved in proprioceptive information processing (Jueptner and Weiller, 1998).

The finding that the cerebellum but not the basal ganglia are selectively involved in central processing of proprioceptive signals contradicts results from several clinical and psychophysical studies. Although the cerebellum receives major sensory input from the spinocerebellar tracts (Bloedel and Courville, 1981; Bosco and Poppele, 2001), sensory deficits were not found in patients with acute cerebellar injury (Holmes, 1917). Patients with a degeneration of the cerebellum exhibited impairments in perceiving durations and velocities, but not amplitudes, of kinaesthetic stimuli (Grill et al., 1994). In contrast, recent studies have suggested that a dysfunction of the basal ganglia leads to proprioceptive deficits (Schneider et al., 1986, 1987). Zia and colleagues showed that patients with Parkinson’s disease were impaired in unilateral elbow-joint position sense (Zia et al., 2000, 2002). However, it remained unclear whether their findings could be attributed solely to impaired kinaesthesia. In their studies, participants had to visually match the actual angle of the elbow joint on a scale or to compare the position of one elbow with the other under time restriction. Knowing that Parkinson’s disease patients may exhibit disturbances of visual processing and cognitive slowing (Antal et al., 1998; Diederich et al., 2002; Sawamoto et al., 2002), such dysfunctions might, at least in part, have contributed to the above results.

The aim of the present study was to investigate the contributions of the cerebellum and the basal ganglia to the perception of limb position. We employed a psychophysical paradigm to examine the ability to detect a change in elbow joint position without involving time computations or visuospatial processes. The study population consisted of nine patients with a diagnosis of idiopathic Parkinson’s disease, six patients with spinocerebellar ataxia (SCA) type 6 or 8, which is characterized by hereditary pure or predominant cerebellar degeneration, and 11 healthy, age-matched control subjects. Patients with SCA6 and 8 are especially suited for testing cerebellar involvement in upper limb kinaesthesia. Autopsy studies revealed intact dorsal columns and spinocerebellar tracts and nerve conduction studies have shown only a mild sensorimotor neuropathy of the lower (but not upper) limbs in 50% of patients with SCA6 (Gomez et al., 1997). Also, patients with SCA8 showed no signs of sensory nerve or tract involvement (Day et al., 2000).

Methods

Subjects

Six patients with degenerative cerebellar disorders (mean ± SD age 47.3 ± 7.1 years, range 24–63 years; two females, four males), nine Parkinson’s disease patients (mean ± SD age 52.3 ± 9.8 years, range 38–70 years; two females, seven males) and 11 age-matched healthy control subjects (mean ± SD age 50.3 ± 8.1 years, range 39–65 years; five females, six males) with no neurological or general medical limitations participated. Prior to testing, each subject underwent a neurological examination including sensory testing (vibration sense, light touch, pinprick sensation and position sense at index finger and first toe), and patients were scored according to the standardized clinical rating scales described below.

All patients with cerebellar disease were recruited from the cerebellar ataxia outpatient clinic at the University of Minnesota and were diagnosed as having a genetically defined spinocerebellar ataxia of type 6 (n = 4) or type 8 (n = 2). Each had moderate to severe cerebellar ataxia based on the International Cooperative Ataxia Rating Scale of the World Federation of Neurology (WFN scale) (Trouillas et al., 1997). The main symptoms were gait and stance instability, limb ataxia predominantly involving the lower limbs, cerebellar dysarthria, and a variable severe cerebellar oculomotor dysfunction (gaze-evoked nystagmus, saccadic dysmetria). Neurological examination revealed no extracerebellar signs, such as peripheral nerve disease or motor neuron involvement. Descriptive characteristics of the SCA patients are summarized in Table 1.

Parkinson’s disease patients were recruited from the movement disorders outpatient clinic at the University of Minnesota. All were diagnosed as having idiopathic Parkinson’s disease with young (21–40 years, n = 3) or late (>40 years, n = 6) onset of disease. None of them had juvenile onset (<20 years) or a known mutation in the parkin gene. According to their Hoehn and Yahr classification, the Parkinson’s disease patients were at a mild (n = 6) or moderate (n = 3) stage (Hoehn and Yahr, 1967). Severity of disease was further determined by use of the Unified Parkinson’s Disease Rating Scale (UPDRS) (Fahn and Elton, 1987). None of the patients had intellectual impairment exceeding mild forgetfulness. Formal neuropsychological testing [Mini-Mental State Examination (MMSE) (Folstein et al., 1975)] was performed in seven Parkinson’s disease patients and did not reveal a cognitive decline in them (mean ± SD MMSE score 29.3 ± 0.8 points, range 28–30 points). Neurological examination did not reveal signs or symptoms of peripheral nerve disorders. All patients were tested on medication, i.e., they were told to take the medication with the same dose and time schedule as regularly. Daily doses of medications were standardized by the use of a formula for levodopa-equivalent doses using the following equation: 100 mg standard levodopa = 125 mg sustained-release levodopa, 1.5 mg pramipexole, 6 mg ropinirole, 10 mg bromocriptine or 1 mg pergolide (Pahwa et al., 1997; Thobois...
et al., 2002). The mean ± SD levodopa equivalent dose was 644 ± 533 mg. Descriptive data for Parkinson’s disease patients, including their medication, are summarized in Table 2.

All study subjects except one Parkinson’s disease patient were right-handed on the basis of results of the Edinburgh Handledness Inventory (Oldfield, 1971). All patients and healthy subjects gave their informed consent to participation in the study. The study was approved by the institutional review board of the University of Minnesota.

**Testing apparatus**

The apparatus consisted of a rectangular wooden splint (50 × 7.5 cm), on which the subject’s forearm was rested (Fig. 1). The splint was connected via a short rod to an aluminium sled. The sled glided linearly on two tracks in the frontoparallel plane of the subject. The tracks were mounted to the base of a table. The joint between the splint and the rod allowed rotation of the splint around the rod’s longitudinal axis. Three ceiling suspension points supported the weight of the arm on the splint through nylon rope fixed to the splint.

A torque motor (DC motor, 24 V, torque capacity 17.5 cm/500 mg; RAE Corporation) provided the necessary force via an interlocking gear system and a gear belt. The direction of sled motion (left or right) was controlled by two buttons. Sled speed was constant and initial accelerations from 0°/s² were not detected by the subjects. Top speed varied slightly with the weight of the subject’s arm. Therefore, measurements were taken in both directions in the loaded position for each subject at the conclusion of testing. The mean ± SD angular velocity was 0.5 ± 0.1°/s and did not differ between the two patient groups and healthy subjects (P > 0.2).

**Positioning of subjects**

First, the correct vertical chair position was established by adjusting the height until the subject’s shoulder reached 90°
abduction while the arm lay on the splint. Then, an elbow joint position of 90° of flexion was ascertained using a goniometer while the sled and the splint were in the starting position. The surface of the splint was padded with foam (4 cm) to ensure the subject’s comfort and to prevent any motor vibrations being transmitted to the subject’s arm. Subjects were instructed to maintain a loose fist throughout testing to exclude the possible use of haptic information. This hand posture prevented haptic sensations from the sensitive palmar aspect of the hand.

**EMG recordings**
To ensure that the subjects did not actively move the arm during trials, EMGs of the biceps and triceps muscles of the tested arm were recorded via silver chloride surface electrodes (gain 2500, bandwidth 30–500 Hz, sampling rate 200 Hz). EMG recordings were monitored online by one of the investigators. Any trial exhibiting EMG activity was excluded from further analysis and repeated.

**Procedure**
Both arms were tested in each subject. Each forearm was moved passively in 80 trials consisting of 40 flexion and 40 extension movements with elbow joint angular displacements of 0.2, 0.6, 1, 2, 3, 4, 5, 6, 7 and 8°. Angular displacements and their directions were presented pseudorandomly, twice in both directions for every displacement. The right arm was tested first. Each trial was signalled to the subject by a tactile cue on the subject’s shoulder prior to the start of the movement. The end of each trial was announced by administering a second tactile cue on the left forearm. After each passive movement, subjects had to judge and express verbally whether the forearm was moved ‘towards’ or ‘away’ from their body or if they ‘could not tell’. There were no time limitations for subjects to respond. Both incorrect responses and ‘could not tell’ responses were scored as an incorrect response. Subjects were further instructed to give full concentration to the task after experiencing the first cue. If, at any time, a loss of concentration was experienced, a break in testing could be taken at the subject’s request. Subjects wore goggles to exclude all visual input, and headphones with pink noise masked all auditory cues during testing. The total testing time was ~40 min.

**Measurements**
The exact amount of movement of the sled (millimetres) required to achieve a distinct angular displacement (°) was calculated individually for each subject using the formula:

\[ \text{required sled displacement (mm)} = \left\{ \tan\left(\text{desired arm displacement} \left(\frac{\pi}{180}\right)\right) \right\} \text{forearm length (mm)}. \]

To initiate sled motion, the experimenter pressed a button and tracked its movement on a rule attached to the metal base of the apparatus and a high-precision potentiometer. The potentiometer signal was calibrated and fed to a digital reader that provided an exact value for the linear displacement of the sled. The accuracy of the reading was determined to be 0.1 mm. For each trial the subject’s verbal response and the precise sled movement were recorded.

**Statistical analyses**
The percentage of correct responses for each degree of angular displacement was calculated for each of the three groups (Parkinson’s disease patients, SCA patients, controls). Group differences in the percentage of correct responses were determined using separate Kruskal–Wallis tests for each displacement (SPSS for Windows 10.0.7®; SPSS, Chicago, IL, USA). The performance data for both arms of the Parkinson’s disease patients were entered in this analysis. Following Fechner’s (1860) technique for determining sensory thresholds, we defined as the threshold for correct responses the point midway between guessing and a perfect response. A curve-fitting procedure (Box Lucas exponential fit) was performed to determine the threshold for 75% correct responses. The model equation was as follows:

\[ y = a[1 - e^{(-bx)}] \]

where \( y \) is the number of correct responses (%), \( x \) is the displacement (°), \( a \) and \( b \) are coefficients and \( e \) is Euler’s number (2.718…).
Subjects (1.03° displacements (0.2°) combined flexion/extension movements. We found no differences in the percentage of correct responses between passive forearm extension and flexion observations, differences between the three groups were significant. Differences were found, Mann–Whitney U tests were performed to further elucidate which difference (affected arm versus less affected arm; affected arm versus control subjects, less affected arm versus control subjects) was significant. Thresholds were calculated using the same curve-fitting procedure as that described above. Moreover, the severity of disease as expressed by the total UPDRS score in Parkinson’s disease patients, the duration of disease and the daily levodopa-equivalent dose were correlated with the percentage of correct responses over all displacements (bivariate correlations, computing Spearman’s ρ). For this analysis, the percentage of correct responses for both arms of all Parkinson’s disease patients was used, given that the motor score of the UPDRS also included both arms in the analysis. P values <0.05 were taken to be significant.

Results
Comparison of kinaesthetic thresholds between groups
We found no differences in the percentage of correct responses between passive forearm extension and flexion movements (P > 0.2). For the sake of simplicity, we therefore collapsed these two data sets and report all results for the combined flexion/extension movements.

Control subjects had difficulty detecting very small displacements (0.2°), but rapidly showed improvement in correct responses with increasing angular displacement (Fig. 2, Table 3). A 0.6° displacement was detected in 51% of trials and a 1° displacement in >82% of trials by the control subjects. SCA patients had a similar rate of detection compared with control subjects. In contrast, Parkinson’s disease patients were clearly impaired. They detected angular displacements of 0.6° in only 22% of trials and of 1° in only 55%. At 2° displacement, SCA patients and control subjects showed ≥94% correct responses, whereas Parkinson’s disease patients showed only 76% correct responses. Although the differences in the performance between Parkinson’s disease patients and SCA patients and control subjects were smaller at 4 and 5° displacements, only at ≥6° displacement was the mean percentage of correct responses not significantly different between groups. Reflecting these observations, differences between the three groups were significant for 0.6, 2, 3, 4 and 5° displacements (all P values <0.05) and showed a trend for the 1° displacement (P = 0.078) (Table 3). In keeping with these results, thresholds for 75% correct responses were different between the three groups. Parkinson’s disease patients had approximately a twofold higher threshold (2.10°) compared with control subjects (1.03°) and cerebellar patients (1.15°) (Fig. 2, Table 4). The mean percentage of correct responses over all displacements underlined the impairment of Parkinson’s disease patients in

![Graph](image.png)

Fig. 2 Percentage of correct responses for each displacement and group. Parkinson’s disease (PD) patients showed a clear impairment in detection of joint displacements, whereas SCA patients showed a performance similar to that of control subjects. The threshold for 75% correct responses of Parkinson’s disease patients (2.10°) was twice that of SCA patients (1.15°) and control subjects (1.03°).

In a second analysis, separate Kruskal–Wallis tests for each displacement were used to determine the within-group differences in the Parkinson’s disease group for percentages of correct response between the two arms and between each of the arms and the performance of the control group. If significant differences were found, Mann–Whitney U tests were performed to further elucidate which difference (affected arm versus less affected arm; affected arm versus control subjects, less affected arm versus control subjects) was significant. Thresholds were calculated using the same curve-fitting procedure as that described above. Moreover, the severity of disease as expressed by the total UPDRS score in Parkinson’s disease patients, the duration of disease and the daily levodopa-equivalent dose were correlated with the percentage of correct responses over all displacements (bivariate correlations, computing Spearman’s ρ). For this analysis, the percentage of correct responses for both arms of all Parkinson’s disease patients was used, given that the motor score of the UPDRS also included both arms in the analysis. P values <0.05 were taken to be significant.

Table 3 Percentages of correct responses per group and displacement

<table>
<thead>
<tr>
<th>Displacement</th>
<th>Controls</th>
<th>SCA patients</th>
<th>Parkinson’s disease patients</th>
<th>P&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.2°</td>
<td>17 ± 26</td>
<td>11 ± 14</td>
<td>11 ± 26</td>
<td>n.s.</td>
</tr>
<tr>
<td>0.6°</td>
<td>51 ± 20</td>
<td>50 ± 34</td>
<td>22 ± 26</td>
<td>0.004</td>
</tr>
<tr>
<td>1°</td>
<td>82 ± 20</td>
<td>75 ± 23</td>
<td>55 ± 37</td>
<td>0.078</td>
</tr>
<tr>
<td>2°</td>
<td>96 ± 13</td>
<td>94 ± 15</td>
<td>76 ± 27</td>
<td>0.005</td>
</tr>
<tr>
<td>3°</td>
<td>97 ± 10</td>
<td>97 ± 9</td>
<td>82 ± 25</td>
<td>0.035</td>
</tr>
<tr>
<td>4°</td>
<td>100</td>
<td>100</td>
<td>96 ± 9</td>
<td>0.044</td>
</tr>
<tr>
<td>5°</td>
<td>99 ± 7</td>
<td>100</td>
<td>89 ± 16</td>
<td>0.009</td>
</tr>
<tr>
<td>6°</td>
<td>97 ± 14</td>
<td>100</td>
<td>98 ± 7</td>
<td>n.s.</td>
</tr>
<tr>
<td>7°</td>
<td>98 ± 9</td>
<td>100</td>
<td>100</td>
<td>n.s.</td>
</tr>
<tr>
<td>8°</td>
<td>99 ± 4</td>
<td>100</td>
<td>97 ± 8</td>
<td>n.s.</td>
</tr>
<tr>
<td>Total</td>
<td>84 ± 30</td>
<td>83 ± 32</td>
<td>73 ± 37</td>
<td>n.s.</td>
</tr>
</tbody>
</table>

<sup>a</sup>P < 0.05 = significant (Kruskal–Wallis test).

Table 4 Results of curve-fitting procedure

<table>
<thead>
<tr>
<th></th>
<th>Threshold</th>
<th>a</th>
<th>b</th>
<th>R&lt;sup&gt;2&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.03°</td>
<td>99.397</td>
<td>1.370</td>
<td>0.979</td>
</tr>
<tr>
<td>SCA patients</td>
<td>1.15°</td>
<td>100.728</td>
<td>1.184</td>
<td>0.982</td>
</tr>
<tr>
<td>PD patients</td>
<td>Total</td>
<td>2.10°</td>
<td>97.942</td>
<td>0.6915</td>
</tr>
<tr>
<td></td>
<td>Less affected arm</td>
<td>1.50°</td>
<td>102.298</td>
<td>0.883</td>
</tr>
<tr>
<td></td>
<td>Affected arm</td>
<td>2.50°</td>
<td>99.208</td>
<td>0.571</td>
</tr>
</tbody>
</table>

PD = Parkinson’s disease. a and b are coefficients.
Further analysis showed that the percentage of correct responses was 73% for the affected arm and 15% for the less affected arm.

detecting changes of their elbow-joint position. Parkinson’s disease patients had an overall accuracy of 73% and SCA patients and control subjects showed 83% and 84% accuracy, respectively.

Percentages of ‘could not tell’ responses and incorrect responses concerning directions (‘away’ instead of ‘towards’) were different between the three groups. Control subjects and cerebellar patients gave only 14.9 and 15.2% ‘could not tell responses’, respectively, whereas Parkinson’s disease patients were indecisive in 25.3% of trials. Differences in overall accuracy and ‘could not tell’ responses were statistically significant ($P < 0.0001$).

**Comparison of kinaesthetic thresholds between the affected and less affected arms of Parkinson’s disease patients and control subjects**

Five of the Parkinson’s disease patients showed a prominent clinical difference between the more affected and less affected arms, and were therefore included in this analysis. Three patients had symptoms only or predominantly on the right side, two on the left side.

The ability to detect changes of elbow position appeared to be impaired in the affected arm compared with the less affected arm (Fig. 3, Table 5). Angular displacements of 2 and 3° were detected correctly in 95% of trials with the less affected arm, but in only 70% of trials with the affected side. At 4° displacement, Parkinson’s disease patients exhibited almost a similar response rate on the two sides. Differences in performance between the affected arm and the less affected arm of Parkinson’s disease patients and both arms of control subjects were significant for 0.6, 2 and 3° (all $P$ values <0.05). Further analysis showed that the percentage of correct responses was significantly different between the affected arm of Parkinson’s disease patients and control subjects for 0.6, 2, 3, 4 and 5° displacements. In contrast, differences between the less affected arm and control subjects were only significant for 0.6 and 5° displacements. Significant differences between the affected arm and the less affected arm of Parkinson’s disease patients were identified for 2 and 3° displacements ($P = 0.006$). The corresponding thresholds for 75% correct responses were 1.5° for the less affected arm and 2.5° for the affected arm (Fig. 3, Table 4). Percentages of indecisive responses (‘could not tell’) were also higher for the affected arm compared with the less affected arm (28.5 versus 22.2%).

**Correlation of performance with severity and duration of disease, medication and cognitive function in Parkinson’s disease patients**

The severity of disease in Parkinson’s disease patients, as measured by the UPDRS total score, correlated significantly and inversely with the percentage of correct responses over all displacements ($r = -0.7, P = 0.03$). Figure 4 shows this correlation in relation to the performance of all SCA patients and control subjects. Three of the Parkinson’s disease patients revealed percentages of correct responses that were within the range of performance of the control subjects and SCA patients. The remaining six Parkinson’s disease patients exhibited response rates that were clearly below those of the control subjects and SCA patients. However, one SCA patient (Subject 4, Table 1) had a response rate that was below the range of the other five SCA patients but within the range of the more severely affected Parkinson’s disease patients. Moreover, there was a significant inverse correlation between the duration of Parkinson’s disease and correct responses over all displacements ($r = -0.7, P = 0.05$), indicating that longer disease duration was accompanied by poorer performance.

**Table 5 Percentages of correct responses per arm and for each displacement for Parkinson’s disease patients with unilateral disease or bilateral disease with a clear predominance of one arm in comparison with healthy controls**

<table>
<thead>
<tr>
<th>Displacement</th>
<th>Correct responses [mean ± SD (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Controls</td>
</tr>
<tr>
<td>0.2°</td>
<td>17 ± 26</td>
</tr>
<tr>
<td>0.6°</td>
<td>51 ± 20</td>
</tr>
<tr>
<td>1°</td>
<td>82 ± 20</td>
</tr>
<tr>
<td>2°</td>
<td>96 ± 13</td>
</tr>
<tr>
<td>3°</td>
<td>97 ± 8</td>
</tr>
<tr>
<td>4°</td>
<td>100</td>
</tr>
<tr>
<td>5°</td>
<td>99 ± 7</td>
</tr>
<tr>
<td>6°</td>
<td>97 ± 14</td>
</tr>
<tr>
<td>7°</td>
<td>98 ± 9</td>
</tr>
<tr>
<td>8°</td>
<td>99 ± 4</td>
</tr>
<tr>
<td>Total</td>
<td>84 ± 30</td>
</tr>
</tbody>
</table>

$^aP < 0.05 = $ significant (Kruskal–Wallis test).

![Fig. 3](https://example.com/image3.png) Comparison of percentages of correct responses between the less affected arm, the affected arm of Parkinson’s disease patients and control subjects. Impairments of kinaesthesia were most prominent in the affected arm for displacements between 0.6 and 4°. The threshold for 75% correct responses was 2.5° for the affected arm and 1.5° for the less affected arm.
In contrast, there was no significant correlation between the daily levodopa-equivalent dose and the percentage of correct responses (Fig. 5; \( r = -0.29, p > 0.2 \)). Cognitive function, as measured by the MMSE, also did not correlate with the impairment in kinaesthesia (\( r = 0.19, P > 0.5 \)).

**Discussion**

The main finding of the present study is that Parkinson’s disease patients exhibited distinct impairments in the conscious perception of kinaesthetic stimuli, whereas patients with pure or predominantly cerebellar degeneration revealed no kinaesthetic deficit compared with control subjects. Our results indicate that intact cerebro-basal ganglia loops are essential for kinaesthesia. They also reveal that the cerebro-cerebellar loop is seemingly not involved in the detection of limb position and movement. The second conclusion is surprising, given that the cerebellum receives substantial proprioceptive inputs from the somatosensory cortex and spinal afferents, and it seems to contradict the findings of earlier fMRI studies of a prominent role of the cerebellum in kinaesthesia. However, before entering into a more detailed discussion about the implications of these results in defining the differential roles of the basal ganglia and the cerebellum in kinaesthesia, it is important to understand the nature of the kinaesthetic stimulus in our study.

**What aspects of kinaesthesia were tested?**

The experiment required a verbal response to the direction of a passively induced forearm displacement. There were two potential sources of information that could form the basis of a perceptual judgement. First, participants compared the final elbow joint position with its initial angular position prior to the start of the trial (position sense, i.e. stataesthesia). Secondly, they detected the movement of the forearm itself (passive movement sense, i.e. kinaesthesia). Signals from muscle spindles and joint receptors probably provided the bulk of the proprioceptive input, whereas the contribution of Golgi tendon organs was small or negligible, because the attached muscles were silent and their tendons were not stretched substantially.

Previous studies investigating joint position sense in patient populations performed passive joint rotations at speeds between 10 and 35°/s (Grill et al., 1994; Zia et al., 2002), whereas our apparatus moved the limb at a much lower speed, 0.5°/s. Yet for the ankle and the metacarpophalangeal joint it is known that humans can detect small excursions (<3.5°) at speeds as low as 0.25–0.5°/min and that only speeds <2°/min prevent the elicitation of a movement sensation (Clark et al., 1985). Thus, our experiment tested predominantly passive motion sense (kinaesthesia) and probably to a lesser extent position sense (stataesthesia).

In the present study, passive movements were performed at a constant speed and participants did not have to discriminate between various movement speeds. Consequently, exact time computations were not necessary to respond correctly. In addition, no differences in speed existed between patient groups. Therefore, speed cannot account for differences in kinaesthesia. This has to be considered because it is known that differences in speed are accompanied by differences in the ability to detect joint displacements (Hall and McCloskey, 1983; Clark et al., 1985).

**Kinaesthesia is impaired in Parkinson’s disease patients**

While the healthy participants in our study perceived forearm displacements with a threshold for 75% correct responses of ~1°, Parkinson’s disease patients required joint excursions of

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**Fig. 4** Correlation between the percentage of correct responses in all trials and the severity of disease as expressed by the UPDRS for Parkinson’s disease (PD) patients. The severity of disease correlated inversely with the deficit in kinaesthesia in Parkinson’s disease.

**Fig. 5** Correlation between the percentage of correct responses in all trials and the levodopa-equivalent dose in Parkinson’s disease (PD) patients. There was no significant correlation between the dose of medication and the kinaesthetic deficit (\( r = -0.29, P > 0.2 \)).
As discussed above, there is a need to consider both sensory input and motor output signals in the basal ganglia. The basal ganglia is used not only for movement feedback and sensorimotor integration but also for the discrimination of somatosensory stimuli that leads to the awareness of limb motion. Other studies have revealed that Parkinson’s disease patients also have impairments in the perception of visual (Bandini et al., 2001; Muller et al., 2002) and auditory (Philipova et al., 1997; Pekkonen et al., 1998) stimuli. This indicates that the basal ganglia process multimodal sensory information that is critical for perceptual discrimination between stimuli, which would indirectly be important for motor planning and control. If the basal ganglia indeed function as a sensory analyser for motor systems, which has been suggested in the past (Lidsky et al., 1985), then movement disorders would be the result of a primary sensory dysfunction that causes faulty computation of relevant movement parameters. Such a notion is supported by research in systems neuroscience that attempts to understand the physiological mechanisms of focal dystonia, another movement disorder. A computational model recently demonstrated that the properties of dystonia, such as co-contraction and overflow movements, can be explained by excessive gain caused by an altered sensorimotor loop (Sanger and Merzenich, 2000).

Could other factors account for the kinaesthetic deficits of our Parkinson’s disease patients?

There are several factors that might contribute to the impairment of kinaesthesia in Parkinson’s disease patients. First, it could be argued that in this study Parkinson’s disease patients, but not SCA patients, had peripheral neuropathy or sensory tract involvement. This is unlikely, given that the clinical examination did not reveal any clinical signs of sensory impairments in our Parkinson’s disease patient group. Moreover, peripheral neuropathy is an uncommon feature in idiopathic Parkinson’s disease and, if present, is due to compression or rare side-effects of medication in advanced stages rather than to the disease itself (Shulman et al., 1999; Valls-Sole and Valldeoriola, 2002). Yet we tested neither patients with juvenile onset of Parkinson’s disease, who might have had involvement of the peripheral nervous system (Byrne et al., 1982; Taly and Muthane, 1992), nor patients with advanced stages of akinetic Parkinson’s disease, at risk of compression neuropathies.

Secondly, the dopaminergic medication might have impaired kinaesthesia in Parkinson’s disease patients rather than the disease itself. In a recent study, O’Suilleabhain and colleagues demonstrated that administration of levodopa and dopamine agonists was associated with suppression of position sense, by comparing results of Parkinson’s disease patients off medication with their performance after they had taken 1–1.5 times their usual morning dose of levodopa and/or dopamine agonist (O’Suilleabhain et al., 2001). In our study, we tested Parkinson’s disease patients on medication. We found that the daily levodopa-equivalent dose and the
ability to detect joint displacements did not correlate significantly (Fig. 5). In contrast, the UPDRS total score was highly correlated ($r = -0.7$) with perceptual performance, indicating that the severity of disease is the critical factor for impaired kinaesthesia in Parkinson’s disease patients (Fig. 4). More supportive, the fact that we saw only minor differences between the less affected arm in Parkinson’s disease patients taking antiparkinsonian medication and control subjects clearly indicates that the medication itself cannot be the single cause of the observed kinaesthetic deficits.

Thirdly, SCA patients and control subjects might have had a higher level of background muscle contraction during passive displacements compared with Parkinson’s disease patients, giving rise to increased fusimotor action, which, in turn, would lead to increased muscle spindle activity and, thereby, to improved movement detection (Matthews, 1982; Taylor and McCloskey, 1992). This seems an unlikely explanation for the impaired performance of Parkinson’s disease patients, given that previous studies have revealed normal function of muscle spindles in Parkinson’s disease (Burke et al., 1977). In addition, we excluded from the analysis all trials in which the EMG recordings of the biceps and triceps muscles showed activation.

Finally, attention and decision-making or other cognitive deficits of Parkinson’s disease patients might have resulted in impairments in the ability to detect joint displacements. This argument is strengthened by the fact that Parkinson’s disease patients had higher rates of indecisive responses (‘could not tell’) than SCA patients and controls. It is known that Parkinson’s disease patients have greater distractibility in sensory attention tasks and more difficulty in lexical decision tasks than control subjects, and have difficulty in extracting relevant information from competing stimuli or in shifting attention, which cannot be solely explained by impaired motor performance (Levin et al., 1989; Sharpe, 1990, 1992; Spicer et al., 1994; Brown et al., 1997; Ravizza and Ivry, 2001). Recent studies have also suggested a role of the cerebellum in attention (Couachersne et al., 1994; Akshoomoff et al., 1997; Allen et al., 1997). Therefore, one may argue that if only attention deficits account for the impaired kinaesthesia in Parkinson’s disease patients, one would also expect at least some impairment in SCA patients. Furthermore, deficits in attention and/or decision-making ought to be general, affecting the performance of both arms. Yet when compared with the performance of control subjects, only the deficits at the affected arm were significantly different (Fig. 4). Furthermore, there was a difference in the rate of indecisive responses between the affected and the less affected arm. Moreover, there were no obvious signs of fluctuations in attention, such as a decrease in task performance over time or high intra-subject variability. In summary, although we cannot completely rule out the possibility that attention and/or decision-making deficits contributed to the impairment of kinaesthesia in Parkinson’s disease patients, they were highly unlikely to be the determining factor. This is underlined by the fact that the performance in neuropsychological testing (MMSE) did not correlate with the grade of impairment in kinaesthesia.

**Kinaesthesia is not affected by a dysfunction of the cerebellum**

The cerebellum receives major proprioceptive input via the spinocerebellar pathways from a variety of receptors (Bloedel and Courville, 1981; Bosco and Poppele, 2001). Functional imaging studies have shown broad activations of the cerebellum during passive and active movements, leading to the assumption that the cerebellum plays an important role in proprioception (Gao et al., 1996; Jueptner et al., 1997; Jueptner and Weiller, 1998). Furthermore, recent studies have shown an involvement of the cerebellum in proprioceptive-driven motor adaptation (Nezafat et al., 2001). In contrast, clinical studies could not reveal any sensory impairment in patients with cerebellar injuries (Holmes, 1917) and the present study did not detect kinaesthetic deficits in patients with genetically defined pure or predominant cerebellar degeneration.

How can these seemingly different findings be reconciled? Deficits in the perception of the duration and velocity of passive displacements of the elbow joint in patients with cerebellar degeneration have been reported in the past (Grill et al., 1994). Yet the ability of cerebellar patients to detect the amplitude of the displacement was not significantly different from the performance of control subjects, which coincides with our findings. Perception of duration as well as velocity, but not of movement amplitudes, strongly depends on correct time computations. Thus, it is plausible that these deficits are rather due to impairment in the processing of time-relevant information than in position sense.

The view that the cerebellum is involved in the timing of motor acts, originally proposed by Braitenberg (1967), has been supported by demonstrating timing deficits in cerebellar patients (Ivry et al., 1988; Ivry and Keele, 1990), by functional imaging studies showing timing-related activations within the cerebellum (Jueptner et al., 1995), and by animal experiments (Braitenberg et al., 1997). Magnetoencephalographic recordings revealed that the cerebellum might play a role in processing the temporal features of the sensory stimuli (Tesche and Karhu, 1997, 2000).

In conclusion, the present study provides evidence that the integrity of a cerebro-basal ganglia loop is essential for the detection of limb position. Our data also demonstrate that an intact position sense does not depend on the integrity of cerebellum. Human cerebro-cerebellar processing of proprioceptive information does not promote the ability to discriminate between two static limb positions and does not give rise to the awareness of limb position. It further suggests that impairments of cerebellar patients in proprioceptive–motor learning (Konczak et al., 2001) are not due to abnormal kinaesthetic thresholds.
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