Abstract

Objective  To quantitatively evaluate motor activity, its fluctuations, and drug effects in patients with Parkinson’s disease (PD), the Lifecorder®, a new monitoring device, was attached to a group of patients for several weeks. This enabled the continuous recording of motor activity in ten scaled magnitudes at two-minute intervals for 6 weeks.

Patients and Methods  Thirteen patients with PD who required dopamine receptor agonist therapy were monitored with Lifecorder, and seven healthy subjects served as the control group. The data obtained with this device correlated well with the Unified Parkinson’s Disease Rating Scale (UPDRS) and Hoehn-Yahr grading. The dose of cabergoline, a D2-receptor agonist, was increased every 2 weeks, until optimum improvement was achieved.

Results  By adding cabergoline, the mean UPDRS improved from 40.5 to 28.4, which was significant. In parallel, the mean daily walking count (WC) also increased from 2,459 to 3,315 steps (p<0.01) and movement-related calorie consumption (MCC) increased from 56 to 74 kcal (p<0.05). UPDRS thus correlated well with WC and MCC obtained with this device. The improvement ratio of WC and MCC of each individual patient was compared with that of UPDRS. WC, and MCC shifted in parallel with UPDRS with one exception. The daily time-dependent fluctuation of motor activity was clearly shown by the Excel-generated graphs to improve with D-agonist therapy. In contrast to enhanced daytime activities, nocturnal restfulness was also clearly documented with this device.

Conclusion  The unique properties of Lifecorder make this device a useful adjunct to the UPDRS for the objective evaluation of Parkinsonian motor activity. The device has a significant advantage over conventional clinical scales, as daytime as well as nocturnal motor activity can be objectively evaluated over long time periods ranging from one hour to one month, and the magnitude of motor activity is quantifiable in relation to the time-course.

Key words: Parkinson disease, monitoring device, cabergoline, UPDRS, movement

Introduction

Although the Unified Parkinson’s Disease Rating Scale (UPDRS) is a standard measure for the evaluation of Parkinson disease (PD), there are drawbacks to its use since it relies on the interpretations of physicians, and it may not adequately reflect the fluctuation of motor symptoms.

The Calorie Counter® (Suzuken Co., Nagoya, Japan) was originally developed for physical exercise management of diabetics and athletes; it enables the measurement of daily calorie consumption and step numbers (1). Recently the same company has developed the Lifecorder® (Suzuken Co.), a small solid state recorder (62.5×46.5×26 mm, 40 g), containing an acceleration sensor with piezoelectric, an amplifier, a microprocessor and memory. This enables the recording of acceleration magnitude every 2 minutes, together with daily calorie consumption and step numbers. When attached to the waist belt, it continuously monitors bodily movements. It is specifically sensitive to axial movements because the acceleration sensor is vertically oriented. Once initialized, it stores data in a memory chip for 6 weeks. There is also a “Remarks” button on the recorder for the input of pertinent information. Developed for physical exercise programs, this device has not previously been utilized for the monitoring of Parkinsonian motor activity. In this report the usefulness of this new device was evaluated in a group of Parkinsonian patients in relation to evaluated dopaminergic therapy.
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Methods

Twenty patients, enrolled in this study with a clinical diagnosis of PD, were 30 years of age or older and were all outpatients (nine men and eleven women, mean age 66.0±9.5). Cerebrovascular and symptomatic Parkinsonism were excluded. All patients had resting tremor, rigidity, and impaired gait that had shown some improvement by the use of levodopa. However, as the rate of improvement was less than satisfactory, dopamine receptor agonist therapy was to be instituted. Lifecorder was attached to them and they were instructed as to the use of the “Remark” button. WC (daily pedometric step count) and MCC (movement-related calorie consumption) are stored together with the MM (motor magnitude) in the Lifecorder from 0:00 to 24:00, and it continuously operates for six weeks or longer.

The MM is digitally divided into 10 grades by the acceleration sensor for every 2 minutes. MM 0 represents the quiet resting state and MM 0.5 subtle movements (movements with less than 1.3 METs; metabolic equivalents score). MMs 1 to 9 are for walking and exercise. MM 1 is for gentle walking (about 1.3 METs) and 9 is for running (about 9.1 METs) (Fig. 1). Movements of MMs 1 to 9 are counted as step numbers, but the subtle movements of grades MM 0 and 0.5 are not recorded as steps. The MCC, calorimetry with this device, is calculated by the computed data of METs, body height and weight, subtracting the basal metabolic consumption.

Age-matched subjects without PD and motor disability were evaluated with Lifecorder as a control group, that consisted of seven persons (three men and four women, mean age 66.6±7.6).

Prior medications that included levodopa with benserazid, amantadine, trihexyphenidyl, and/or selegiline were unchanged for at least two weeks for the baseline assessment. After the baseline study, cabergoline, a long-acting D2 receptor agonist, was added in an increasing manner (0.5, 1, 2,

Table 1. Profiles of Each Patient and Normal Control Subjects; Age, Sex, Duration of PD (years), Hoehn-Yahr, and UPDRS at Entry

<table>
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<th>No.</th>
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<th>duration of PD</th>
<th>Yahr</th>
<th>UPDRS</th>
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<td>F</td>
<td>7</td>
<td>3</td>
<td>59</td>
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<td>F</td>
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<td>79</td>
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PD: Parkinson disease, UPDRS: unified Parkinson’s disease, rating scale.

Figure 1. The magnitude of movements (MM) corresponds to the metabolic equivalents score (METs; kcal/kg/h). The graph shows the relation between MM and METs. For example, movement of less than 1.3 METs is recorded as MM 0.5 with Lifecorder, and the movement of this magnitude is not counted as steps, and walking of 1.8 METs is recorded as MM 2.

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3, 4 mg oral, once a day) every 2 weeks, until optimum improvement was achieved. Before cabergoline administration and 4, 8 and 12 weeks after, the Lifecorder data was assessed and correlated with UPDRS. UPDRS was evaluated at each clinic morning visit. The examiner was not aware of the results of the Lifecorder analysis at this time, as the data was gathered later. The Lifecorder data was transferred to a computer through an exclusive ultra-red interface, and was subjected to statistical analysis with Excel® spreadsheet software. Cabergoline dose, WC, and MCC were correlative analyzed by ANOVA for multiple comparisons, followed by Dunnett’s test. MM for each 2-minute period was averaged.

Figure 2. Twenty-four-hour recordings of the magnitude of movements (MM) per two minutes. A is a record of patient 1 prior to cabergoline administration. At most points in time during daytime, MM is as low as 0.5. When walking, MM only registers up to 2. Pedographically, the patient walked only 433 steps a day. The nocturnal record shows the patient probably tried to turn over in bed, as MM 0.5 activity is occasionally seen, as the arrows indicate. B is a record of the same patient with cabergoline 3 mg per day. The rate of MM 1 and 2 clearly increased during daytime. The patient walked 3,570 steps per day. On the other hand, nocturnal minor motor activity decreased. C is a record of a healthy control subject. When walking in daytime, MM is between 2 to 6, indicating high motor activity. The subject walked 6,600 steps per day. Nocturnal bathroom visit is identifiable with MM 1 or 2, as the arrow indicates.
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hourly, and graphically shown as a daily movement profile (2, 3). The group was divided into two subgroups; those with improvements of more than 10% of UPDRS, and those with less than 10%. To estimate bodily activities like turning over in bed, subtle nocturnal movements in the MM 0.5 range were also assessed from 0:00 to 4:00 AM.

**Results**

**An exemplified case study**

A 74-year-old woman (patient 1; Table 1) had deteriorating walking ability, together with festination, tremor of upper limbs and fluctuating motor activity. The off period occupied approximately 25–50% of daytime, and thus cabergoline was added. The baseline study showed a limited activity in the MM 0.5 range, but small motor activities of MMs 1 and 2, were also recorded (Fig. 2A). After the dose was increased to 3 mg per day, she was much more mobile and content with the drug effect (Fig. 2B, Fig. 3A, B). The symptoms had clearly improved, as UPDRS decreased from 59 to 25. The off-period decreased to less than 5% of daytime, while WC increased from 665 to 1,682 steps and MCC from 9.8 to 21.8 kcal (Fig. 4). Moreover, subtle movements presumably due to restlessness while in bed were reduced with dopaminergic therapy (Fig. 5).

**The baseline characteristics of control and Parkinsonian groups**

Seven control subjects (three men and four women, mean age 66.6±7.6) and thirteen Parkinsonian patients completed the study (six men and seven women, mean age 65.5±8.2, Hoehn-Yahr rating from 1.5 to 4) (Table 1). Before cabergoline administration, the average UPDRS was 40.5. WC 2,459±2,522 steps (mean±S.D., normal control, 5,332±2,368) and MCC 56±67 kcal (mean±S.D., normal control, 133±67.3 kcal) (Fig. 6) were distinctly lower in the disease group than in the control group by t test (p<0.01). Mean WC was 2,912, 3,796±2,716, 469±180, and 611 steps for patients
with Yahr 1.5 (one case), 2 & 2.5 (seven cases), 3 (four cases), and 4 (one case). Mean MCC was 58.3, 91±7, 4, 6.1±2.9, and 12 kcal. UPDRS also correlated well with WC (p<0.05) and MCC (p<0.05).

Mean cabergoline dose at the completion of the study was 2.3 mg per day. The mean UPDRS improved from 40.5 to 28.4 (p<0.01). The mean WC increased from 2,459±2,522 to 3,315±2,668 steps (p<0.01) and the MCC from 56±67 to 74±70 kcal (p<0.05) by t test (Fig. 6). Thus, the UPDRS improved in parallel with WC and MCC after cabergoline administration except for patients 5 and 11 (Fig. 7).

Eight patients (No.1–4, 6, 10, 11, 13) were judged to have improved by UPDRS for more than 10%, whereas five (No.5, 7, 8, 9, 12) did not (Table 1). The mean UPDRS in the former group was 42.5±11.8, and improved to 21.4±12.8 (p<0.0005). The mean WC increased from 2,558±3,118 to 3,902±3,104 (p<0.005) and the MCC from 58.8±83.2 to 88.1±81.4 (p<0.01). One patient (case 11) showed improvement by UPDRS, but the WC and MCC did not (Fig. 7). On the other hand, the mean UPDRS in those without improvement was 37.4±18.1 and 39.6±17.4 (p=0.15) after cabergoline. The mean WC changed from 2,301±1,420 to 2,375±
1,639 (p=0.41), and the MCC from 52.3±35.6 to 52.8±44.1 (p=0.48). Thus, no statistically significant changes were recorded when data was compared before and after cabergoline usage. As an exception, one patient (the case 5) showed clear improvements of WC and MCC but the UPDRS did not (Fig. 7). The cabergoline treatment of these five patients was discontinued, or changed to another D-agonist.

Nocturnal restfulness, in contrast to enhanced daytime activity, was clearly shown with Lifecorder, when daytime improvements did occur (mean UPDRS-12; before, 1.8; after, 0.9). Mean nocturnal restlessness decreased from 32.6±21.2 minutes to 16.8±17.5. The UPDRS-12 also correlated well with the nocturnal restless period (p<0.05).

Figure 6. Walking step counts (WC) and movement-related calorie consumption (MCC) prior to and after cabergoline administration in all cases are shown in graph A (WC) and B (MCC). The open circles are the mean WC and MCC, and vertical bars indicate the standard deviation. Both WC and MCC significantly increased with cabergoline therapy by paired t test (p<0.05).

Figure 7. The percentages of improvement of WC, MCC and UPDRS with cabergoline. Each number indicates an individual case in Table 1; the numbers in open circles indicate the patients who improved more than 10% of UPDRS. Most patients improved on UPDRS also shows enhanced performance on WC and MCC except for cases 5 and 11 who did not.
Discussion

When each patient was assessed with WC and MCC in relation to UPDRS in the majority of cases, the UPDRS was positively correlated with these data, but some parameters of the UPDRS were not necessarily in parallel with Lifecorder data. This is mainly due to the fact that the Lifecorder data exclusively depends on the motor activity, whereas the UPDRS does not. Case 5, that was interpreted to be unimproved on total UPDRS, showed a motor improvement on UPDRS part III, a motor performance scale, in parallel with the Lifecorder data.

Therefore, the Lifecorder data are not necessarily parallel with the total UPDRS score, that contains the scores of UPDRS part I (behavior, mental and mood), part II (activity of daily living), part III (motor performance) and UPDRS part IV (drugs side effects). The major usefulness of the Lifecorder is, however, not simply to evaluate the total daily, weekly or monthly motor activity. It is of value for evaluating the time-dependent motor activities throughout the entire day and to identify the change or fluctuation of motor activity in relation to one’s daily life. We may thus state that the Lifecorder data correlates with the UPDRS with some exceptions, as Lifecorder exclusively represents the motor aspect of Parkinsonian performance.

A variety of attempts have been made for the objective, quantitative, and simple assessment of motor disability in PD (3–5). The UPDRS, widely utilized, is useful for semi-quantitative clinical assessment of the entire performance and not simply the motor performance, but it requires interpretation by physicians and is thus not a fully objective scale. For quantitative analysis of tremor and movement of an upper limb, the Actigraph® (6, 7), attached to the wrist, has been utilized for evaluation of Parkinsonian motor activity, but it has the drawback of recording all hand-related movements, and picks up not only volitional hand activity (4) but also tremor and involuntary movements. Accordingly, its usefulness tends to be rather restricted. In contrast, the Lifecorder objectively interprets and records the movements of the body axis, but not the upper limbs (2, 8).

Lifecorder is attached to the waist belt. This implies that it records the axial motor activity in terms of vertical acceleration and deceleration, as the built-in sensor is gravity/antigravity sensitive. This operates continuously while walking with varying magnitude, sitting and even sleeping. This appears to be the first report in which improved nocturnal quiescent state, as opposed to enhanced daytime motor activity, has been clearly demonstrated after dopaminergic therapy, as seen in Fig. 3.

The motor activity profiles displayed visually by averaging the daily recording on a weekly or monthly basis are useful for objective assessment of improvement and deterioration in relation to drug therapy.

One of the problems in the use of the Lifecorder is to clearly differentiate dyskinesia from non-dyskinetic motor activity. The majority of dyskinesia occurs in the limbs while the body axis is less involved, but there is a problem with the Excel-generated data to discriminate normal daily motor functions from dyskinesia. However, there are solutions to this problem. One is that the patient can be instructed to push the “Remark” button on the Lifecorder when dyskinesia starts and ceases. In this way it is possible to know the time, the duration, and the severity of the dyskinesia. Another is to let the patient record in the “Parkinsonism” diary when dyskinesia occurs, its time of onset, severity and time of cessation. However, difficulties still remain in being able to completely distinguish voluntary movements from axial dyskinesia, and also on occasion shuffling type gait is likely counted as steps although the motor magnitude is lower in range than more physiological walking.

The nocturnal problems in PD have not been well-focused upon in previous studies (9). However, these certainly impair daytime activities, as a quiescent sleep is not achieved for a variety of reasons; for example, difficulties experienced in turning over in bed, or in getting out of bed (10) for nocturia. These nocturnal disabilities are perhaps the major cause of insomnia and shallow sleep in Parkinsonian patients (11). The failure of attempts to turn over in bed were clearly recorded as MM 0.5, nocturnal minor movements, in contrast to larger movements of MM 1 when the patient actually got up and walked. Another aspect of the usefulness of this device is to evaluate the magnitude of akinesia (4). Since the axial motor activity is scaled to 10 divided grades, viewing the record allows insight into what a patient was doing at a certain point in time. When motor activity improves, the Lifecorder clearly shows the enhanced and prolonged high-range peaks. Furthermore, the accumulated data may be used for both short-term and long-term analysis, as the device continues to operate for more than 6 weeks. Accordingly, this device serves as an exceptionally useful adjunct to conventional UPDRS for objective evaluation of Parkinsonian motor disabilities and improvements.

Acknowledgements: Mr. Tadao Kubota, Pfeizer, Japan, suggested the necessity of evaluating the nocturnal motor behavior in Parkinsonism. His idea prompted us to consider the use of this device.

References