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ORIGINAL COMMUNICATION

Assessment of Wearing Off in Parkinson's disease using objective measurement

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Abstract

Background Development of "Wearing Off" (WO) of motor and non-motor function in Parkinson's disease (PD) adversely affects quality of life. This suggest that identifying and treating WO is important. However, identification of WO depends on people with PD (PwP) recognising and reporting WO and there is a perception that WO may be significantly underestimated.
Objective We investigate the feasibility of identifying "Wearing Off" using objective measurement and assess the clinical benefit in rectifying it.
Method In this study, 200 PwP were studied for evidence of WO using a continuously worn wearable system. Eighty-five patients (43%) were found to have WO and treatment was changed to mitigate the effects of WO.
Results Factors, such as duration of disease, high baseline MDS-UPDRS (motor component), high Percent Time in Bradykinesia (PTB), high Levodopa Equivalent Daily Dose (LEDD), frequent Levodopa doses and younger age of onset, are associated with severity of motor complications. Patients with more severe WO experienced worse motor and non-motor symptoms and lower quality of life. Quality of life significantly improved in PwP when WO was treated.
Conclusion The findings reported in this study provide evidence that identifying and treating WO improves outcomes of PwP and that objective measurements may help clinicians to identify and treat WO.

Keywords Parkinson's · Disease · Wearing off · Motor complications · Objective measurements · Wearable sensors

Introduction

Following diagnosis of Parkinson's disease (PD), the benefit provided by a dose of levodopa may last many hours, and commonly, people with PD (PwP) are unaware of increasing bradykinesia following a dose even when a dose is overlooked. However, within a few years from diagnosis, the duration of therapeutic effect from each dose of levodopa shortens [1, 2] and PwP become aware of a transition from receiving benefit from levodopa ("on") to loss of benefit ("off") [3], frequently known as "Wearing Off" (WO) (2, 4). WO can commence as early as two years after diagnosis [2, 5, 6], and within ~ 3 years ~ 25% have WO and ~ 40% by 5 years [5, 7, 8].

WO is thought to reflect the reduced storage capacity of dopaminergic terminals [9–11] and significantly reduces quality of life [12, 13]. It seems likely therefore that identifying the presence, characteristics and timing of WO, and treating it in a timely manner would improve quality of life. However, there have been surprisingly few studies directly confirming this [14].

WO is recognised through history provided by the PwP to the assessing clinician. This interchange can be improved using self-rated questionnaires/diaries [15–17] and a structured interview by an experienced clinician [18] that aids the PwP in reporting motor [19–21] and non-motor transitions [21–23] from "on" to "off". Nevertheless, it is likely that 25% of WO remains undetected [24] with 30–50% of non-demented PD patients having impaired self-awareness of their motor complications [25]. Additionally, detecting fluctuations probably depends on clinician's experience and time available at the clinic visit [2, 26].

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Objective measurements of PD symptoms using wearable devices is now possible [27] and previous pilot studies suggested that they may assist clinicians in the detection of WO [28, 29]. These systems can correctly identify the levodopa response in a challenge test which is a key feature of fluctuations [30]. This entails recognition of "off" to "on" and therefore implies that recognition of "on" to "off" with objective measurement systems should also be possible. In this study, the data from one of these systems (the Parkinson's KinetiGraph or PKG, Global Kinetics CorporationTM, Australia) were examined for evidence of WO and whether treating this WO improved scores as measured by clinical scales and quality of life scores. This was a retrospective analysis of 200 PwP in whom both a range of clinical scales were collected and a PKG was also worn. WO was identified by visual inspection of the PKG for the presence of an obvious increase in PKG's bradykinesia scores and the scores from clinical scales were compared in those with and without WO. The benefit gained from treating WO in terms of changes in scores from clinical scales was assessed. Objective measurement allows the opportunity to set a therapeutic target range [31] which was important in assessing the benefit in optimising therapy to treat WO.

The primary purpose of this study was to assess the feasibility of identifying WO using objective measurement and to assess the clinical benefit in rectifying it.

Methods

The subjects in this study were 200 people with idiopathic PD (PwP) who had previously been recruited into two studies undertaken in nine hospitals across Australia. These studies had ethics approval provided by St Vincent's Hospital Melbourne Human Research & Ethics Committee to use data for investigations related to PD. One study was conducted on a "whole population" of PD in northern Tasmania [32] and the other study completed between March 2018–December 2019 recruiting patients with (a) idiopathic PD of either 4 or more years of disease or on 4 or more doses per day of levodopa (i.e., selection criteria likely to be weighted toward those with WO); (b) no contraindications to increase levodopa and (c) MoCA > 21 and aged between 59 and 75 years. At the outset of both studies, all subjects wore a PKG logger on the arm most affected by PD for at least 6 days, clinical scales (MDS-UPDRS I-IV, PDQ39 and NMS) were administered and a clinician took a history, examined the PwP (with access to the PKG in 155 and without knowledge of the PKG in 45) and wrote an assessment of the clinical state, including whether WO was present and whether further treatment was required.

In this current study, all PKGs and their written reports were reviewed and sorted into those that showed WO and those that did not (see below for sorting criteria). The treating clinician's assessment of WO was made with the support of the PKG in 155 PwP, whereas in 45 cases, clinical assessment was made without knowledge of the PKG. Then, clinicians were asked to make incremental changes to therapy over subsequent visits ~ 1 month apart, until their therapy was optimised. At this point, clinical scales were again administered along with a final PKG and the subject was discharged from the study. The clinical scales and PKG data from the first and last visit were compared to each other in PwP with WO.

Statistical analyses

As many of the data were not normally distributed and with small populations, non-parametric tests were used. Mann–Whitney test was performed to compare two groups with different subjects, while Wilcoxon test was used to compare same subjects before and after treatment. Chi square test was performed to compare suitability for device-assisted therapy (DAT) in WO PWP. In all tests, P values of < 0.05 were considered statistically significant. GraphPad Prism software version 8.0 was used for conducting statistical evaluations and making graphs.

Diagnosis of WO

In this study, PKG reports and clinician's assessment letters of 200 PwP attending for their first assessment in these two studies were examined for evidence of WO. The primary criteria for the presence of WO were its identification on the PKG. The PKG graphically presents a bradykinesia score plotted against time of day and in relation to the time of medications (Fig. 1 and see cBKS in Glossary of PKG terms below). This plots the PKG's bradykinesia levels as they vary in relation to taking medications but also with respect to a therapeutic target range [31], shaded blue in Fig. 1. The PKG was interpreted qualitatively and independent of knowledge of the MDS-UPDRS scores, using the following criteria:

- Evidence of a decrease in bradykinesia scores in response to levodopa (a levodopa response);
- A subsequent increase in bradykinesia scores at some time prior to the next dose;
- Re-emergence of tremor provided supporting evidence only.

In those cases where the doctor had access to the PKG, this was used as verification. There were no cases where the PKG showed WO but the doctor's correspondence showed that the doctor believed otherwise. When WO was identified, it was further classified according to whether or not,

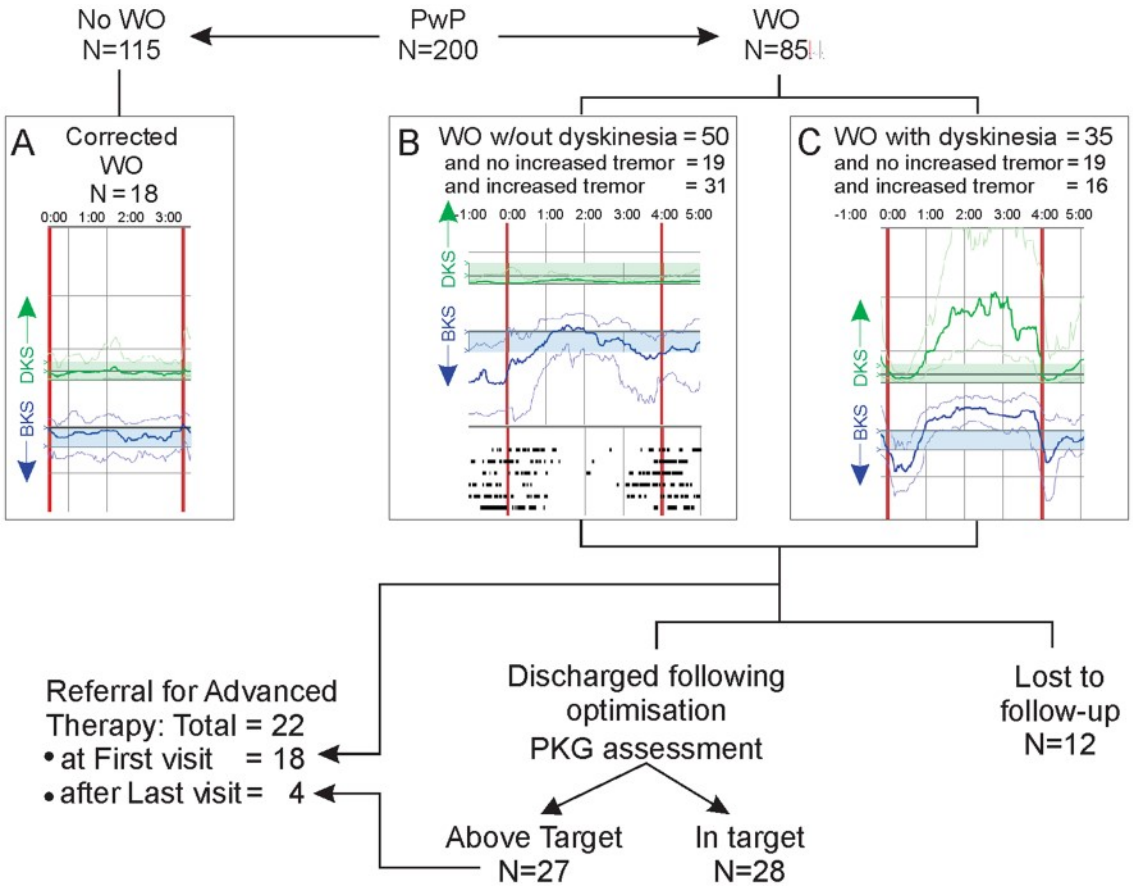

Fig. 1 Flow chart of study showing how PwP were sorted into subjects with "Wearing-OFF" (WO) and "Corrected Wearing-OFF". There are three figures taken from different PKGs to illustrate the three categories of WO. In all three figures, the vertical red lines indicate the time that dose reminder was delivered and the thin dark vertical lines indicate 1-h interval. The dark blue line is the cBKS, with increased bradykinesia towards the bottom of the figure. The shade blue area indicates the target range. The dark green line is the cDKS, with increased dyskinesia towards the top of the figure. The shade green area indicates the target range. **a** the doses are 3 ½ hours apart and both the cBKS and cDKS are in target. **b** the dose interval is 4 h and cBKS is out of target at the time of the first dose but reaches target in ~ 45 min and increases above target ~ 2½ hours later. The dotted lines below the figure are tremor rasters with each line indicating a day and each dot indicating a 2-min epoch in which tremor was present: it shows that tremor is present at times when the cBKS is above target. **c** shows the cBKS entering the target range ~ 30 min after the first dose and abruptly increasing above target just prior to the second dose. There is concomitant increase in the cDKS when the cBKS enters the target range

following a dose of levodopa, the PKG's bradykinesia trace fell below the therapeutic target as follows:

- WO with peak response to levodopa being above target;
- WO with peak response to levodopa falling within target;
- WO with re-emergence of tremor;
- WO where the peak was associated with dyskinesia.

Corrected WO

A further category of WO was identified. When levodopa is first introduced as a therapy, it is conventionally prescribed as a t.d.s. dose. Over time, the interval between doses is reduced in response to WO. PwP who had dose intervals of ≤ 4 h, whose cBKS were in target and without WO, were presumed to previously have had WO which was adequately treated at the time of the examination (referred to as "corrected WO").

The PKG

The PKG system consists of a data logger, a series of algorithms that produce data points every two minutes and a series of graphs and scores that synthesise these data into a clinically useful format known as the PKG [33–39]. Each patient wore a PKG logger continuously for 6 days 2–4 weeks prior to appointment with clinician. The reader is referred to the manufacturer's website and to other publications for a more comprehensive definition of terms. The following is a glossary of PKG terms relevant to this study.

Glossary of PKG terms

BKS: The Bradykinesia Score (BKS) is a score of a subject's level of bradykinesia obtained from 2 min of data. BKS are provided continuously over the entire 6 days of recording time. A BKS > 80 is indicative of sleep [40] and a BKS < 80, > 40 is indicative of inactivity.

cBKS: The continuous BKS from the 6 days is plotted against time of day and in relation to the time of medications (Fig. 1). At a particular time of day (say 10:00 am), the plot shows the median of the BKS recorded on the 6 days at 10:00 am [36]. It is a smoothed 15 BKS moving median centred on the seventh (middle) BKS.

mBKS: This is the median of the two-minute BKS in the period 09:00–18:00 for all days that the PKG was worn (usually 6 days) excluding BKS > 80.

aBKS: The active BKS is the median of the two-minute BKS in the period 09:00–18:00 for all days that the PKG was worn (usually 6 days) excluding BKS > 40.

mDKS: The median DKS is the mean of the dyskinesia score obtained from the same two-minute epochs used to estimate the BKS in the period 09:00–18:00 for all days that the PKG was worn.

PTT: The Percent Time Tremor is the proportion of 2-min epochs containing between 09:00–18:00 for all days that the PKG was worn (43).

PTB: The Percent Time in Bradykinesia is estimated using the Severity levels described in (44): The threshold for target was a Severity level of 2.5 or ~ 35 MDS-UPDRS III points. The PTB is the number of 2-min epochs Levels 3, 4 and 5 between 09:00–18:00 on the 6 days that the PKG was worn, in Severity level 3 or above, expressed as a percent of all the available epochs in that period.

PTD: Percent Time in Dyskinesia is the proportion of time that DKS were over target (DKS = 7), not include epochs with high levels of walking.

Dose: Reminder. The PKG logger is programmed to deliver reminders in the form of a vibration at the time when levodopa doses were due. The number of *Doses of levodopa/day* is the sum of the number of reminders. The *Dose interval* is calculated from the interval between dose reminders.

Results

Figure 1 shows a flowchart of the study. Eighty-five PwP (43%) were identified and treated for WO. Most (59%) had WO without dyskinesia, and of these, 62% (of 50) were associated with re-emergence of tremor (Fig. 1b). Peak dose dyskinesia accompanied the WO in 41% of subjects (Fig. 1c) and re-emergence of tremor was less frequent (46%) in these cases. Table 1 compares the demographics of all PwP in this study including those with and without WO. The main significant differences were age, age of onset of PD, duration of disease, the use of D2 agonists and MDS-UPDRS IV scores.

Table 1 Demographic characteristics of patients

	All Participants (*N* = 200)	No WO (*N* = 115)	WO (*N* = 85)	Corrected WO (*N* = 18)	*P* No-WO v WO	*P* WO v Corrected WO
Age	71 (66–77)	72 (66–77)	70 (65–74)	71 (64–75)	0.04	0.8
Age of onset	64 (59–71)	67 (61–73)	61 (56–67)	65 (59–71)	0.0001	0.1
Disease Duration	5.5 (3–9)	4 (3–7)	7 (5–11)	4 (2–7.5)	0.0001	0.001
Number of doses	4 (4–5)	4 (4–5)	4 (4–6)	4 (4–5)	0.7	0.7
LED	629 (500–900)	620 (500–900)	600 (400–848)	600 (411–863)	0.3	0.6
LED D2%	0 (0–21)	0 (0–26)	0 (0–13)	0 (0–22)	0.05	0.2
MDS-UPDRS I	10 (7–15)	11 (7–15)	10 (8–15)	11 (6–13)	0.7	0.6
MDS-UPDRS II	11 (6–16)	10 (6–16)	11 (7–16)	9 (3.8–14)	0.4	0.03
MDS-UPDRS III	38 (29–46)	36 (29–46)	39 (30–47)	32 (23–40)	0.2	0.008
MDS-UPDRS IV	4 (0–6)	3 (0–6)	5 (1–7)	3.5 (0.7–5)	0.07	0.1
MDS-UPDRS total	64 (48–78)	60 (47–79)	67 (53–78)	51 (38–65)	0.1	0.007
PDQ39	26 (15–44)	29 (16–47)	25 (15–42)	24 (8.5–44)	0.3	0.9
NMS	9 (7–13)	10 (7–13)	9 (6–12)	7 (4.8–11)	0.2	0.1
aBKS	24 (19–27)	24 (20–28)	24 (20–27)	21 (20–23)	0.6	0.01
mDKS	1.9 (0.9–3.9)	1.6 (0.8–3-4)	2.2 (1.2–4.7)	2.9 (2–4)	0.01	0.3
PTB	34 (13–62)	37 (13–74)	39 (24–59)	19 (13–30)	0.7	0.0003
PTT	1.8 (0.6–6)	0.01 (0–0.05)	8.6 (1.5–23)	0.4 (0.2–1.9)	0.0001	0.0001

All values show median and interquartile range in brackets

However, there was a trend for most MDS-UPDRS scores to be higher in the WO group.

Dose interval in WO and its effect on symptom severity

The scores of PwP categorised as having WO were then compared with PwP who had corrected WO (dose intervals of ≤ 4 h, but whose PKG scores were corrected, Table 1). The proposition is that a dose interval less than 4 h (typically 3 or 3½ hours) would be unlikely; unless at some stage in the past, these PwP were considered to have WO which was corrected by shortening the dose interval of levodopa. It is relevant that the PTB of PwP with corrected WO was in the normal range compared to an elevated PTB in their counterparts with "wearing-OFF". Their MDS-UPDRS total scores were significantly lower, as were their MDS-UPDRS II, III, aBKS and disease duration.

Next, PwP with WO were sorted according to the time interval between doses [< 3 h ($n = 28$) and > 3 h ($n = 57$)]. Their clinical and PKG scores were compared along with those from PwP with corrected WO (Fig. 2a-d). PwP with WO < 3 h had longer duration of disease and lower age of onset. Similarly, their motor (MDS-UPDRS III, IV sub scores) and non-motor (MDS_UPDRS II, PDQ39, NMS) scores were higher than the other two groups and received higher LEDD and more frequent levodopa doses (Fig. 2a-d).

Change in clinical scores following therapeutic interventions to correct WO

Eighteen of the 85 PwP with WO were immediately referred for device-assisted therapy (DAT) at first visit and 12 did not attend the final visit. Optimising control of bradykinesia was attempted using oral medications in the remaining 55 subjects. By the final visit, PKG scores were in the target range in 28 PwP, but in 27, scores remained above target and 4 of them were then referred for DAT. The improvement in the two groups for various scores are shown in Table 2. The MDS-UPDRS III, MDS-UPDRS total and PDQ39 were significantly improved in both arms; however, the MDS_UPDRS I, II and IV were only significantly improved in the optimally controlled arm. In that arm, NMS changes were close to significant ($P = 0.05$). Interestingly the change in LEDD and in number of doses was similar in the two arms, whereas the use of D2 agonists was higher in non-optimally controlled arm. Only 27% of PwP with WO < 3 h were optimally controlled compared with 66% when WO > 3 h. This was not significant ($P = 0.10$, Fisher's exact) mainly because of the small number of PwP with WO < 3 h.

Suitability for DAT in the 22 (26%) WO PwP was further examined by reviewing the doctors' correspondence. Based on examination of doctors correspondence, most PwP with WO < 3 h were considered to be ready for DAT/heading towards DAT, while PwP with WO > 3 h were mostly treated with oral medications (Chi square test, p value < 0.0001). Likewise, PwP on 5 or more doses of L-dopa were mostly referred for DAT, whereas those on 4 or less doses were predominantly treated with oral medications (Chi square test, p value < 0.0001). Subjects with WO > 3 h who developed significant dyskinesia were also considered as DAT candidates. These data support previous commentary (45) that frequent L-dopa doses, WO < 3 h and developing troublesome dyskinesia are contributing factors for consideration of DAT.

The impact of PKG on therapeutic decision making

The difference between MDS-UPDRS III and MDS-UPDRS total scores from first and final visits were obtained and those PwP whose doctors had access to PKG information at the time of consultation (PKG +, $N = 43$) were compared with those PwP who did not (PKG, $N = 12$). The change in MDS-UPDRS scores (shown as Δ in Fig. 2f) was significantly larger in PKG + group ($P = 0.03$ and 0.003 for MDS-UPDRS III and total MDS-UPDRS, respectively). The size of the change in the PKG + arm was 5 MDS-UPRDS III points and 13.3 MDS-UPDRS Total points compared to −1.0 and 0.45 (UPDRS III and MDS-UPDRS Total, respectively) for PKG- arm.

Discussion

Recognition of WO by history requires experience [18], even so it is likely that ~ 25% remain undetected [24]. As wearable technologies, such as the PKG, can measure the transition from "off" to "on" by reliably predicting response to the levodopa challenge test [30], they should also provide the opportunity to directly measure motor transitions from "on" to "off". Objective measurement provides the opportunity of not only identifying WO but also measuring the duration of benefit obtained from a dose of levodopa. It also provides the opportunity to assess the effect of the levodopa dose (i.e., whether it achieved target) in much the same way as can be achieved by a levodopa challenge test. WO questionnaires were not collected in the studies that provided the data for this study and so could not be compared to the methods described here.

The incidence of "wearing-OFF" in this study was similar to those in previous studies. In this study of 200 PwP, most of whom were in the first 10 years of disease [median disease duration 5.5 (IQR: 3–9)], 43% were diagnosed with "wearing-OFF" compared to 40% (5, 46) and 41% [1] reported previously. While the similarity between this and previous studies in incidence of WO suggests that objective measurement does not increase the rate of detection

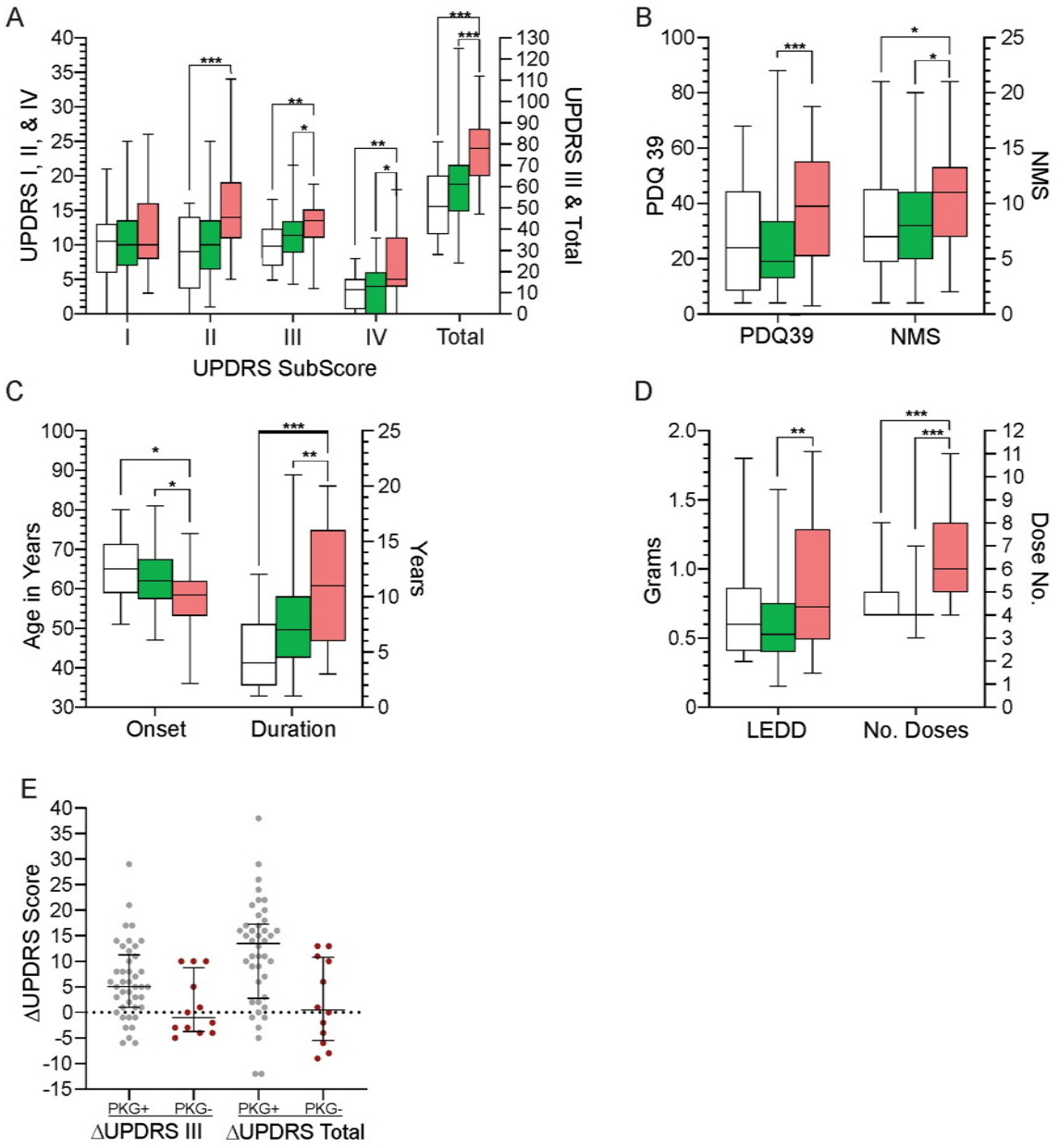

Fig. 2 Comparison of clinical scales of fluctuators separated according to their dose interval. **a-d** are box and whiskers (10th and 90th percentiles) plots showing subjects with corrected WO (white boxes, WO > 3 h (green boxes) and WO < 3 h red boxes. Asterisk shows *P* values: * = < 0.05, ** = < 0.01, *** = < 0.001. Findings are discussed in text. **e**. This is a plot of the difference (Δ) between MDS-UPDRS scores at first and final visits in subjects managed with and without access to the PKG information. The change in both MDS-UPDRS III and total MDS-UPDRS was greater in PKG + group than in the PKG- (*P* value 0.03 and 0.003, respectively, Mann–Whitney test)

above that of an expert clinician, pilot studies [26] suggest that in about 25% of cases of WO, PwP were unaware of their presence even though objective measurement showed them to be present. Furthermore, most of the 200 PwP in this study were usually managed by neurologists and their WO had gone undetected. The question of the contribution of objective measurement to the detection of otherwise unrecognised WO requires further study.

PwP with WO were substantially younger at diagnosis with longer disease duration than those without WO, with a non-significant trend to higher MDS-UPDRS scores. There was also a significant difference between the MDS-UPDRS II, III and Total of PwP with WO and those with corrected WO, suggesting a benefit in identifying and treating "wearing-OFF". Table 2 shows that there is a substantial change in MDS-UPDRS scores and PDQ39 when WO is treated.

Table 2 Motor and non-motor outcomes post WO treatment

Clinical scores		WO optimally controlled ($N=28$)		WO non-optimally controlled ($N=27$)	*P* value
Age		70 (64–74)		67 (63–74)	0.6
Disease duration		6 (4–8)		7 (5–10)	0.05
Age of onset		62 (59–68)		59 (55–67)	0.1
CLINICAL SCALES		values	*p*	values	*p*
Number of doses	*Baseline*	4 (4–4)	*0.0001*	4 (4–5)	*0.006*
	Final	5 (4–5)		5 (4–6)	
LEDD	*Baseline*	500 (397–700)	*0.0001*	613 (400–775)	*0.02*
	Final	650 (548–831)		675 (475–969)	
D2% of LEDD	*Baseline*	0 (0–0)	*0.01*	0 (0–14)	*0.02*
	Final	4.5 (0–23)		11 (0–21)	
MDS-UPDRS I	*Baseline*	10 (7.3–13)	*0.0006*	8 (7–14)	*0.2*
	Final	6.5 (5–9.8)		10 (6–15)	
MDS-UPDRS II	*Baseline*	7.5 (5–13)	*0.03*	12 (9–16)	*0.3*
	Final	7 (3.3–9.8)		9 (5–15)	
MDS-UPDRS III	*Baseline*	31 (28–40)	*0.003*	39 (36–46)	*0.0003*
	Final	30 (21–36)		28 (19–40)	
MDS-UPDRS IV	*Baseline*	4 (0–6)	*0.002*	5 (0–9)	*0.3*
	Final	0 (1–2)		6 (3–18)	
Total MDS-UPDRS	*Baseline*	55 (48–66)	*0.0001*	68 (56–77)	*0.0006*
	Final	47 (33–53)		53 (28–65)	
PDQ39	*Baseline*	20 (14–33)	*0.0001*	19 (10–37)	*0.01*
	Final	14 (9.3–19)		14 (7–30)	
NMS	*Baseline*	8 (5–11)	*0.05*	8 (5–11)	*0.5*
	Final	7 (4–11)		9 (5–14)	
Active BK	*Baseline*	24 (23–25)	*0.005*	27 (21–29)	*0.04*
	Final	23 (20–25)		25 (22–27)	
PTB	*Baseline*	40 (31–53)	*0.001*	56 (39–79)	*0.02*
	Final	30 (20–39)		44 (33–67)	
PTD	*Baseline*	5 (0.6–11)	*0.01*	2.5 (0.7–25)	*0.1*
	Final	8.9 (5.8–15)		6.7 (2.9–24)	
PTT	*Baseline*	3.6 (1.1–7.8)	*0.03*	3.9 (2.1–9.2)	*0.1*
	Final	1.3 (0.5–3.8)		3 (1.1–7.3)	

The justification for the "corrected WO" classification is that dose intervals of 3 or 3½ hours are likely to have been deployed with the intention of treating WO. As the post-treatment scores are similar to the "corrected WO" cohort suggesting that it is achieving "control" that matters rather than previous history of WO. Indeed, while those in whom optimal control could not be achieved did have improved motor scores, they did not achieve the same benefit in quality of life and non-motor scales as those who achieved optimal control. With regard to PKG scores, the percent time in bradykinesia (PTB) was the most sensitive with people whose WO was optimally controlled having PTB at the upper limit of corrected subjects (30%).

Treating WO in this study required bringing the cBKS into the target range for the whole period between 09:00–18:00. The target range was set based on the advice of expert opinion [31] and resulted in change in UPDRS III to 28–30, suggesting that it constitutes an acceptable target. This target was achieved by increasing the number of doses and increasing the LEDD by ~ 150 mg, half of which was due to an increase in D2 agonists. This increase in LEDD not only resulted in a fall in MDS-UPDRS III but also in UPDRS IV, implying that dyskinesia was not a consequence of this change in LEDD. This is supported by the PKG scores where the percent time in dyskinesia (PTD) was well below the upper limit of normal subjects (30%).

WO after a shorter interval of benefit from levodopa (i.e., < 3 h) generally indicated that optimal control was less likely, and that device-assisted therapy would be required. This concurs with previous recommendations [45]. The data reported here suggest that factors predicting more severe motor complications in PD are duration of disease, high

baseline MDS-UPDRS (motor component), high PTB, high LEDD, frequent Levodopa doses and younger age of onset and in keeping with early findings [1, 46].

When examining the PKGs for WO, a proportion of subjects were found whose PKG scores for bradykinesia (aBKS) were high throughout the day and without evidence of a response to levodopa. For the purpose of this study, these participants were not considered to be fluctuators. However, there are two possibilities for these participants: either they do not respond to levodopa and thus are truly non-fluctuators or their bradykinesia is undertreated and an increase in levodopa would reveal levodopa responsiveness. If the latter were the case, it is possible that a proportion of these PwP would become fluctuators. Because this distinction cannot be made at the first visit, the number of PwP with WO may have been underestimated in this study.

This study was not directly designed to address the question of whether management of WO benefits from the use of the PKG or whether objective measurement is superior to usual clinical care in this regard. However, the data from some subjects were collected from clinics that did not use the PKG. The numbers are small and anecdotal but do suggest that without objective measurement, it is difficult to effect change in MDS-UPDRS scores in people with WO compared to when it is used. This is not surprising because recognition of WO by history is difficult and in as many as ~ 25% of subject it remains undetected [24]. Clearly a prospective blinded study addressing this question is required.

Conclusion

The primary purpose of this study was to assess the feasibility of identifying WO using objective measurement and to assess the clinical benefit in rectifying it. The study confirms that WO can be identified by objective measurement and treating it to reach a target provides improvement in motor function, non-motor function and quality of life. Further prospective studies are required to validate these findings.

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Author contributions HW contributed in co-ordinating subjects and collecting data related to clinical scales. PF did the data analyses. PF and MH wrote the manuscript and all the authors reviewed the paper.

Compliance with ethical standards

Conflicts of interest Global Kinetics Corporation (GKC) is the manufacturer and distributor of the Parkinson's KinetiGraph (PKG). PF has no financial interests in GKC. MH has equity in GKC. HW is supported by a grant provided by GKC to the Florey Institute. GKC management had no role in the instigation, design, data collection, analyses, interpretation of data or writing of the manuscript, nor have they been consulted as to whether the data should be published.

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