SAHLGRENSKA ACADEMY

Evaluation of Two Commercial Sensor Systems for Monitoring Parkinsonism and Their Possible Influence on Management of Parkinson's Disease

Degree Project in Medicine

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Programme in Medicine

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ABSTRACT

Degree Project in Medicine, Programme in Medicine.

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Keywords: *Parkinson's disease. Motor fluctuations. Wearable sensors. PKG. STAT-ON.*

BACKGROUND

Wearable sensors can be used to monitor motor symptoms in Parkinson's Disease. The Parkinson's KinetiGraph (PKG) and STAT-ON are two promising single-sensors. No previous studies have been made comparing these two, neither in terms of agreement nor in terms of usability.

AIMS

Compare agreement between PKG, STAT-ON, a resident physicians' assessment, and patients' medical records. Describe usability from the patients' view.

METHOD

Ten patients recruited from Sahlgrenska University Hospital wore two sensor systems (PKG and STAT-ON) and reports were assessed for typical categories of motor symptoms. A resident physician categorized the patients in the same way after taking the patients' history of motor symptoms and fluctuations. Agreement was evaluated with Cohen's kappa, and usability surveys and self-assessment scales were filled out.

RESULT

Compared to information derived from the patients' medical records, agreement was seen for the resident physician (kappa = 0.747, p = 0.015) and for one of two STAT-ON raters (kappa = 0.673, p = 0.023). Agreement between STAT-ON and the resident physician was significant for one of two raters (kappa = 0.783, p = 0.014). No significant agreement was seen between PKG and STAT-ON evaluations nor between PKG and the resident physician. Both sensors had a low mean rating score in the usability survey (1-5, lower better), PKG = 1.67 ± 0.56, and STAT-ON 2.01 ± 1.10.

CONCLUSION

The STAT-ON sensor provides information on motor symptoms that is more consistent with the resident physician than PKG. However, PKG might to a greater extent provide different information. Future studies are needed to understand the implications of this. The low mean rating score for usability indicates potentially high acceptability for sensors.

ABBREVIATIONS

BKS	Bradykinesia score
DKS	Dyskinesia score
FOG	Freezing of Gait
H&Y	Hoehn and Yahr scale
LID	Levodopa-induced dyskinesia
MDS	Movement Disorder Society
PD	Parkinson's Disease
PDQ-8	Parkinson's Disease Questionnaire 8
PKG	Parkinson's KinetiGraph
PRO-PD	Patient Reported Outcomes in Parkinson's Disease
QoL	Quality of Life
UPDRS	Unified Parkinson's Disease Rating Scale
WOQ	Wearing-off Questionnaire

BACKGROUND

Parkinson's Disease (PD) is the second most common neurodegenerative disease after Alzheimer's Disease. The prevalence worldwide is estimated to approximately 6 million and will very likely increase in the upcoming decades (1), making it a disease of particular current interest. Historically, PD was first described in 1817 by James Parkinson's *Essay of the shaking palsy*. Later in 1850, Jean-Martin Charcot refined and broadened the symptomatology separating the disease from other tremor-like diseases. However, it was not until the middle of the twentieth century that the key role of dopamine in the pathophysiology and treatment of the disease was discovered (2). Today, most evidence suggests that the pathological feature of the disease is explained as a decrease in nigrostriatal dopaminergic signaling depending on a loss of dopaminergic neurons in the brain, particularly in substantia nigra pars compacta (3). Additionally, cell dysfunction with misfolding of proteins, especially α-synuclein leading to Lewy Body inclusions, are thought to play a key role in the degeneration of dopamine neurons, potentially starting in other regions of the nervous system (4).

CLINICAL MANIFESTATIONS

The loss of dopaminergic signaling eventually gives rise to the classic parkinsonian motor features with the following four cardinal symptoms. Bradykinesia, which is the slowness and decrement of movement. Rigidity, which often appears as "cogwheel"-like rigidity. Tremor at rest, which is characterized by a 4-6 Hz tremor at rest, initially unilateral. And lastly, postural instability due to the loss of postural reflexes. However, the spectrum of motor symptoms is heterogeneous, also including other symptoms like dystonia and gait disturbances (e.g., freezing of gait, decreased arm-swing, or shuffling gait) (5). Among patients with PD, a wide variety of non-motor symptoms also occur, like autonomic dysfunction (e.g., sialorrhea, constipation,

urinary urgency), sleep disturbances, depression, and cognitive impairments (6), and some of these precede the motor symptoms (7).

TREATMENT

No treatment is available which prevents the disease from progressing. The treatment is instead symptomatic, substituting the deficiency of dopamine in the brain. Levodopa, a precursor to dopamine, is the most commonly used. Furthermore, dopamine agonists can be used for direct stimulation of dopamine receptors. Other alternatives include monoamine oxidase type b inhibitors and catechol-O-methyltransferase inhibitors, which reduce the rate of dopamine and levodopa degradation and preserves the levels of dopamine (8). In later stages of the disease, the therapeutic window may become narrower and patients can be considered for advanced treatment, including subcutaneous apomorphine infusion (9), levodopa/carbidopa intestinal gel infusion (10), or deep brain stimulation (11).

MOTOR COMPLICATIONS

During the first years of treatment, motor symptoms are often easily kept under control. However, as the disease progresses the majority of PD patients develop motor complications, including fluctuations, wearing-off, dyskinesias and other phenomena (see ***Figure 1***). According to a meta-analysis from 2001, approximately 40% of PD patients experience motor fluctuations after 4-6 years of treatment with levodopa. After > 9 years of treatment, the proportion reaches 70% (12). The umbrella term motor complications include several phenomena. Firstly, patients' motor symptoms can fluctuate between different motor states, called “OFF” or “ON” state. Briefly, OFF is described as periods where the parkinsonian symptoms are prominent and there is reduced treatment effect. In contrast, ON is described as periods with good motor function where the effect of treatment is satisfying (13).

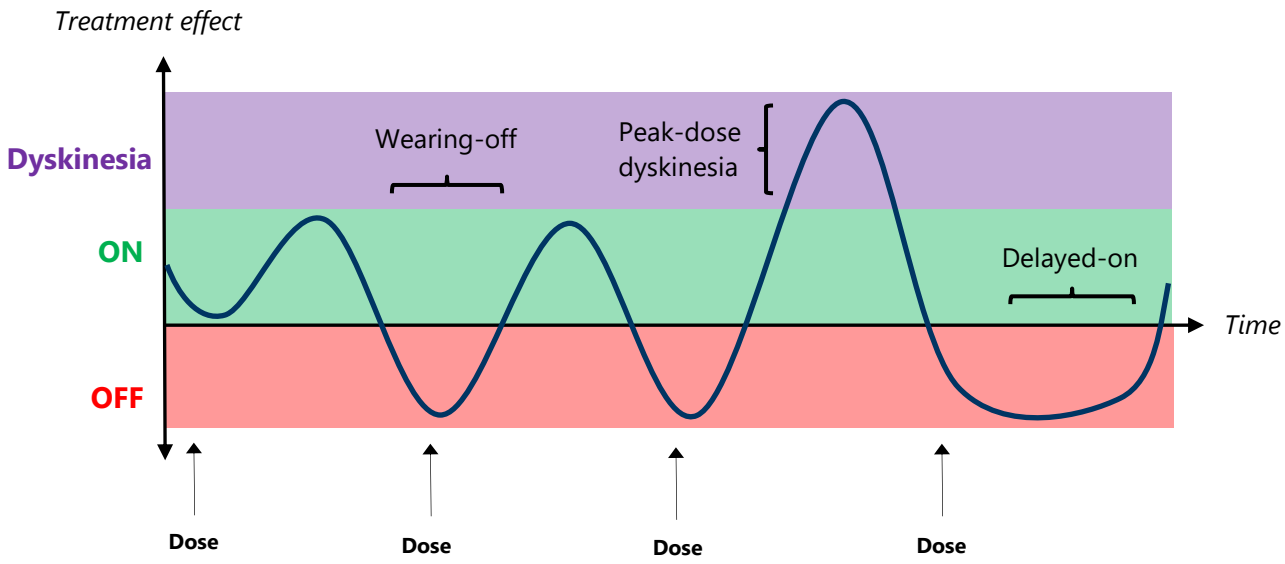

Figure 1. *Schematic illustration of motor complications.*
ON (green) illustrates periods with good treatment effect. OFF (red) illustrates poor treatment effect where parkinsonian symptoms are prominent. Wearing-off is the reappearance of symptoms prior to the next dose. Delayed-on is the latency in response to a dose of levodopa. Dyskinesia (purple) can occur as peak-dose dyskinesia, a form of levodopa-induced dyskinesia. Dose = Dose of levodopa.
(Author's illustration, based on some of the articles presented in the background (13-15))

WEARING-OFF, DELAYED-ON, AND DOSE-FAILURE

One phenomenon, usually one of the earliest motor complications, is "wearing-off". Basically, it is a reappearance of parkinsonian symptoms prior to the next scheduled medication, indicating insufficient duration of action of a dose. Wearing-off could be classified as either predictable, i.e., always arriving before each dose, or unpredictable, where the phenomena appear unrelated to medication intake (14). Two examples of unpredictable fluctuations are what is referred to as "delayed on" and "dose failure". As the names suggest, "delayed on" is a delayed response to a dose of levodopa, whereas "dose failure" is the absence of response to a dose of levodopa. Both these phenomena are believed to result from aberrant gastric emptying (14).

LEVODOPA-INDUCED DYSKINESIA (LID)

Moreover, many patients eventually experience levodopa-induced dyskinesias (LID). Dyskinesia can be explained as involuntary, often choreatic, movements, dystonia, or ballism,

which can involve different body parts from the head-and-neck to the trunk, extremities, or facial muscles. With disease progression, the therapeutic window for dopaminergic treatment becomes narrower. Consequently, patients can experience dyskinesia as a symptom of high dopamine levels, often referred to as peak-dose dyskinesia. However, some patients also tend to experience dyskinesia at the beginning-of-dose and end-of-dose, instead referred to as diphasic dyskinesia (15). The self-awareness of LID among PD patients is modest. In a study from 2013, almost one-fourth of the patients were unaware of having LIDs when video recorded and assessed as LID by physicians (16).

ON-OFF FLUCTUATIONS

Fluctuations in motor states affect many patients with chronic levodopa treatment. In the beginning, patients often experience these fluctuations as short periods of predictable wearing-off, in this study referred to as "regular OFF-fluctuations". Later in the disease, patients can regularly switch between being ON with peak-dose dyskinesia to being OFF, instead referred to as "regular ON-OFFs". With further disease progression and aberrant gastric emptying, patients' motor states can instead switch rapidly and unpredictably between the ON- and OFF-state, sometimes also called "yo-yoing". The pathophysiology behind these phenomena is not yet fully understood, however, altered pharmacodynamics, as well as pharmacokinetics, are feasible explanations (14).

FREEZING OF GAIT (FOG)

Furthermore, one of the most bothersome motor complications among patients with PD is Freezing of Gait (FOG). It is characterized as an inability of lifting the feet and taking a step forward, thus making the patient stuck at a place. By patients, it is often described as having the feet "glued to the floor". FOG can occur in different situations, however, it is mostly seen during gait initiation, turning, or passing through a narrow space (i.e., a doorway). Even though

the incidence is higher during the OFF-state, it also appears in the ON-state. The phenomenon is more frequently observed in later stages of the disease (17).

To summarize, various complications develop with disease progression. Some truly bothersome and some that are not always recognized. The impact of these motor complications on Quality of Life (QoL) has previously been studied, indicating a substantial negative effect (18), probably also when the complications are not recognized. An important part in the management of motor complications is optimizing the patient's medication scheme based on which medicines are used, treatment response, duration of action, and therapeutic window (13). Thus, mapping and understanding patients' motor complications to manage them, becomes an important part of routine care in patients with PD.

LIMITATIONS OF PATIENT DIARIES

The golden standard to evaluate motor fluctuations, both in clinical practice and clinical trials, has for a long time been different patient diaries. After proper training patients are asked to evaluate their motor state, for instance, classify whether they are *OFF*, *ON*, or *ON with dyskinesias* once every half hour for some days. However, these often-paper diaries suffer from several limitations (19). To begin with, studies argue that the level of compliance as measured as diary entries within target time is notably low (20). Furthermore, recall bias, hoarding (several entries filled out later) and diary fatigue occur. Equally important is the problem following alterations in motor status within a particular diary entry (19). Moreover, a sufficient observation period is needed, and a period of two days may be too short to recognize patterns (21). Despite this, paper diaries are still considered acceptable because it lowers the risk of physician bias and interpretation, as well as giving more rigorous information compared to the medical history obtained by a physician (19). In conclusion, there is a need for better alternatives. Wearable sensors, if they are sufficiently correct and validated, would be a great opportunity for replacing paper diaries as a golden standard in quantifying motor symptoms.

WEARABLE SENSORS

There has been a growing interest during the past decades in technology-based sensor systems assisting in the assessment of clinical manifestations of Parkinson's disease, demonstrated in a systematic review of articles from 2005-2015 (22). On the other hand, until now, very few studies have primarily investigated the acceptability among PD patients of wearing these sensors in everyday life. In a study from 2016, the acceptability of wearing bilateral wrist sensors for one week was studied, demonstrating a high degree of willingness in wearing sensors at home (94%) and in public (85%). Additionally, only one of the thirty-four participants (3%) opposed the statement of rather using a sensor than filling out patient diaries (23).

In this current study, we are interested in evaluating two different brands, each followed by an introduction below.

PARKINSON'S KINETIGRAPH (PKG)

Parkinson's Kinetigraph (PKG) is a wrist-worn watch-like device developed by Global Kinetics Corporation in Melbourne, Australia (see ***Figure 2***). It weighs 35 grams and consists of a 3-axis accelerometer. The device is worn on the most affected side continuously for approximately one week, and measurements are summarized in a report. Bradykinesia Score (BKS) and Dyskinesia Score (DKS) are calculated for every 2 minutes epochs using algorithms based on acceleration variables, and visualized on a time chart over the day (24). The correlation between the PKG report and patient diaries has been studied, indicating a significant correlation when looking over the whole day. However, when comparing hour for hour the relationship was poorer. The poorer relationship could be explained either by an actual disagreement or possibly because of the continuous recording of the PKG while patient diaries are filled in more seldom and suffer from recall bias and diary fatigue (25). The BKS and DKS also correlate against established rating scales such as the Unified Parkinson's Disease Rating Scale (UPDRS)

and Abnormal Involuntary Movement Scale (AIMS) (24). The UPDRS is a clinical rating scale for PD, nowadays revised by the Movement Disorder Society (MDS) into a newer version (MDS-UPDRS). MDS-UPDRS consists of four parts, “non-motor experiences of daily living” (part I), “motor experiences of daily living” (part II), “motor examination” (part III), and “motor complications” (part IV). Each part consists of several questions, rated on a 0-4 ordinal scale based on the severity (26). Potential treatment targets for BKS and DKS have been proposed by a movement disorder specialist panel, which are meant to assist the treating physician in his decision-making (27). Moreover, the PKG report quantifies the percent of the time that tremor was present (PTT), where a value of 1.0 % or higher indicates clinical meaningful tremor (28) and proportion of time immobile (PTI) which for instance can be used as a measure of daytime sleep (29).

Figure 2. *Parkinson’s Kinetigraph (PKG). (Author’s picture)*

A blinded, controlled trial of the use of PKG in the management of patients with PD has recently been completed and published. Physicians in one group had access to patients’ PKG reports with targets for BKS, while physicians in the other group clinically assessed the patients conventionally. If needed, changes in therapy were made between baseline and follow-up. The study compared outcomes such as improvements on the MDS-UPDRS total score, as well as improvements on the MDS-UPDRS part III (motor examination). The group of patients where the physician’s management was aided by PKG-recordings showed significantly better improvements (30).

STAT-ON

The STAT-ON sensor is a waist-worn single sensor commercialized by Sense4Care in Barcelona, Spain (see ***Figure 3***). STAT-ON consists of a device with an inertial sensor (3-axis accelerometer), worn in a neoprene belt with the device positioned just above the left iliac crest (31). The algorithms for processing data generated by the sensor are based on an analysis of the power spectra of the patient's gait. In general, the algorithm first detects when the patient starts walking. Subsequently, strides are recorded regarding the power spectra of the acceleration measurements which depicts the patient's gait fluidity. Before analyzing, the first two and last two steps in each walking bout are removed to avoid artifacts by gait initiation and finalization. Finally, the average stride fluidity provides an output for each 10-min epoch, resulting in the presence or absence in each epoch of bradykinetic gait or dyskinesia respectively (32). Since the algorithm is based on analyzing gait, the patient must be able to walk independently. If the patient is unable to walk, no data on motor status is provided.

Figure 3. *STAT-ON sensor with neoprene belt. (Author's picture)*

The capability of detecting motor states (on/off) have been compared to patient diaries, indicating a high specificity and sensitivity (both > 90%) in a study by the shareholders of Sense4Care (31), later validated by the same researchers in other articles (32, 33). Although these findings may be somewhat limited by the comparison with patient diaries, few study participants, and a limited measurement period of 1-3 days, the results indicate that STAT-ON

can be used to measure motor fluctuations in PD patients. The correlation between the STAT-ON algorithm output and the motor examination of UPDRS (part III) has also been studied, suggesting a good correlation (Spearman's rho = –0.73) when compared against the gait-specific part (item 22) of the UPDRS part III, although only a moderate overall correlation (Spearman's rho = –0.56) of UPDRS part III was seen (34). Furthermore, STAT-ON also detects and quantifies episodes of FOG (35), something not done by the PKG. On the other hand, STAT-ON does not measure tremor or sleep-like immobility, which is done by the PKG.

The clinical utility of STAT-ON has been investigated in a newly published study based on surveys from 27 Spanish neurologists, which for three months had the possibility of using the device in their clinical setting. Seventy-four percent of the neurologists found STAT-ON to be "quite" or "very" useful, and a majority (70%) considered it superior to patient diaries (36).

To our knowledge, no studies are made comparing these two sensors, neither in terms of correlation nor in terms of usability.

AIM

This study aims to compare the agreement between two commercial sensor systems for monitoring PD, their usability from the patients' view as well as the possible influence of management on PD. Two systems are used in this study, PKG and STAT-ON. We hypothesize that there will be different evaluations of patients' motor fluctuations between sensor systems compared to less experienced physicians and patients' medical records. Additional information from the sensors might indicate a potential use in routine care of patients with PD.

This concludes into the following research questions: Do the sensors, after blinded evaluations by MDS-specialists, give an equivalent assessment of motor symptoms? Do the evaluations from the objective measurements differ from the clinical assessment by a resident physician in neurology? Do the evaluations from sensors and the resident physician agree with

patients' medical records? Furthermore, we aim to describe the usability of each sensor, respectively, and to correlate the evaluations of motor symptoms against established rating scales for PD.

MATERIAL AND METHODS

POPULATION

A study population of 10 patients with Parkinson's disease was obtained from the clinic of neurology at Sahlgrenska University Hospital. Since the PKG sensor has been available at the hospital for some years, all subjects had been measured at earlier time points with the PKG sensor. To get a broad variety of motor symptoms and fluctuations, the study population was obtained by including patients from each of three different categories: patients with a good correlation between previous PKG and symptom history, patients with a history of symptom fluctuations not detected by the previous PKG and lastly, patients who are on the waiting list for advanced therapy (e.g., deep brain stimulation, apomorphine pump). When on the waiting list for advanced therapy, considerable fluctuations are expected.

DATA COLLECTION

Two sensor systems were used in this study, namely PKG and STAT-ON. The measurements were carried out for one week using the two sensor systems simultaneously. PKG sensors were programmed to monitor the patients during six consecutive days, throughout day and night (approx. 144 hours), while STAT-ON sensors were worn during daytime. The patients were seen at the beginning and end of the measurement period (see ***Figure 4*** for timeline of study design). During the first visit baseline characteristics including age, years of disease, treatment, and Hoehn & Yahr (H&Y) classification were collected. The H&Y scale can be used as a measure of disease progression (37). Education on how to use the sensors was given. At the end of the week of measurement, the patients met with a resident physician, a physician

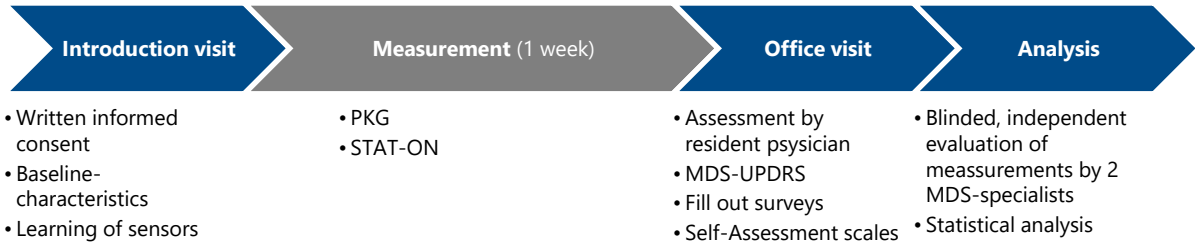

Figure 4. *Timeline of study design.*
PKG = Parkinson's Kinetigraph. UPDRS = Unified Parkinson's Disease Rating Scale. MDS = Movement Disorder Society. The resident physician works in the field of neurology.

independent from the research team, whose assignment was to take the patients' history of motor symptoms and fluctuations with a time limit of fifteen minutes. The patient's symptoms and fluctuations were classified in different categories ranging from mostly OFF to mostly dyskinetic (see ***Table 1***). The presence of gait disturbances, falls and sleep disturbances were also examined, as well as giving a rough estimate on the duration of action by single doses of medication at daytime. Considering the patient's current treatment plan, the resident physician also had to decide on whether he considered that a change in therapy was warranted.

Table 1. *Categories for evaluation of patient's motor fluctuations. For the complete examination form, see Appendix B – Assessment forms (resident physician / objective measurement report).*

Category	Explanation
Mostly OFF	*Poor effect of treatment, undertreated*
Stable and sufficient effect	*Generally, well treated. Possibly with morning symptoms*
Regular OFF-fluctuations	*i.e. predictable wearing-off, well treated in between*
Irregular or sporadic OFF periods	*i.e. unpredictable wearing-off, "delayed on" or "dose failure"*
Regular ON-OFF	*OFF and ON with dyskinesias*
Unpredictable ON-OFF	*Can include biphasic dyskinesias*
Mostly dyskinetic	*Overtreated with few and short off-periods*
Not assessable	*i.e., the sensor was worn incorrectly or insufficient time; the patient is unable to describe symptoms.*

Furthermore, the patients filled out a usability survey for each sensor system individually. The surveys consisted of Likert rating scale questions with the possibility of leaving an optional comment below each question. Lastly, the surveys included an open-ended question if patients wished to make further comments about their experience. The full survey can be reviewed in ***Appendix A*** – Usability survey.

Also, three different PD symptom self-assessment scales (Patient-Reported Outcomes in Parkinson's Disease (PRO-PD) (38), Wearing-off questionnaire (WOQ) 19 (39), and Parkinson's Disease Questionnaire 8 (PDQ-8) (40)) were filled out by the patients. The PD symptom self-assessment scales were used in the study as a measure of the study populations' disease burden. Moreover, the patients' disease burden was rated using the MDS-UPDRS by a trained rater in the research team (research team consisting of the author, supervisor, and a research nurse). The MDS-UPDRS also includes a self-estimation of time in OFF or with dyskinesia during the week by patients (part IV). This self-estimation was collected after the interview by the resident physician to avoid bias.

Every patient generates two different objective measurement reports, one from PKG and STAT-ON, respectively. Both reports were examined independently by two trained specialists in Movement Disorders (MDS-specialists), coded R1 and R2. In other words, reports from the same patient were evaluated twice, thus amounting to twenty report evaluations for each sensor. Before examination, reports were blinded and labeled with a unique code, preventing the examiners from identifying patients or influence each other. Using recent historic data in patients' medical records, the research team categorized the patients from mostly OFF to mostly dyskinetic as well. The reason for categorizing patients' motor symptoms by the MDS-specialists and the resident physician was to be able to test for agreement since the sensor systems and the resident physician do not generate the same outcome variables. These categories are also canonical descriptions of treatment scenarios that should result in different treatment decisions.

STATISTICAL METHODS

The statistical analysis was performed using SPSS V.27.0 (IBM Corp, Armonk, NY). Descriptive statistics with mean, standard deviation, median, range, number, and frequencies, was used to describe the baseline characteristics. Calculations of the agreement between raters

were accomplished by using weighted kappa with quadratic weights. Kappa statistics can be used to look for the proportion of agreement between raters, corrected for chance, providing a value between -1 (perfectly disagreement) and 1 (perfectly agreement). The weighting of kappa takes the seriousness of disagreement into account (41). In this study, values of kappa between 0.4-0.6 were considered a moderate agreement, values between 0.6-0.8 were considered a good agreement, and lastly, values above 0.8 were interpreted as almost perfect agreement. P-values of < 0.05 were considered significant. At first, sensors and the resident physician were tested for agreement towards the categorization based on all available historic data in patients' medical records. Subsequently, specific comparisons were conducted between raters of PKG and STAT-ON, PKG and physician's interview, and STAT-ON and physician's interview. Reports denoted by one rater as not assessable were excluded before the analysis of agreement in that specific comparison. Categorizations made by the different raters are also tested for correlation towards MDS-UPDRS total score. In addition, patient-reported OFF-time in the MDS-UPDRS section IV was tested for correlation towards STAT-ON monitored OFF-time. Correlation analysis was conducted using Spearman's correlation coefficient.

The estimation of duration of action by single doses of medication was presented in minutes for all patients and raters individually, as well as in mean for the raters. To test the potential statistical differences in the estimation of duration of action between sensors and between sensors and the resident physician, Wilcoxon signed-rank test was used. For the usability survey, non-parametric tests like Wilcoxon signed-rank test and binomial test were used, since the survey answers have an ordinal scale, and the lengths of each step cannot be assumed equal. Graphical illustrations were made using GraphPad Prism V.9.0 (GraphPad Software, San Diego, CA).

ETHICS

This study has been approved by the Regional Ethical Review Board in Gothenburg (application 507-15). Written informed consent was provided before inclusion in the study. The study was completely voluntary and the choice of not participating or drop out of the study did not affect the patient's treatment. There were no identified risks of wearing the sensor systems. Due to the COVID-19 pandemic, all patient-doctor contact was done outside office hours so that the study participants only met with the research team using appropriate protective measures like visors and face masks.

RESULTS

A total of 10 patients completed the study, eight men and two women. Due to the COVID-19 pandemic resurgence, all the 15 planned patients could not be enrolled. The mean age was 70.6 years (SD = 6.6 years) and the mean duration since onset of PD was 8.0 years (SD = 4.0 years). Further, the mean MDS-UPDRS score among patients was 50 (SD = 33, median = 50, IQR = 61). Most patients had an H&Y score of 1-3, whereas one patient was classified as H&Y 5 (and therefore not appropriate for assessment with STAT-ON). For full baseline characteristics, see ***Table 2***. The average score in the three different PD symptom self-assessment scales (PRO-PD, WOQ, and PDQ-8) can be found at the bottom of the same table.

The mean time monitored with PKG was a little less than the 144 hours programmed. The time off wrist for PKG was on average approximated to less than 10 hours during the entire measurement period. However, most patients had minimal time off wrist (< 4 hours), while three patients had higher (8.5, 21, and 48 hours respectively). The patient with the highest time off wrist did not sleep with the PKG sensor on. STAT-ON sensors were only used during the daytime. The mean time monitored with STAT-ON was 69 hours (SD = 22 hours). Most

patients were monitored with STAT-ON for 54-95 hours, however, one patient had a limited time monitored of 20 hours.

Table 2. *Baseline characteristics of patients in the study.*

Characteristic	N (%)	Mean ± SD	Min–Max
Age (y)		70.6 ± 6.6	58–78
Gender			
Male	8 (80%)		
Female	2 (20%)		
Duration of PD (y)		8.0 ± 4.0	2.9–13.9
MDS-UPDRS		50 ± 33	11–103
Section I		10 ± 8	0–23
Section II		12 ± 12	0–32
Section III		21 ± 12	6–44
Section IV		7 ± 5	0–16
Levodopa equivalent daily dose (mg)		1437 ± 1178	105–3858
H&Y Scale		2.2 ± 1.3	1–5
1. Unilateral disease	3 (30%)		
2. Bilateral disease, without impairment of balance	2 (20%)		
3. Mild to moderate bilateral disease, some postural instability, physically independent	4 (40%)		
4. Severe disability, still able to walk or stand unassisted	0 (0%)		
5. Wheelchair-bound or bedridden unless aided	1 (10%)		
PRO-PD		778 ± 630	130-1740
WOQ			
Nº symptoms experienced		8 ± 5	1-16
Nº symptoms improved after the next dose		4 ± 3	0-10
PDQ-8 (summary index)		20.0 ± 15.4	0-40.6

N = Number, SD = Standard deviation, PD = Parkinson's Disease, MDS-UPDRS = Movement Disorder Society - Unified Parkinson's Disease Rating Scale, H&Y scale = Hoehn and Yahr scale, PRO-PD = Patient Reported Outcomes in Parkinson's Disease, WOQ = Wearing Off Questionnaire, PDQ-8 = Parkinson's Disease Questionnaire 8.

ANALYSIS OF AGREEMENT

Excerpts from the PKG and STAT-ON reports can be seen in ***Figure 5*** and ***Figure 6***, which illustrate the measurement of the same individual. The resident physician found that they would perform a change in therapy in six patients (60%).

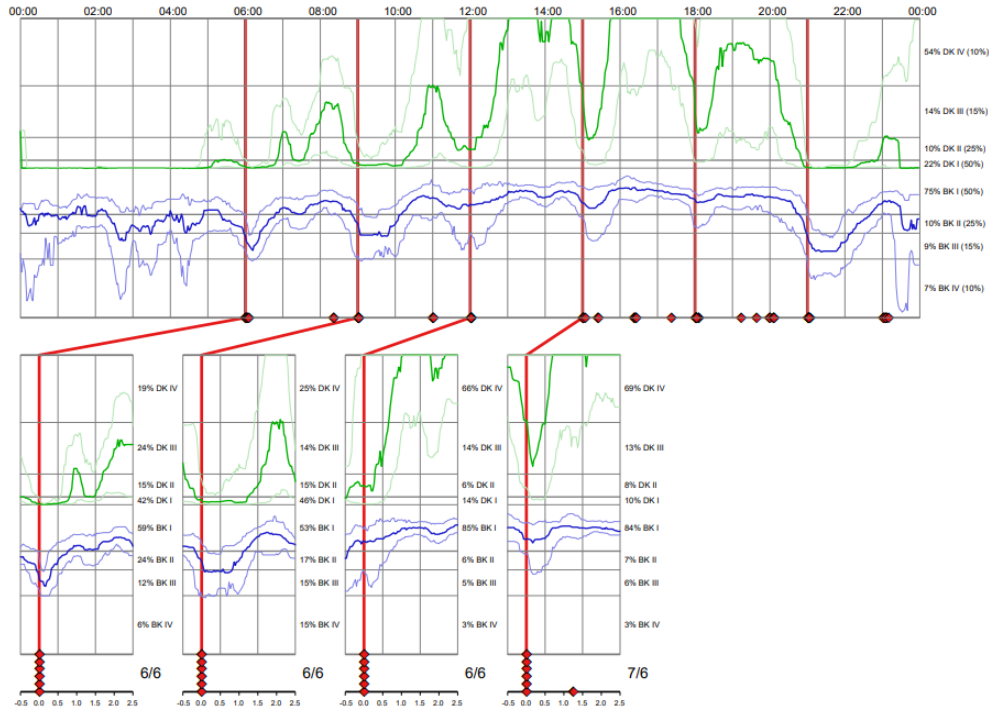

Figure 5. *Example from the PKG report. Same patient in figure 5 and 6.*
Green line represents weekly mean of Dyskinesia Score throughout the day (higher value = more dyskinesia), where blue line represents Bradykinesia Score (lower value = more bradykinesia). Red vertical lines illustrate medication intake.

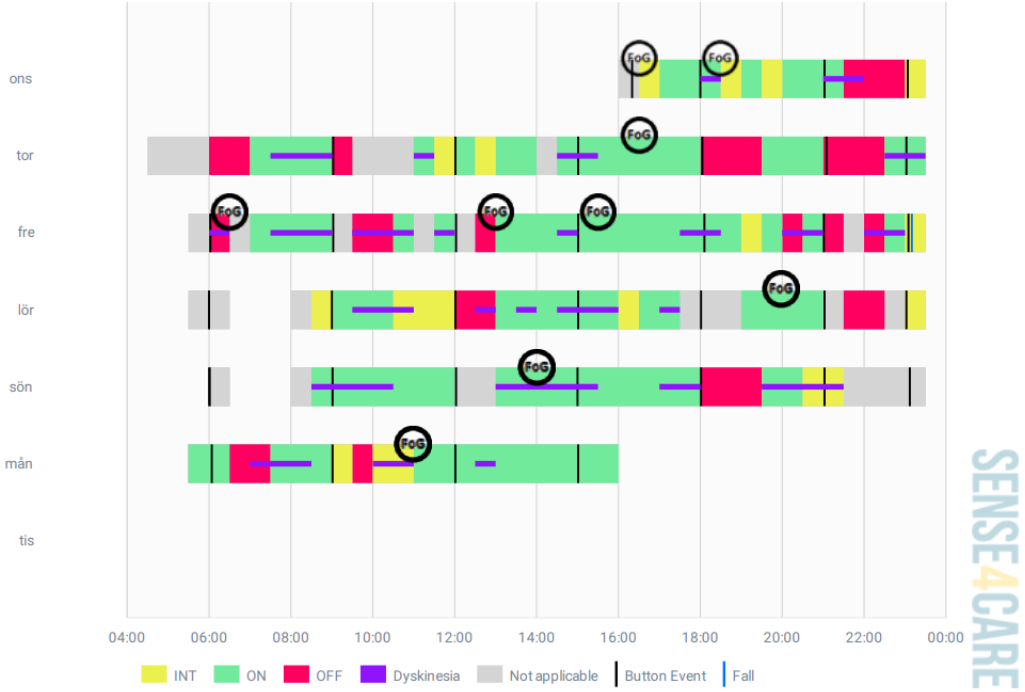

Figure 6. *Example from the STAT-ON report. Same patient in figure 5 and 6.*
Green areas illustrate ON periods, red OFF periods, yellow intermediate, and grey equals not applicable. Purple horizontal lines represent presence of dyskinesia. FoG = Freezing of Gait. Black vertical lines indicate button events (patients were told to press the button at medication intake).

Correlation analysis between the categories of assessing patients' motor fluctuations used in this study, with the established rating scale MDS-UPDRS is illustrated in ***Figure 7***. The category "Mostly OFF" is excluded from correlation analysis since being "Mostly OFF" can be expected to generate higher scores on MDS-UPDRS than if the patient is stable with decent treatment effect. There was a significant correlation between the STAT-ON evaluations (Spearman's rho = 0.86) and the resident physician assessment (Spearman's rho = 0.74) towards the MDS-UPDRS total score. On the other hand, the correlation between PKG evaluations and the total score of MDS-UPDRS was poor (Spearman's rho = 0.04). However, 60% and 40% of patients were classified as "Mostly OFF" by the raters of PKG, respectively. Consequently, many PKG evaluations were excluded from this correlation analysis.

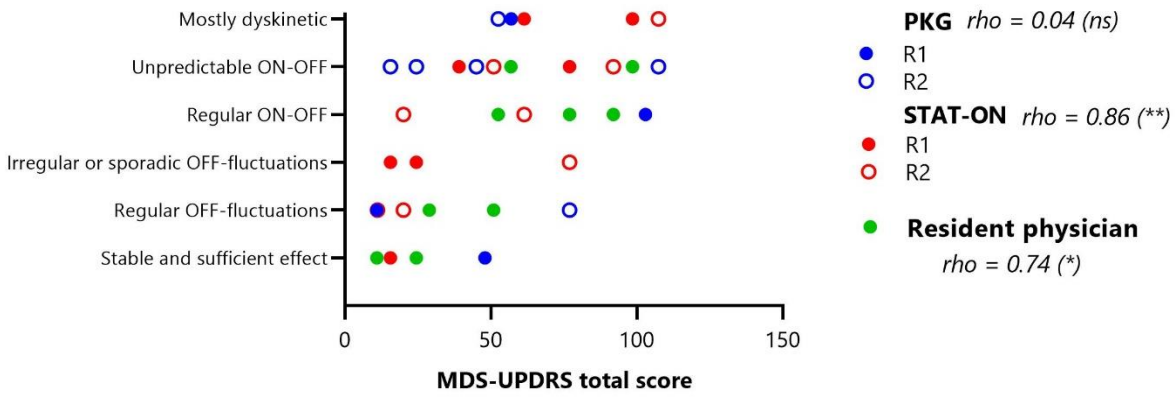

Figure 7. *Correlation analysis of categorization of patients' motor fluctuations towards total score of MDS-UPDRS. Each dot represents one evaluation of the patient's category of motor symptoms, divided by different colors to represent which rater conducted the assessment. Rating on the MDS-UPDRS was conducted by the research team. Spearman's correlation coefficient (rho) is used to describe correlation, p < 0.05 is considered significant. A significant correlation is seen for STAT-ON and the resident physician. P < 0.05 = (*), P < 0.01 = (**), ns = not significant. PKG = Parkinson's Kinetigraph. R1 = Rater 1, R2 = Rater 2. MDS = Movement Disorder Society, UPDRS = Unified Parkinson's Disease Ratina Scale.*

COMPARISON WITH MEDICAL RECORD

First, agreement is tested toward the categorization based on patients' medical record. This categorization's agreement with sensors (PKG and STAT-ON) and the resident physician is presented in ***Table 3***. All PKG reports were assessable, while one STAT-ON report was deemed not assessable (the same specific report for both raters). The number of categorizations analyzed is presented in ***Tables 3-5*** in the column on the far right (n = number of pairs analyzed). The categorization from the resident physician had a good agreement with patients' medical records (kappa = 0.747), also illustrated in a crosstabulation (see ***Table 4***). For STAT-ON, R2 has a good agreement with medical records (kappa = 0.673). However, there was no evidence for an agreement between STAT-ON and medical records for R1. For PKG, none of the raters provided a significant statistical agreement with medical records, even though R1 had a moderate agreement close to significant. When comparing the information provided by the sensors with what is already known in the medical records, PKG provided new information in five cases (50%). STAT-ON provided new information in four cases (40%).

Table 3. *Rater agreement with patients' medical records.*
Agreement between raters is analyzed with weighted kappa. A statistically significant agreement for categorization of patients' motor symptoms is seen for STAT-ON (R2) and the resident physician.

			Agreement with medical record			
Question	**Rater**		**Weighted kappa [a]**	**95% CI**	**Sig.**	**n**
Categorization of motor symptoms [b]	*PKG*	R1	0.495	0.044-0.946	0.067	10
		R2	0.280	-0.276 to 0.837	0.365	10
	STAT-ON	R1	0.308	-0.309 to 0.924	0.315	9
		R2	0.673	0.421-0.925	**0.023**	9
	Resident physician		0.747	0.364-1.129	**0.015**	10

n = number of pairs analyzed, R1 = MDS-specialist 1, R2 = MDS-specialist 2
[a] *Quadratic weights*
[b] *Categorization according to Table 1*

Table 4. *Crosstabulation of categorization of motor symptoms between resident physician and medical record. If perfect agreement between raters, all assessments will follow the grey boxes in a diagonal line. Numbers in the crosstabulation represent number of patients. In this crosstabulation, two patients were assessed as "stable and sufficient effect" by both the resident physician and the medical record. However, one patient was assessed by the resident physician as "regular ON-OFF" while according to the medical record the patient is categorized as "mostly OFF". Statistical agreement with the medical record for the resident physician is good (kappa = 0.747, p = 0.015).*

		Resident physician						
	Category*	Mostly OFF	Stable and sufficient effect	Regular OFF-fluctuations	Irregular or sporadic OFF-periods	Regular ON-OFF	Unpredictable ON-OFF	Mostly dyskinetic
Medical record	Mostly OFF	**1**	-	-	-	**1**	-	-
	Stable and sufficient effect	-	**2**	**1**	-	-	-	-
	Regular OFF-fluctuations	-	-	**1**	-	-	-	-
	Irregular or sporadic OFF-periods	-	-	-	-	-	-	-
	Regular ON-OFF	-	-	-	-	-	-	-
	Unpredictable ON-OFF	-	-	-	-	**2**	**2**	-
	Mostly dyskinetic	-	-	-	-	-	-	-

** Category of motor symptoms according to table 1.*

COMPARISON BETWEEN PHYSICIAN AND PKG

The analysis of agreement between the PKG sensor and the resident physician is presented in ***Table 5***. There was no significant agreement in the categorization of motor symptoms, neither among R1 or R2. The PKG sensor is unable to detect FOG and falls, while the STAT-ON sensor is unable to detect sleep disturbances. Therefore, analysis of agreement of these three aspects cannot be done for both sensors and between the sensors. Regarding sleep disturbances, R1 has a significant agreement with the resident physician (kappa = 0.630), however no significant agreement for R2. The number of reports classified as not assessable for PKG is between zero and one.

Table 5. *Sensor evaluations vs. resident physician.*
Agreement is analyzed with weighted kappa. A statistically significant agreement is seen of categorization of patients' motor symptoms for STAT-ON (R2), freezing of gait for STAT-ON (R1), and sleep disturbances for PKG (R1).

			Agreement with resident physician			
Question	**Sensor**	**Rater**	**Weighted kappa [a]**	**95% CI**	**Sig.**	**n**
Categorization of motor symptoms [b]	*PKG*	R1	0.317	-0.038 to 0.672	0.098	10
		R2	0.298	-0.223 to 0.819	0.314	10
	STAT-ON	R1	0.585	0.175-0.995	0.065	9
		R2	0.783	0.627-0.939	**0.014**	9
Freezing of Gait? [c]	*STAT-ON*	R1	0.474	0.154-0.794	**0.048**	8
		R2	0.259	-0.066 to 0.583	0.263	9
Falls? [d]	*STAT-ON*	R1	-0.500	-0.832 to -0.168	0.128	8
		R2	0.129	-0.679 to 0.937	0.688	9
Sleep disturbances? [c]	*PKG*	R1	0.630	0.388-0.872	**0.020**	9
		R2	0.471	0.089-0.852	0.140	9

n = number of pairs analyzed, R1 = MDS-specialist 1, R2 = MDS-specialist 2
[a] *Quadratic weights*
[b] *Categorization according to Table 1*
[c] *Assessed as either "no", "yes mild" or "yes severe"*
[d] *Assessed as either "no", "yes seldom" or "yes severe"*

The estimation of duration of action by a single dose of levodopa at daytime for the resident physician and raters of the PKG report is presented in ***Table 7***. No significant differences are seen between the resident physician and any of the raters of PKG reports. When comparing specific individuals, the difference in assessed duration of action is within 60 minutes for most patients. However, three patients were assessed very differently by the resident physician with an inconsistency of between 120-480 minutes.

COMPARISON BETWEEN PHYSICIAN AND STAT-ON

The agreement between the STAT-ON sensor and the resident physician is shown in ***Table 5***. The agreement of categorization of motor symptoms between R2 and the resident physician was good (kappa = 0.783). In addition, there was a potentially moderate agreement between R1 and the resident physician as well (kappa = 0.585), however, kappa was statistically significant only for R2. Assessment of FOG had a moderate agreement for R1 (kappa = 0.474), although

there was no significant agreement for R2. There was no significant agreement considering the assessment of falls. It was more common that R1 and R2 assessed problems with falls as worse compared to the assessment by the resident physician. For STAT-ON, one to two reports were denoted as not assessable. The estimated duration of action for the raters of STAT-ON is presented in ***Table 7***. No significant differences in the estimated duration of action were seen between the resident physician and any of the raters of STAT-ON reports.

In addition, ***Figure 8*** illustrates a comparison between the percent of time classified as OFF by STAT-ON with the patient-reported OFF-time. No correlation was seen regarding time in OFF (Spearman's rho = 0.02, two patients were excluded from analysis since the STAT-ON sensor could not provide an estimation).

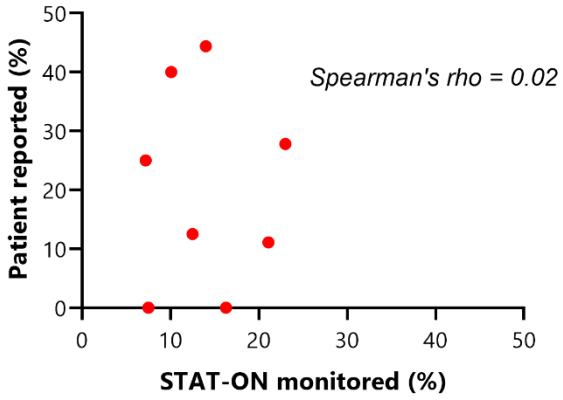

Figure 8. *Comparison of OFF-time.*
Correlation analysis is conducted using Spearman's rho. Each red dot represents one patient. As the figure illustrates, no correlation between patient-reported and STAT-ON monitored OFF-time is seen. OFF-time represents % of time OFF during hours awake.

COMPARISON BETWEEN SENSORS

The agreement of evaluation between the two sensor systems regarding the categorization of patients' motor symptoms is presented in ***Table 6.*** Evaluations of R1 for PKG are compared to R1 for STAT-ON and the same for R2. Kappa values for each rater between sensors are 0.431 and 0.452 respectively, however, neither of them is statistically significant. In other words, no significant agreement between the different sensor systems is seen in this study.

Table 6. *PKG vs STAT-ON evaluations.*
Agreement is analyzed with weighted kappa. No statistically significant agreement of categorization of patients' motor symptoms is seen between the sensors.

		PKG sensor vs. STAT-ON sensor			
Question	**Rater**	**Weighted kappa [a]**	**95% CI**	**Sig.**	**n**
Categorization of motor symptoms [b]	R1	0.431	0.037-0.825	0.057	9
	R2	0.452	-0.086 to 0.990	0.150	9

n = number of pairs analyzed, R1 = MDS-specialist 1, R2 = MDS-specialist 2
[a] Quadratic weights
[b] Categorization according to Table 1

The estimated duration of action presented in ***Table 7***, found no significant differences between raters of the sensors. The differences between the two sensors were for all patients within sixty minutes.

Table 7. *Estimated duration of action by single doses of medication at daytime. Values for each estimation by the resident physician and raters of the two sensors are presented in minutes. No significant differences are seen between any of the ratings. Although, large individual differences are seen between ratings of some patients (e.g., patient 8-10) where the resident physician differs from sensors.*

		PKG		STAT-ON	
Patient	**Resident physician**	**R1**	**R2**	**R1**	**R2**
1	60	90	90	120	60
2	120	180	120	120	120
3	45	90	90	60	120
4	75	60	60	*n.a*	*n.a*
5	180	120	120	60	180
6	*n.a*	120	*n.a*	60	60
7	180	120	120	180	120
8	360	120	90	120	*n.a*
9	0	120	120	120	180
10	540	60	*n.a*	60	90
Mean	173	108	101	100	116

n.a = not assessable
R1 = MDS-specialist 1
R2 = MDS-specialist 2

USABILITY

All ten individuals returned fully answered questionnaires. When asked whether they rather use a wearable sensor than filling out patient diaries, after giving a brief introduction about the sensors' possibilities and limitations, the majority (90%, CI = 53-91%) agreed or strongly agreed to rather use a sensor (one-sample Wilcoxon signed-rank test, p = 0.005). Further, if the two sensors gave equal information, seven patients (70%, CI 33-82%) would prefer PKG, while three patients (30%, CI 4-53%) would prefer STAT-ON, however, due to the small sample size, no significant difference was seen (binomial test, p = 0.344). The next section of the questionnaire required the patients to rate the two sensors regarding different aspects on a one-to-five Likert rating scale. The median rating score for each question is presented in ***Table 8***.

In the same table, the median difference in patients' ratings of sensors for each question is reported. Question 6 regarding charging of the sensors was excluded from analysis since very few patients needed to charge them. The difference in patients' ratings between sensors can range from -4.0 (best score for PKG combined with the worst score for STAT-ON) to 4.0 (worst score for PKG combined with the best score for STAT-ON). Both the median for each question as well as the overall mean of patients' mean rating score for all questions on the one-to-five rating scale are low for both sensors (PKG = 1.67 ± 0.56, STAT-ON = 2.01 ± 1.10, lower is better), and there were no significant differences between the sensors (Wilcoxon signed-rank test, p = 0.23), see ***Table 9*** and ***Figure 9***.

Table 8. *Usability survey. Eight rating scale questions from 1-5 (lower better). The median rating for all questions is between 1-2. Question 1 (STAT-ON) and questions 3-4 (both sensors) had the highest median rating. No significant difference is seen between sensors on any of the questions. Question 6, regarding charging of the sensors, was excluded.*

			PKG and STAT-ON rating			***Difference in patient's ratings between PKG and STAT-ON***			
Question	**Sensor**	**N**	**Median**	**Min**	**Max**	**Median**	**Min**	**Max**	**Sig.***
Q1: How easy was it taking the sensor on? [a]	PKG	10	1	1	3	-0.5	-2.0	0.0	0.06
	STAT-ON	10	2	1	5				
Q2: How easy was it taking the sensor off? [a]	PKG	10	1	1	3	0.0	-2.0	0.0	0.25
	STAT-ON	10	1	1	5				
Q3: How did you experience the sensor system regarding comfort? [b]	PKG	10	2	1	3	0.0	-3.0	1.0	0.38
	STAT-ON	10	2	1	5				
Q4: What are your opinions about the sensor's shape and design? [c]	PKG	10	2	1	4	0.0	-3.0	2.0	0.81
	STAT-ON	10	2	1	5				
Q5: How easy was it learning how to use the sensor? [a]	PKG	10	1	1	4	0.0	-1.0	2.0	1.00
	STAT-ON	10	1	1	3				
Q7: What is your experience in using the sensor in public? [d]	PKG	10	1	1	2	0.0	-1.0	1.0	0.63
	STAT-ON	10	1	1	3				
Q8: Does the sensor limit you in your everyday activities? [e]	PKG	10	1.5	1	3	0.0	-1.0	1.0	1.00
	STAT-ON	10	1	1	4				

[a] *Rating scale from 1 (very easy) to 5 (very difficult)*

[b] *Rating scale from 1 (very good) to 5 (very bad)*

[c] *Rating scale from 1 (very positive) to 5 (very negative)*

[d] *Rating scale from 1 (very comfortable) to 5 (very uncomfortable)*

[e] *Rating scale from 1 (no, not at all) to 5 (yes, all the time)*

** Wilcoxon Signed Rank Test*

Table 9. *Overall usability from patients' view.*
The mean value can range between 1.00 (best score) to 5.00 (worst score). The mean rating score for both sensors is low.

	Sensor	**N**	**Mean ± SD**	**Min**	**Max**	**Sig.***
Patient's mean rating score [a]	PKG	10	1.67 ± 0.56	1.00	2.57	0.23
	STAT-ON	10	2.01 ± 1.10	1.00	4.00	

[a] Total sum of all answered questions (q*uestion 6 excluded) divided by the number of questions.*

** Wilcoxon Signed Rank Test*

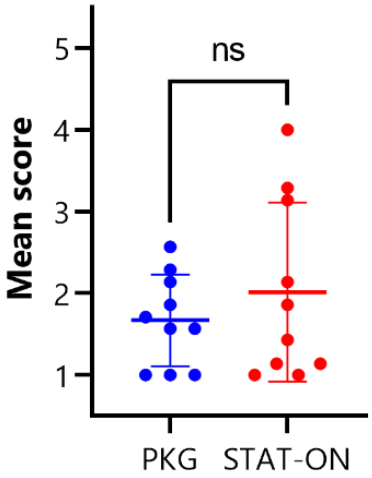

Figure 9. *Overall usability from patients' view.*
The mean value can range between 1.00 (best score) to 5.00 (worst score). Each dot represents one patient's rating for the sensor (blue = PKG, red = STAT-ON). The thick horizontal line represents the mean and the thin one's standard deviation. PKG = Parkinson's Kinetigraph, ns = not significant.

In the final part of the questionnaire, patients had the possibility of leaving open-ended answers of their experience of using the sensors. Two patients (20%) complained about the PKG watch band as being clumsy and oversized for a small wrist. As for the STAT-ON, six patients (60%) had complaints regarding the waist strap. It was explained as not sitting secure and often getting out of position. One participant even expressed fear of dropping it when visiting the toilet. Further, due to the sensor positioning, one of the patients also found it difficult to press the event button.

DISCUSSION

The present study aimed to compare the agreement between PKG and STAT-ON, as well as the agreement between the sensors, a resident physician's assessment, and the patients' medical records. Furthermore, this study also set out the aim to assess the usability of the two sensors from the patients' view through a survey.

DISCUSSION OF RESULTS

The first research question was if the sensors gave an equal categorization of patients' motor symptoms. In this study, we found no statistically significant agreement between PKG and STAT-ON. It is possible that with a larger sample size, a statistically significant moderate agreement could have been seen. Unfortunately, no previous studies have been made directly comparing these two sensors and our results can thus not be compared with earlier studies. Therefore, further studying with larger sample sizes is needed to get more evidence before making more conclusions about differences between PKG and STAT-ON.

The next research question was whether the evaluation of the sensors' objective measurement reports differs from the clinical assessment by a resident physician. Interestingly, there is a potentially moderate to good agreement between STAT-ON and the resident physician. In comparison, this study found no statistically significant agreement between PKG and the resident physician. Therefore, one could argue that the information presented by STAT-ON is more relevant than PKG. On the other hand, wearing the STAT-ON sensor for several days and it only presents us with the information a resident physician can gather during fifteen minutes of talking with the patient, raises thoughts of the sensor's usefulness. Consequently, another question that emerges from this is: What depicts the reality most accurately? Categorization based on all available information in the patients' medical records can be considered the best available data, provided that the information is not too old. Even this

information can however be questioned. Interestingly, the resident physician's high agreement with medical records speaks for the strengths and importance of the patient-doctor interaction. Still, medical records are to a great extent consisting of evaluations made by physicians, thus an agreement is very likely to be seen. The resident physician's ability to capture patients' symptom fluctuations over the whole day, is also affected by patients' recall bias. Besides this, the only statistically significant agreement with the medical record is for one of two raters of the STAT-ON report. With our study method, agreement of categorization based on PKG reports and the patients' medical records were not found to be significant. Although, one of the raters' PKG categorizations was close to being significant at the p=0.05 level.

Equally important, what does it mean that sensors evaluate the patients differently from a resident physician? Indeed, if new information shall be presented, it will always equal different information. Although, there are two potential answers to this question. Certainly, the different information may be due to an actual falseness. Equally important is the possibility that it adds useful information to what is already known, therefore providing different information. Although, most previous studies on PKG and STAT-ON are compared to patient diaries since it has for a long time been the golden standard in assessing fluctuations. One previous study on PKG conducted in the USA by Joshi et al. has primarily analyzed the agreement between the PKG sensor and a physician as the frequency of disagreement of symptoms reported (42). In the study, 48% of the objective measurements reported a symptom not being told to the physician. On the contrary, 24% of patients reported a motor symptom not reported by the PKG report. Moreover, another study from the USA by Santiago et al. found that PKG provided additional information to the physician anamnesis in approximately 40% of the cases (43). The findings in our study that PKG provides new different information from the physician, is in line with these previous studies.

Nevertheless, this study was not designed to answer the question of whether the information from the sensors was useful or not. However, because of the small sample size, the research team had the possibility of analyzing deeper into individuals whether the sensors generated new information, and if it could be of potential use. In summary, PKG provided new information to the physician in five out of ten cases and STAT-ON provided new information in four out of ten cases. It is important to bear in mind that new information does not necessarily equal correct information. Some examples from specific cases are discussed below.

One patient was categorized as having stable and sufficient effect of treatment by both the medical record and the resident physician. Despite this, both sensors provided new information that the patient had obvious OFF-fluctuations. In this case, the sensors' information could contribute to a change in the treatment plan, potentially to the patient's benefit. In two other patients, issues with fluctuations and dyskinesia are described in the medical records. This is easily understood by the resident physician when talking with the patients. However, in these two cases, the PKG was unable to detect the fluctuations, rather providing an image of mostly off or a stable situation. On the other hand, STAT-ON was in these cases slightly better in detecting these symptoms. Consequently, the new and different information provided by PKG in this case could be deceptive. Furthermore, there are some cases where the STAT-ON sensor provides new information depicting fluctuations and a lot of questionable time in OFF, which neither the PKG, resident physician or the medical record provide. In these cases, PKG probably presented information more accurately. Even though there are obvious disparities in some cases, there is also an example of a patient with troublesome fluctuations and dyskinesia, which were captured both in the medical record, by the physician, and by both sensors. In conclusion, new and different information from the sensors should be interpreted with some caution since they could both be valuable or potentially misleading.

Some previous articles have investigated the influence of PKG recordings on treating physicians' decisions. Santiago et al. found that the information from PKG recordings influenced the physician to change the patient's treatment plan (i.e., the timing of doses), from the initial plan based on only the physician's anamnesis, in approximately 32% of cases (43). Similar, in a newly published Swedish study, Sundgren et al. demonstrated that PKG contributed to a change in almost one-third (31.8%) of the patients (44). Another study on PKG by Farzanehfar et al. reported a higher frequency of change, over 60% of the cases (45). In summary, these studies argue that there is additional information by PKG that might to a substantial degree influence patients' treatment plans. To the author's knowledge, no similar studies have been conducted primarily investigating the influence of STAT-ON on the treating physician's decisions. Further studying on the impact of STAT-ON on treatment decisions is therefore requested.

Even though information regarding patients' motor fluctuations can be gathered in several different ways, the most important will be if, and which, of the sources of information that contributes to the most favorable outcomes for patients. In the study from Woodrow et al., PKG have shown to be promising with improved treatment results for patients, illustrated by a decline in total MDS-UPDRS score (30), which might suggest that there is valuable information provided by the PKG sensor, not captured in the physician's anamnesis. However, further studies are needed to fully understand the implications of the different information provided by the sensors.

Moving to another aspect, the assessment of falls, we found that there might be an overestimation made by the STAT-ON sensor when compared to the resident physician. This has previously been reported in other studies as well (36). A possible explanation is that artifacts or something in patients' everyday activities are interpreted by the sensors as falls.

In one aspect, the estimation of duration of action by single doses of medication, the agreement between the two sensors was good. For all patients where the raters of sensors were possible to estimate the duration of action, the difference between the two sensors' assessment in minutes was within sixty minutes. In comparison with the agreement towards the resident physician's assessment, some patients were assessed very differently by the physician with up to 120-480 minutes of difference from estimations based on sensors.

Moreover, something worth discussing is the fact that there is a big difference in time monitored during the week since PKG is worn throughout both day and night whereas STAT-ON only is worn during the daytime. The question remains whether this additional time monitored with PKG is needed. To be able to fully answer the question of whether nighttime monitoring adds useful information to the assessment of motor fluctuations, more studies are needed comparing the use of PKG during all-day versus only daytime use.

Turning now to usability. In this study, we conclude that the overall mean scores in the usability survey were notably low for both sensors (lower is better). In addition, the median rating for each question was also low. This indicates that the acceptability of wearing PKG and STAT-ON is potentially high. However, with this small sample size, caution must be applied when interpreting these findings. Nevertheless, our results are in line with previous acceptability studies from 2014 (using a set of five sensors including one on the hip) (46) and 2016 (using a set of two sensors) (23), both with a high willingness in using the sensors. The current study found no differences in acceptability between the sensors from the patients' view. Both sensors had their worst rating scores in the aspect "shape and design", potentially explained by the multiple complaints received regarding the sensors' wrist strap (PKG) and waistband (STAT-ON). An implication of this is the importance of designing a slim and secure holder for the sensors. Currently, the PKG can be perceived as large and clumsy, especially among those with smaller wrists. Developing different sizes of wrist straps could perhaps

slightly reduce this issue. Certainly, technological advances will also minimize the required size for a sensor. As for STAT-ON, the soft waistband, as a holder for the sensor, could easily spin or lose its position. This could be solved either by developing a more rigid band, a belt holster for pants, or the possibility of attaching the STAT-ON using a belt clip, the latter something requested by a patient.

Another interesting finding was that most patients (90%) would prefer a sensor rather than filling out diaries, also in line with the previous acceptability study from 2016 (23). This result may be explained by the fact that patient diaries require a lot of effort and time in filling out, while it can be considered easier to wear a sensor. In contrast, a similar question was asked in the newly published study on STAT-ON utility (36), instead directed to physicians. A majority of the 27 neurologists were in favor of the sensor (STAT-ON) over diaries (70%). Both these results strengthen the motives for further development of sensors and future research in how the sensors best can be used in routine care of patients with PD.

METHODOLOGICAL CONSIDERATIONS

The findings in this study are somewhat limited by the relatively small number of included patients. The COVID-19 pandemic made the research team pause the recruitment of study participants, which became the major reason for the reduction in sample size. In addition, the generalizability of these results is also subject to some limitation, since the recruitment strategy of study participants may not depict the whole population of people with PD. Nevertheless, as can be seen in the baseline characteristics (***Table 2***), there is a wide range in disease duration, MDS-UPDRS, and H&Y as well as in the PD symptom self-assessment scales such as PRO-PD, WOQ, and PDQ-8. Presumably, this indicates a broad study population, even though it is small.

Furthermore, in the study design, seven categories for assessing motor symptoms were used. This makes the possibility of detecting an actual agreement more difficult, especially

along with a small sample size. Likewise, another questionable aspect is whether the categories have an ordinal scale, which is an assumption needed to be able to use weighted kappa when analyzing. For instance, the category “mostly off” (= 1) is ranked lower than “stable and sufficient effect” (= 2). Nevertheless, we have treated categories as ordinal in this study since we believe that they depict a continuous worsening in disease progression. In the correlation analysis, after excluding the category “mostly off”, categorizations made by both the resident physician and the STAT-ON sensor have a good correlation towards the MDS-UPDRS total score.

Further, it is important to bear in mind the possible bias in the survey responses since all patients had been measured at earlier time points with the PKG sensor. Consequently, there is a risk that patients find it easier using the PKG sensor compared to the first time or prefer it superior to other sensors since they are more used to it.

The strengths of the study method are the usage of both sensors at the same measurement period on every patient and the blinding of the objective measurement reports before evaluation of MDS-specialists. This removed the possibility of impact from differences in everyday activities between measurement periods, as well as lowering risks of bias in specialists’ interpretation. There is also an advantage in comparing different sensor systems in the same study. Patients can directly compare their experience and possible bias from using different raters for different sensors is removed.

To address the utility of sensors in routine care of patients with PD in a better manner, a randomized controlled trial with either only clinical assessment or a clinical co-assessment with an objective measurement would be a suitable direction for future study design. If sensors would be implemented in routine care, the likely usage would be supportive to the clinical assessment. Therefore, the comparison between clinical assessment alone with the clinical assessment with the support of objective measurement would be the most accurate. Further,

randomization to either co-assessment with PKG or co-assessment with STAT-ON would give a more realistic comparison. As a suggestion, reasonable outcome comparisons would be improvements in quality of life, the established MDS-UPDRS, and different PD symptom self-assessment scales between baseline and a follow-up period. This kind of study design has previously only been implemented for the PKG sensor in comparison with only clinical assessment (30). Moreover, a greater number of study participants would also improve a future study design.

CONCLUSIONS

The findings of this study provide insights that the STAT-ON sensor is more consistent with the resident physician than the PKG sensor. However, PKG might to a greater extent provide different information to the physician. Further studies are needed to fully understand the implications of this and how objective measurements can aid the physician in routine care of patients with PD. Additionally, this study concludes that the acceptability and willingness of wearing wearable single sensors in everyday life are potentially high. Although, the development of a slim and secure holder for the sensors is requested by patients to further improve usability.

Since the existing golden standard to evaluate motor fluctuations is unsatisfactory, the need for a better alternative is evident. Meanwhile, several commercial sensor systems for monitoring parkinsonism have shown to be promising in the replacement of patient diaries. Thus, more comparative studies between sensor systems are needed in the future to improve the management of patients with PD.

POPULÄRVETENSKAPLIG SAMMANFATTNING

Titel: Jämförelse av två bärbara sensorer för att mäta och behandla symtom hos patienter med Parkinsons sjukdom

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Handledare: Docent Filip Bergquist, Institutionen för Neurovetenskap och Fysiologi vid Sahlgrenska Akademin, Göteborgs Universitet

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Går det att mäta hur mycket symtom en patient har? Kan bärbara sensorer hjälpa läkaren att optimera behandlingen för patienter? Vad tycker patienterna om att bära dessa sensorer i vardagen? Detta är några av de frågor som forskare vid Göteborgs Universitet och Sahlgrenska Universitetssjukhuset undersökt hos patienter med Parkinsons sjukdom.

Parkinsons sjukdom är en neurologisk rörelsesjukdom som kan leda till skakningar, stelhet och svårigheter att röra sig. Det finns idag ingen botande behandling för sjukdomen, utan behandlingen syftar till att minska symtomen. Nya sätt för att mäta hur mycket symtom en patient har i förhållande till medicineringen är att använda sig av olika bärbara sensorer som patienterna får ha på sig under cirka en vecka. Genom att få information om patienternas symtom över större delen av dygnet, hoppas läkarna kunna anpassa behandlingsschemat för varje individ på ett bättre sätt.

I denna studie har ett forskningsteam jämfört olika sensorer med varandra, om de ger liknande eller tillför ny information till läkaren, samt hur patienterna upplevde att bära sensorerna. Forskarna testade två olika sensorer, den första lik en klocka som bärs på handleden, och den andra sittande på sidan av höften i ett midjebälte. Patienterna i studien fick bära båda sensorerna samtidigt under en vecka. När en vecka hade gått fick de träffa en läkare som också fick bedöma patienternas symtom. Till sist fick deltagarna fylla i en enkät över upplevelsen.

Intressanta resultat i studien var att sensorerna skiljde sig åt i hur de bedömde patienternas symtom. I studien visades att sensorn som burits på midjan oftare stämde överens med läkarens bedömning. Sensorn på handleden gav i stället oftare ny information till läkaren. Vidare frågor som forskarna därför ställer sig är om den nya informationen given av sensorn på handleden därför är av mer nytta.

Vad det gällde upplevelsen av att bära sensorerna, så tyckte patienterna i studien att det var acceptabelt att bära sensorerna i sin vardag, även om flera deltagare klagade över det mjuka midjebältet som lätt kunde åka snett. De flesta patienter uttryckte ändå att de gärna under kortare perioder skulle kunna tänka sig att bära sensorer för att mäta sina symtom.

Vilken av sensorerna som är bäst i dagsläget har forskarna svårt att säkert uttala sig om, och därför krävs ytterligare studier framåt som jämför hur införandet av de olika sensorerna i sjukvården bidrar till ett bättre mående hos patienter med Parkinsons sjukdom.

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APPENDICES

The following pages show the different usability surveys filled out by the patients after the measurement period. Also, a copy of the assessment forms for the resident physician interview and objective measurement evaluation is attached. The surveys and assessment forms are translated from Swedish.

APPENDIX A – USABILITY SURVEY

Wearable sensors 2020/2021

Survey [sensor] (page 1/2)

This survey examines the usability of [sensor]. To be filled in after the measurement period with [sensor]. Only one answer per question is allowed. Below each question, there is space for an additional optional comment. Note that the survey has two pages.

Picture of sensor

To be filled in by study participant

Date _____ - _____ - _____ (YY-MM-DD)

How easy was it taking the sensor on?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very easy *Very difficult*

Comment:

How easy was it taking the sensor off?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very easy *Very difficult*

Comment:

How did you experience the sensor system regarding comfort?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very good *Very bad*

Comment:

What is your opinion about the sensor's shape och design?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very positive *Very negative*

Comment:

How easy was it learning how to use the sensor?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very easy *Very difficult*

Comment:

Survey [sensor] (page 2/2)

Only one answer per question is allowed. Below each question, there is space for an additional optional comment.

Picture of sensor

To be filled out by study participant

What is your experience in charging the sensor?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ *Did not need to be charged* ☐

Very easy *Very difficult*

Comment:

What is your experience in using the sensor in public?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Very comfortable *Very uncomfortable*

Comment:

Does the sensor limit you in your everyday activities?

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

No, not at all *Yes, all the time*

Comment:

Further comments on the sensor system:

To be filled out by the research team Patient ID _____

Survey Summarizing

This survey is to be filled in after all the sensor measurements have ended. At the bottom, there is space for additional optional comments.

To be filled out by the study participant

Date _____ - _____ - _____ (YY-MM-DD)

If the sensors give equivalent information, which sensor would you prefer?

PKG ☐ STAT-ON ☐ None of them ☐

Wearable sensors can today be used to measure motor symptoms among patients with Parkinson's Disease. However, they are not reliable in measuring non-motor symptoms. Another way to measure symptoms would be to fill out a patient diary, which for example can be filled in once every hour for some days. Considering this, how well do you agree with the following statement?

I rather use a sensor than filling out a patient diary.

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐

Strongly agree *Strongly disagree*

Further comments about the sensors, measurements, or the study:

To be filled out by the research team Patient-ID _____

APPENDIX B – ASSESSMENT FORMS (RESIDENT PHYSICIAN / OBJECTIVE MEASUREMENT REPORT)

Wearable sensors 2020/2021

Interview by a resident physician in neurology

Your assignment is to take up anamnesis in a way that you can evaluate the patient's motor symptoms and eventual fluctuations during the last week. If possible, we would like you to give an estimate on the average duration of action by a single dose of levodopa at daytime. The following questions shall be answered. Timelimit of maximum 15 minutes.

To be filled out by the resident physician in neurology

Date _____ - _____ - _____ (YY-MM-DD)

1. Categorize the patients motor symptoms *(only one answer allowed)*

☐ **Mostly OFF** – *Poor effect of treatment. Undertreated.*

☐ **Stable and sufficient effect** – *Generally well treated. Possibly with morning symptoms.*

☐ **Regular OFF-fluctuations** – *i.e., "wearing-off", well treated in between.*

☐ **Irregular or sporadic OFF periods** – *i.e., "delayed on" or "dose failure".*

☐ **Regular ON-OFF** – *"Off" and "on with dyskinesias".*

☐ **Unpredictable ON-OFF** – *Can but must not include biphasic dyskinesias.*

☐ **Mostly dyskinetic** – *Overtreated.*

☐ **Not assessable** – *i.e., sensor was born incorrect or insufficient time; the patient is unable to describe symptoms.*

2. Do the following symptoms occur?

Freezing of gait?	No ☐	Yes, mild ☐	Yes, severe ☐	Not assessable ☐
Falls?	No ☐	Yes, seldom ☐	Yes, often ☐	Not assessable ☐
Sleep disturbances?	No ☐	Yes, mild ☐	Yes, severe ☐	Not assessable ☐

3. Duration of action by a single dose levodopa at daytime _____ minutes

4. Based on your interview and the patient's current treatment plan, would you perform a change in therapy? No ☐ Yes ☐

Signature _____

To be filled out by the research team Patient-ID _____

Assessment of objective measurement

Your assignment is to evaluate the following objective measurement report, categorizing the patient's motor symptoms and fluctuations, as well as giving an estimate on the average duration of action by a single dose of levodopa at daytime.

To be filled out by MDS-specialist

Date _____ - _____ - _____ (YY-MM-DD)

1. Categorize the patients motor symptoms *(only one answer allowed)*

☐ **Mostly OFF** – *Poor effect of treatment. Undertreated.*

☐ **Stable and sufficient effect** – *Generally well treated. Possibly with morning symptoms.*

☐ **Regular OFF-fluctuations** – *i.e., "wearing-off", well treated in between.*

☐ **Irregular or sporadic OFF periods** – *i.e., "delayed on" or "dose failure".*

☐ **Regular ON-OFF** – *"Off" and "on with dyskinesias".*

☐ **Unpredictable ON-OFF** – *Can but must not include biphasic dyskinesias.*

☐ **Mostly dyskinetic** – *Overtreated.*

☐ **Not assessable** – *i.e., sensor was born incorrect or insufficient time; the patient is unable to describe symptoms.*

2. Do the following symptoms occur?

Freezing of gait?	No ☐	Yes, mild ☐	Yes, severe ☐	Not assessable ☐
Falls?	No ☐	Yes, seldom ☐	Yes, often ☐	Not assessable ☐
Sleep disturbances?	No ☐	Yes, mild ☐	Yes, severe ☐	Not assessable ☐

3. Duration of action by a single dose levodopa at daytime _____ minutes

Signature _____

To be filled out by the research team Report number _____