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Mobile phone sensors can discern medication-related gait quality changes in Parkinson's patients in the home environment

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ABSTRACT

Patients with Parkinson's Disease (PD) experience daytime symptom fluctuations, which result in small amplitude, slow and unstable walking during times when medication attenuates. The ability to identify dysfunctional gait patterns throughout the day from raw mobile phone acceleration and gyroscope signals would allow the development of applications to provide real-time interventions to facilitate walking performance by, for example, providing external rhythmic cues. Patients (n = 20, mean Hoehn and Yahr: 2.25) had their ambulatory data recorded and were directly observed twice during one day: once after medication abstention, (OFF) and once approximately 30 min after intake of their medication (ON). Regularized generalized linear models (RGLM), neural networks (NN), and random forest (RF) classification models were individually trained for each participant. Across all subjects, our best performing classifier on average achieved an accuracy of 92.5%. This study demonstrated that smartphone accelerometers and gyroscopes can be used to distinguish between ON versus OFF times, potentially making smartphones useful intervention tools.

1. Introduction

Parkinson's disease (PD) is a progressive degenerative neurological disease that negatively affects movement ability, impacting most activities of patients' daily living and reducing quality of life. There are 930,000 individuals with PD in the US and demographic trends project a rise to 1,238,000 cases by 2030 [1,2]. PD is the second most common age-related disorder, after Alzheimer's disease [3], and its prevalence increases with age. Even though PD symptoms vary from person to person, patients typically experience hypokinesia, bradykinesia, postural instability, rigidity and tremors [4]. As the disease progresses, these symptoms lead to deteriorated walking patterns characterized by reduced gait speed; unrhythmic, small amplitude movements; gait instability and freezing of gait (FOG). Such gait disturbances place patients at risk for falling, which could result in injuries, fractures, hospitalization, and in extreme cases, death [5,6].

Pharmacological treatments such as levodopa, dopamine agonists or inhibitors of dopamine metabolism can improve PD symptoms and normalize gait abnormalities [7]. However, the effect of these drugs deteriorates with time, leading to fluctuations in medication effectiveness as a function of time since the drug was taken. Time periods during which the medication is effective and patients experience few symptoms and nearly normal gait patterns are referred to as ON states. On the other hand, OFF states occur when medication has worn off and patients show instable, shuffling, and small amplitude gait patterns [8,9]. In addition to pharmacological interventions, external visual, haptic, or acoustic cues have been successfully used to normalize poor walking performance and gait speed [10–12]. For example, rhythmic acoustic cues, like from a metronome or recorded sounds of footsteps on gravel can help PD patients to regularize step frequency, reduce gait variability and increase stride length [13,14]. While external cues are beneficial in improving gait quality, they have been limited to in-therapy settings and are difficult to implement in the real-world. Thus, in their current form, they cannot assist patients in their daily life [15]. However, migrating such treatments to smartphones represents an unparalleled opportunity to track ON versus OFF walking in the real-world and to provide

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real-time external cues in response to deteriorated gait.

Scaling PD treatments to real-world scenarios will inevitably require the use of remote sensors for gait phase detection and preliminary work in this area has recently been performed [13,16]. Typically, spatiotemporal gait outcomes such as step length, and step time were calculated from mobile sensor data via the identification of heel strikes and toe-offs [17]. Gait outcomes were then used to contrast, on a group level, healthy versus clinical cohorts or patients in ON versus OFF medication states [15,18–21]. Importantly, these approaches all investigated changes in ambulation at the cohort level and, therefore, assumed universal gait abnormalities in PD patients. Consequently, results may have masked important information about individual gait signatures, which limited the accuracy of gait impairment detection. In other work, measurement from accelerometers placed around the limbs and pelvis have been used in unsupervised machine learning approaches to establish a patients' individual motor profiles [22,23]. However, the number of sensors used are impractical for sustained daily use by patients in a real-world gait detection scenario.

Built-in smartphone sensors might be an excellent alternative for every-day, real-world gait tracking in PD patients. A large, and increasing number of older people report using such a devices regularly [2]. Furthermore, smartphones can easily provide external auditory or haptic cues, potentially making them an ideal tool to intervene upon deteriorated gait [24]. While products such as STAT-ON from Sense4-Care and PDMonitor from PD Neurotechnology are capable of monitoring Parkinsonian gait, they require patients to buy additional equipment, which we aim to avoid by implementing our study on consumer smartphone devices. Previous research has developed smartphone-based gait classification rules based on the observation of differences in the walking behavior of cohorts, as opposed to a single-subject. Additionally, the learning approaches previously implemented typically functioned over extracted gait outcomes and/or signal features, rather than raw signals; transitioning to the latter is likely advantageous for a future real-time intervention application. Therefore, this study aims to investigate if raw accelerometer and gyroscope signals from a single smartphone are sufficient to identify ON and OFF gait patterns in individual PD patients.

In contrast with other studies, our methodology creates a custom, individualized, classifier for each patient, rather than using an aggregate approach. This allows us to precisely study participants' gait and movement on an individual basis rather than using sample averages. This approach is consistent with personalized medicine that recognizes between-patient heterogeneity and seeks to move away from "one-size-fits all" treatments [25]. With a future real-time application in mind, we aim to minimize computational requirements by investigating raw and smoothed sensor signals and avoiding the prior identification of gait events, spatiotemporal gait measures and signal feature extraction. Our approach's focus on ON vs. OFF outcomes, the use of a smartphone as a measurement device, the utilization of raw data rather than extracted features, and the prioritization of computationally efficient methodologies that have the greatest potential for incorporation into real-time systems represent novel and valuable contributions to the field that we hope will help PD patients fully benefit from the current big data paradigm.

2. Methods

2.1. Participants & experiment

The inclusion criteria for this study were (i) diagnosis with PD and (ii.) a Hoehn and Yahr score between 1 and 5. Twenty PD patients were recruited by public announcement in local patient support groups. Before inclusion, all participants received detailed information about the study in a telephone call and were provided written, informed consent, in accordance with a protocol approved by Chapman University's Institutional Review Board. The study sample consisted of 11 males and 9 females and the average (standard deviation) age, height, weight, and years since diagnosis score was 69 (9) years, 170 (9) cm, 77 (23) kg, and 8 (5) years, respectively. Hoehn and Yahr scores ranged from 1 to 4 with a mean of 2.25 and standard deviation of 3. While the sample size was relatively small, the large data volume collected from every individual allowed us to pursue a single case design (SCD) strategy that identified unique outcomes for each participant. Within SCDs, a large number of measures per participant leads to small standard errors for observations, which compensates for the modest power associated with a small sample.

To begin the measurement collection procedure, patients were visited at their homes, typically early in morning after an overnight abstinence of their prescribed anti-Parkinson medication (i.e. during an OFF time). A second measurement period was arranged the same day, typically 30 min after intake of their regular medication (i.e. ON), in order to remain within the interval of the short-duration response of the medication [26]. Since patients' medication doses and intake routines varied and were not changed for this study, there were likely differences in the amount of active drug during the ON and OFF observation periods for each patient. Not all patients experience equivalent medication-related symptom fluctuations, making ON versus OFF times difficult to visually observe, but, as shown below, ADPM measurements confirmed these differences. To account for this phenomenon, participants were also asked to rate the severity of their motor symptoms throughout the day, using a 10 cm visual analog scale.

During both observation periods, patients were asked to perform short bouts of indoor and outdoor walking, which allowed consecutive intervals of relatively long walking patterns to be observed. Depending on the ability of the patient and local factors, such as available space in their homes, the walking protocol slightly varied between patients. However, all patients were asked to perform a minimum of 10 short indoor walking bouts. During these time periods, patients wore a smartphone (Galaxy S6, Samsung, South Korea) attached to the right side of the pelvis using a common smartphone belt-pouch. The smartphone contained triaxial accelerometer and gyroscopes and was mounted such that the x, y and z axes of these instruments approximately aligned with the cranio-caudal, anterior-posterior and medio-lateral movement direction, respectively. Patients also wore a validated six inertial-measurement unit (IMU) system (Mobility lab, APDM Inc., USA) [27], attached to both feet, wrists and around the pelvis and trunk, that recorded typical gait outcomes such as gait velocity and stride length.

The duration of each visit was approximately 45 min, during which the patient's walking behavior was directly observed by project personnel. This was done to ensure initial proper placement of IMU sensors and smartphones, accurate readings from our devices, and to record when protocol walking activities were performed. A researcher recorded the times (HH:MM:SS) at which the patient performed walking activities, which allowed intervals of smartphone and IMU recorded signals to be labeled as walking versus non-walking. By recording the exact times when protocol activities were performed, we were able to discard all non-walking signals and gain ground truth walking measures during ON/OFF periods that allowed us to train our classification model.

Between the two observation sessions (i.e. OFF vs ON), patients were instructed to wear all sensors so that they could continue to record data during their daily living. Between-visit time periods ranged from 30 min to 6 h, depending on subjects' medication schedule, which varied due to differences in when patients felt least affected by PD. After all data was collected, smartphone acceleration and gyroscopic signals were temporally aligned with the recorded protocolled walking times according to the common Android OS times.

2.2. Processing

Time-stamped three-axial acceleration (m/s^2) and gyroscope (rad/s) signals were recorded at 80Hz while the IMU devices had an acquisition

frequency of 128 Hz. These measures were collected along with the classification state (ON vs. OFF) of each measurement. Raw accelerometer data can be noisy, which can affect the accuracy of gait performance classification in machine learning algorithms [28]. So, both non-smoothed and smoothed versions of the data were used, which allowed us to determine if the additional preprocessing was justified by an improved learning accuracy. A windowing method was used to smooth the data, whereby the original dataset was divided into *n* sets consisting of non-overlapping, 2 s windows. Local Polynomial Regression (Loess) [29] was performed individually on each window to smooth excessive noise produced by the sensors. We considered several values for the Loess *span* parameter, with a final value of 0.16 selected, based on visual inspection. Both the smoothed and non-smoothed data in all channels were normalized using a sigmoidal function. Fig. 1 illustrate representative examples of non-smoothed and smoothed data for each of the data channels. Fig. 2 illustrates the densities of ON versus OFF accelerometer and gyroscope signals, respectively.

2.3. Supervised learning algorithms

Three popular supervised learning algorithms, regularized generalized linear model (RGLM), neural network (NN), and random forest (RF), were used to predict ON versus OFF states based on the six channels of accelerometer and gyroscope mobile phone data (three dimensions for each device). Due to its simplicity and popularity for binary classifications, RGLM was selected as our baseline algorithm [30].

RF was used because of its reputation as a robust, versatile algorithm [31] and NN was chosen due to its ability to handle cyclical data [32]. Each model was trained on each patient individually for both smoothed and non-smoothed versions of the data. All machine learning analyses were repeated using only tri-axial acceleration and only gyroscopic signals.

As is commonly done, a holdout method was used, where, at random, 70% of the data was split into a training set and 30% was considered a testing set [33]. To avoid overfitting, *k*-fold cross validation with k=10 was used for model training. This method divided the training set into *k* subsets and then performed *k* rounds of training, each of which used one the *k* subsets as testing data and the other *k*-1 subsets as training data. The output was combined into a composite model that was used to make predictions about the 30% testing set that was portioned via the holdout method. Importantly, every observation in the 70% training set was used as both training and test data and the 30% testing set used for prediction accuracy played no role in model training. Hyper-parameters were

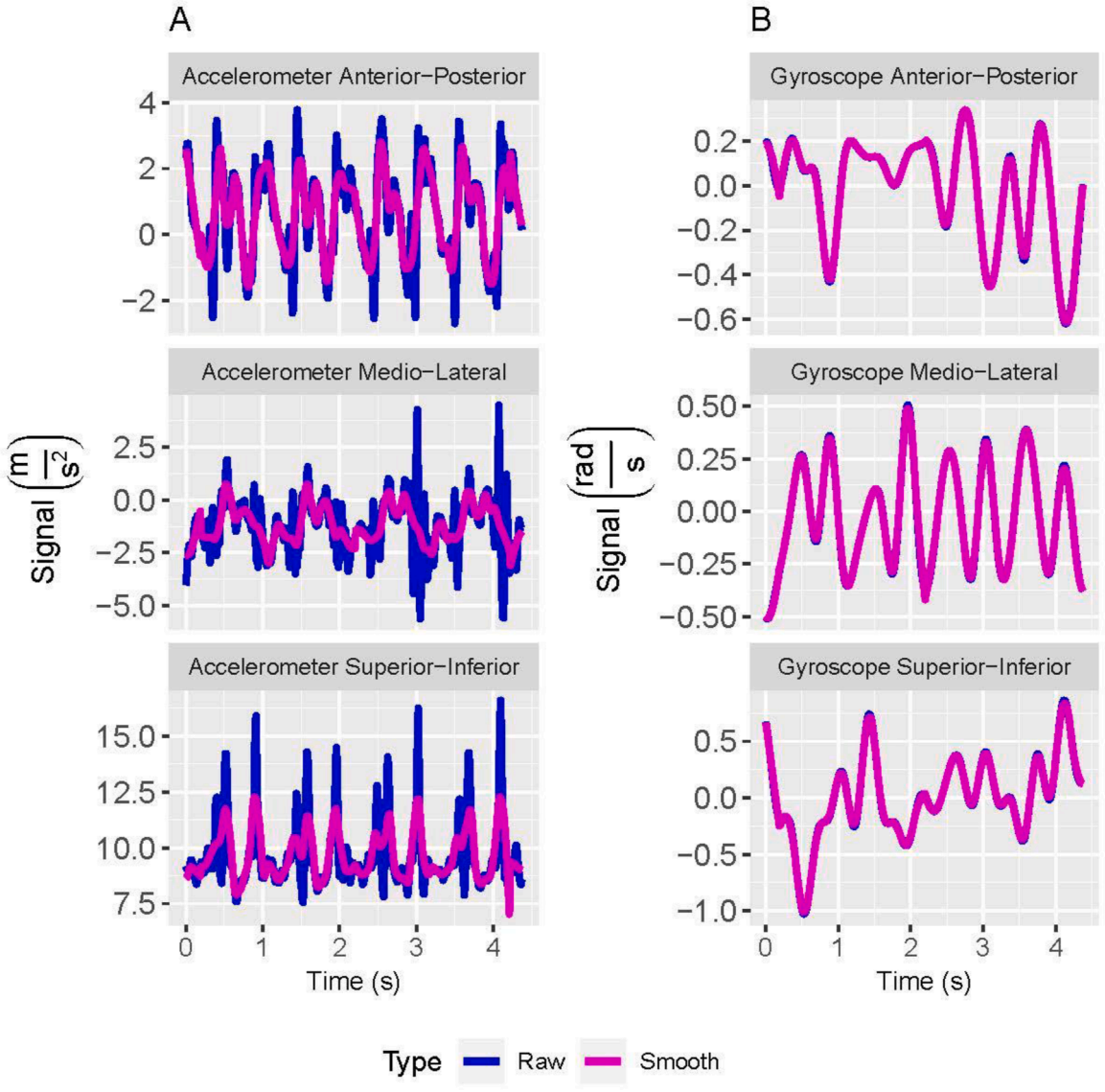

Fig. 1.. Comparison of smooth versus non-smooth three-axial accelerometer (A) and Gyroscope (B) Signals of Subject 8, representative of a typical participant.

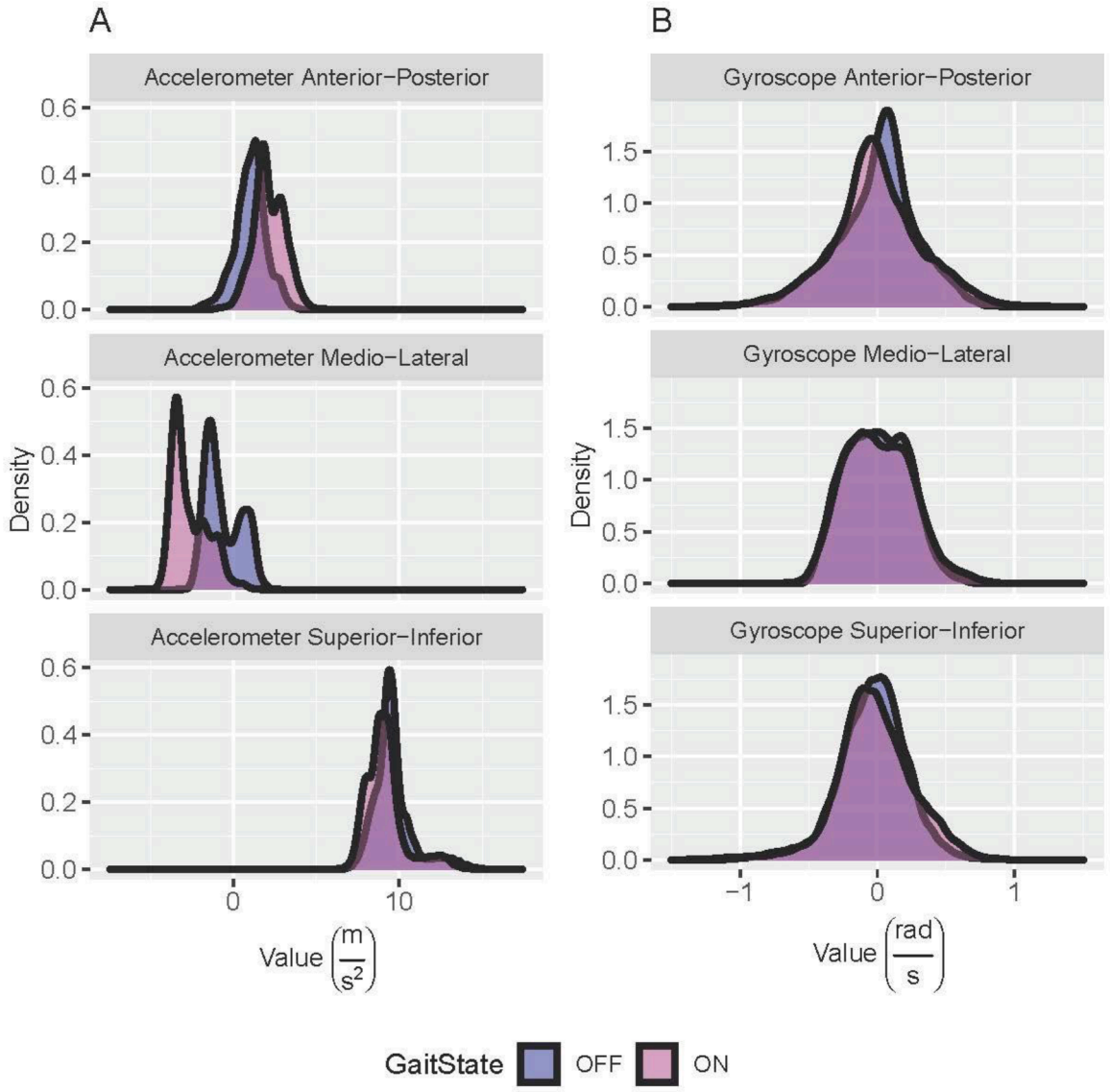

Fig. 2.. Density of ON vs OFF three-axial accelerometer (A) & Gyroscope (B) Signal.

tuned using tuning grids, which are described in Table 1. The optimal model was selected based on which tuning grid hyper-parameter combination resulted in the highest accuracy. The accuracies of each patients' best models were averaged for comparison of the three supervised machine learning approaches. All work was performed using the Caret package in the R Statistical Software [34].

2.4. Statistics

The overall change in gait performance (i.e. gait speed and step length) based on the IMU sensor gait outcomes and self-perceived motor impairment was investigated by comparing measures from ON and OFF walking periods using a paired samples *t*-test. Prior to performing these tests, normality was assessed via Kolmogorov-Smirnov and Shapiro Wilks test for normality. With the exception of stride length during the OFF condition in the Shapiro-Wilk test, all distributions were normal. As a result, we replicated the *t*-test that compared stride length using a Wilcoxon-Mann-Whitney test, which does not assume a normal distribution, and found qualitatively similar results to the ones outlined below (not shown).

Confusion matrices were created for each participant's optimal model and the average accuracies, F_1 and Area Under the Curve (AUC) on both the raw dataset and the smoothed dataset were calculated. Receiver Operating Characteristic (ROC) curves were created to investigate the balance between sensitivity and specificity. Sensitivity refers to the proportion of ON periods that were correctly identified as ON, while specificity is the proportion of OFF periods that were correctly predicted as OFF. The relative importance of each predictor was calculated via the 'varImp' function, which removes each variable one at a time and calculates the change in prediction accuracy; larger changes are associated with more important variables. Importance was ranked on a 0 (low) to 100 (high) scale with the most important variable always having a score of 100 [35]. These values were also averaged over all 20

Table 1.
Input parameters and tuning grid design for three machine learning approaches.

	Parameter	Description	Range	Step
RGLM	α	Elastic-net penalty	0.1 – 1.0	0.01
	λ	Shrinkage parameter	0.0001 – 1.0	0.0101
NN	size	Number of hidden layers	1.0 – 15.0	1
	decay	Regularization	0.1 – 0.5	0.1
RF	mtry	Number of variables at each node	1.0 – 6.0	1.0

participants.

3. Results

3.1. Validated gait performance

Paired samples *t*-tests on the validated gait speed and stride length measures taken from the IMU sensor system revealed that patients walked significantly faster ($t_{(19)} = 2.23$, $p = 0.04$) and with longer strides ($t_{(19)} = 2.4$, $p = 0.03$) during the ON times (see Fig. 3). Patients performed different numbers of walking bouts based on their ability and medication status. On average, they walked for 10 min in ON intervals and 8 min during OFF intervals. The IMU sensor system recorded, on average, 697 and 620 valid gait cycles during ON and OFF, respectively. Also, self-perceived motor impairments significantly decreased by on average 24% ($t_{(19)} = 6.89$, $p < 0.001$). We do not use the IMU data as a classification parameter or input, but rather to validate that there is a difference between gait during ON vs. OFF periods. Since the *t*-tests indicate a significant difference, we aim for our supervised machine learning algorithm using smartphone (and not IMU data) to be able to do the same.

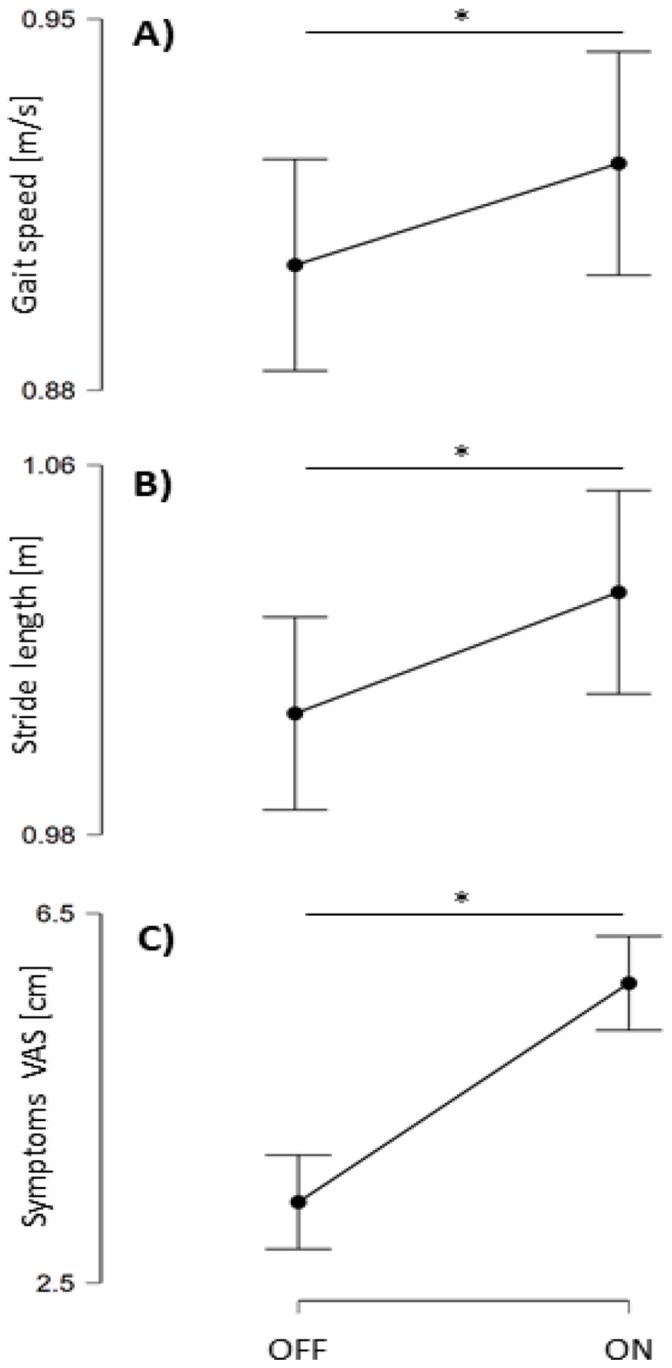

Fig. 3.. Difference in stride length, gait speed, symptom severity stratified by ON versus OFF.

3.2. Supervised machine learning

RF had the highest classification accuracy for both the smoothed and raw data with an average accuracy of 86.8% and 92.5%, respectively (Table 2). Smoothed signals resulted in consistently higher classification results, with generally larger AUC (Table 3).

The ROC curve in Fig. 4 represents one patient from all raw and smooth machine learning models indicates a general well-balanced sensitivity and specificity in all approaches and an overall advantage of smooth data compared to raw signals.

Table 4 presents the sensitivity, specificity, area under the curve as well as the 95% confidence intervals for each signal, raw and smooth. The confidence intervals units are in percentages and values are in regard to the three algorithms we used RGLM, NN, and RF.

Variable importance measures indicate that acceleration signals are more important than gyroscope signals for the classification of walking patterns. In particular, accelerations along superior-inferior and medio-lateral directions (i.e y and z directions) provide the most information about change of gait quality directions (Table 4).

When re-running the models with just the tri-axial accelerometer data (i.e.excluding the gyroscopic signals), the average accuracy fell by 2.0%, 3.5%, 9.8% for RGLM, NN, and RF, respectively. When using smoothed data, RGLM, NN and RF accuracy fell on average 2.0%, 4.0%, and 8.5%, respectively.

4. Discussion

Patients with PD experience fluctuations in their ability to walk safely throughout the day. Conventional smartphones contain accelerometers and gyroscopes that might allow to continually track dysregulated gait patterns, potentially enabling mobile phones to serve as a platform for providing patients with real-time feedback and external cues to maintain safer walking patterns. As a first step in this process, this study aimed to identify if smartphone-recorded raw three-dimensional accelerometer and gyroscope signals are sufficient to distinguish between ON medication and OFF medication walking patterns. Our results indicate that machine learning algorithms can identify ON versus OFF walking patterns from waist-mounted smartphone data without the need for time-consuming preprocessing. The RF approach was particularly promising, with an average correct classification rate of 92.5%.

Previous studies have placed multiple, non-smartphone accelerometers on the body and used the data to construct artificial neural networks to evaluate ON versus OFF, as well as dyskinesia, for PD patients

Table 2.
Average accuracy (95% Confidence Intervals) and F1 score of three machine learning approaches for raw and smoothed signals.

	RGLM Accuracy	F_1	NN Accuracy	F_1	RF Accuracy	F_1
Raw	72.4% (67.7; 77.2)	89.9%	80.2% (76.6; 84.0)	92.5%	86.8% (84.2; 89.6)	97.0%
Smooth	77.0% (71.5; 82.5)	93.9%	86.8% (83.0; 90.7)	92.4%	92.5% (90.4; 94.7)	96.8%

Table 3.
Sensitivity (Sn), Specificity (Sp), Area Under the Curve (AUC) and (95% Confidence Intervals) for three machine learning algorithms applied to raw and smoothed signals.

	RGLM			NN			RF		
	Sn	Sp	AUC	Sn	Sp	AUC	Sn	Sp	AUC
Raw	0.88 (0.750; 0.777)	0.78 (0.879; 0.890)	91.1 (90.8; 91.4)	0.93 (0.870; 0.887)	0.81 (0.932; 0.940)	95.6 (95.4; 95.8)	0.97 (0.979; 0.985)	0.93 (0.977; 0.981)	99.1 (98.9; 99.1)
Smooth	0.93 (0.901; 0.915)	0.87 (0.902; 0.913)	95.7 (95.5; 95.9)	0.94 (0.993; 0.996)	0.80 (0.994; 0.996)	99.6 (99.4; 99.5)	0.97 (0.998; 0.999)	0.92 (0.996; 0.998)	99.8 (99.8; 99.8)

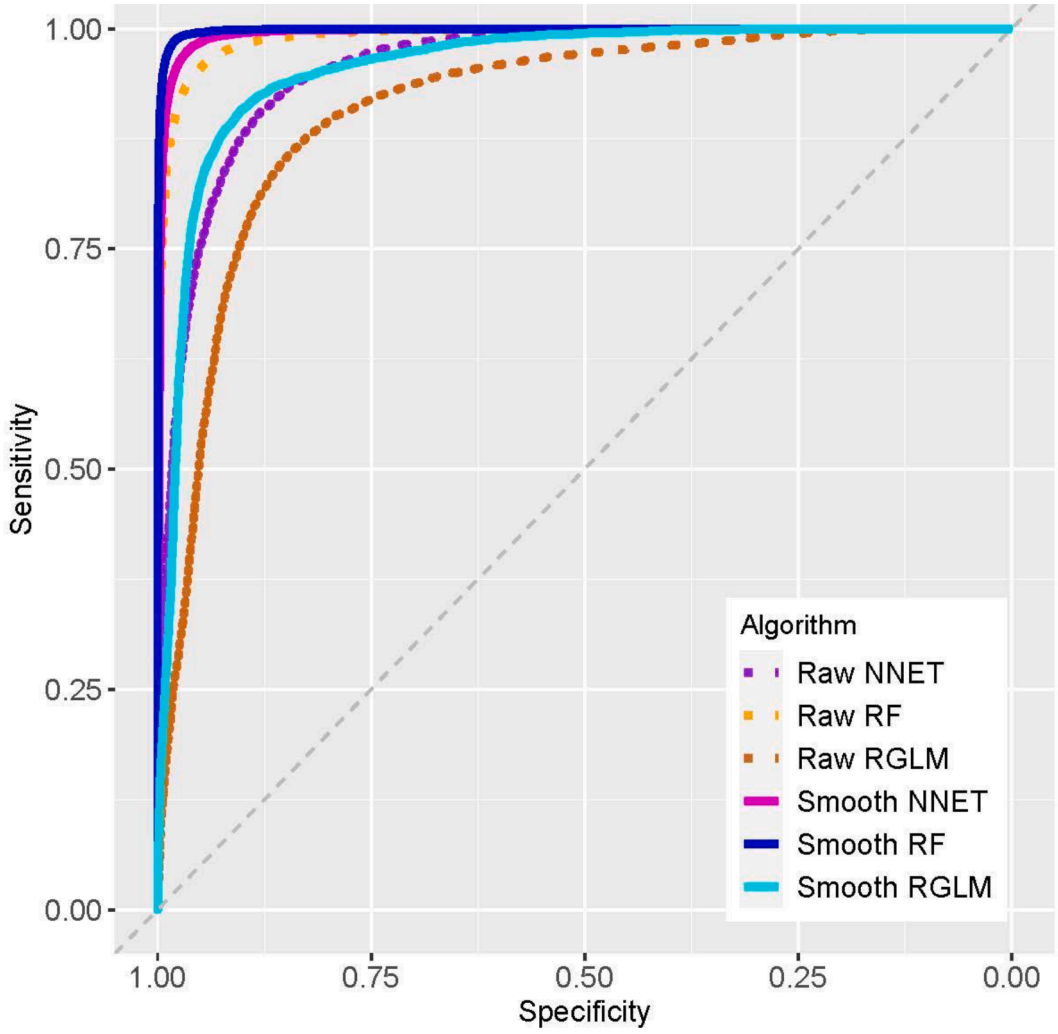

Fig. 4.. Raw and Smooth ROC Curve Comparison.

Table 4.
Accelerometer and gyroscope signal importance.

	AccelAnterior-Posterior	AccelMedio-Lateral	AccelSuperior-Inferior	GyroAnterior-Posterior	GyroMedio-Lateral	GyroSuperior-Inferior
Raw	26.8	60.4	63.4	13.4	22.4	11.6
Smooth	32.5	57.8	78.4	6.42	12.5	8.0

in their homes [23,36,37]. In contrast to the approach presented here, those studies also included upper extremity function, but nevertheless found considerable lower classification accuracy of 84% for [36] and sensitivity/specificity of 51% / 87% [37]. A study by Keijsers et al found excellent sensitivity and specificity of both 97%, but data from six triaxial accelerometers mounted at various body locations were used [23]. Such an approach is not only impractical, but the additional burden is not justified by the gain in accuracy compared to this study. Another study had participants wear a single waist-mounted accelerometer and used machine learning methods to calculate bradykinesia severity [21]. In this study, a support vector machine (SVM) algorithm was used to detect gait and then frequency features were extracted from strides. Two epsilon-support vector regression (SVR) models were used to calculate a threshold that characterized bradykinesia severity. For a real-time application, this complex procedure would likely be too computationally expensive to compute on the fly. This stands in contrast

to our approach which used minimal feature extraction to detect gait abnormality (ON vs OFF) at a high accuracy. Furthermore, rather than introducing a stand-alone device, we use a smartphone to detect gait, which has been shown to be a reliable approach [38,39].

A real-time ON versus OFF classification scheme needs to analyze data as it streams into the device. This stands in contrast to the work outlined within this paper, which operated over complete data sets that were built after all data collection had ended. Therefore, transitioning to real-time analyses will require major modifications to the approaches presented herein, potentially including the consideration of data in windows as it streams in, feature extraction and a blend of labeled training data based on group averages and individual calibration. Many decisions remain to be explored in this framework, including an investigation into the processing power required to complete such a task and a more formal comparison of machine learning approaches. But the benchmarking results outlined in this study, along with the existence of other systems explicitly designed to sense, analyze, and act on streaming data collected by smartphones, makes us optimistic that it will be possible to build a real-time classification/response system. For example, a smartphone-based platform aiming at providing real-time feedback from embedded sensors, was able to process about 9000 samples/second. In the current project, the maximal sample rate was 80 Hz, which given the six sensor channels, would require processing of only 480 samples/second [40]. Future work will focus on defining the specifics of ON versus OFF machine learning classification within this context in a manner that balances accuracy versus computational concerns. We will also focus on the presentation of external cues to determine how quickly they can be activated, for how long they should be provided, and what the best topography is for these alerts. Furthermore, the acceptability of wearing a waist-mounted mobile phone in one's natural environment for extended periods of time among a PD population is unknown. Future work will explicitly assess this issue and will aim to use a design that is most likely to lead to high compliance rates.

This work represents a large departure from traditional approaches that evaluate gait function based on spatiotemporal outcomes (e.g. step length) extracted from accelerometer and gyroscope signals [41]. An important limitation of this deviation is that our classification algorithm acts as a "black-box," which does not provide information on how ON versus OFF walking times differ [42], which may restrict the ability of clinicians to adjust PD treatment protocol as a function of ON versus OFF spatiotemporal outcomes. Additionally, the results only detail a binary classification of ON versus OFF state, but do not allow for the identification of differences in disease severity or progression. The positioning of the smartphone with respect to the human physiognomy can also act as a limitation in a real time application. More precisely, patients would have to be mindful that the smartphone with its attachment must be placed correctly on the body. Patients might have the potential to misposition the smartphone which can have an impact of algorithm performance. In our data gathering process, we ensured that this placement was ideal and correct to further maximize the performance of our algorithms. We also feel that positioning of the smartphone on the hip helps combat asymmetrical walking patterns in patients. It is noteworthy that we did not build a single, generalized model capable of processing pooled data and simultaneously making predictions about all participants since, due to the idiosyncratic nature of individual's presentation of PD, we expect all future applications to use subject-specific models. Future studies could also monitor and detect changes in disease severity over time, which would likely have clinical significance. In addition to these technical issues, our sample size of 20 participants limits generalizability to a wider population. Furthermore, broad recruitment criteria were used and participants were not assessed and included/excluded based on features such as cognitive/physical disorders, freezing-of-gait occurrences, or the stability of drug regimen. Consequently, there is the potential for heterogeneity in the sample, which is appropriate for this proof-of-concept stage and should not affect the individual-level classifiers that were built, but limits the appropriateness of cohort-based statistics.

In conclusion, this study shows that a single waist-mounted smartphone can identify ON versus OFF gait patterns in individual patients, with the best classifier, a RF approach, providing an average accuracy of 93%. By avoiding common gait outcome calculations or feature extraction and focusing on minimally-processed acceleration and gyroscope signals, the approach represents a promising first step for the development of a real-time feedback smartphone application that provides corrective cues to deficient walking patterns in PD patients.

Author contributions

Albert Pierce: Mr. Pierce was the primary author of the original draft of the manuscript and was heavily involved in reviewing and editing subsequent versions He also performed all statistical analyses.

Niklas König Ignasiak: Dr. Ignasiak conceptualized the projet and let data collection and curation activities. He also reviewed and edited drafts of the paper. He also led funding effots.

Wilford K. Eiteman-Pang: Mr. Eiteman-Pang led data curation activities and reviewed and edited drafts of the paper

Cyril Rakovski: Dr. Rakovski supervised the performance of statistical activities, aided with the secruing of funding for the project and reviewed and edited drafts of the paper

Vincent Berardi: Dr. Berardi aided with the conceptualization of the project and the development and implementation of statistical analyses. He also reviewed and edited drafts of the paper

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability statement

The datasets generated for this study can be found in the Chapman University Digital Commons https://doi.org/10.36837/chapman.000166.

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