Real-World Evidence for a Smartwatch-Based Parkinson’s Motor Assessment App for Patients Undergoing Therapy Changes

Aaron J. Hadley\textsuperscript{a}  David E. Riley\textsuperscript{b}  Dustin A. Heldman\textsuperscript{a}

\textsuperscript{a}Great Lakes NeuroTechnologies, Cleveland, OH, USA; \textsuperscript{b}Private Practice, Beachwood, OH, USA

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Parkinson’s disease · Remote monitoring · Wearables · Tremor · Parkinson’s disease-related motor symptoms

Abstract

Introduction: Parkinson’s disease (PD) is poorly quantified by patients outside the clinic, and paper diaries have problems with subjective descriptions and bias. Wearable sensor platforms; however, can accurately quantify symptoms such as tremor, dyskinesia, and bradykinesia. Commercially available smartwatches are equipped with accelerometers and gyroscopes that can measure motion for objective evaluation. We sought to evaluate the clinical utility of a prescription smartwatch-based monitoring system for PD utilizing periodic task-based motor assessment. Methods: Sixteen patients with PD used a smartphone- and smartwatch-based monitoring system to objectively assess motor symptoms for 1 week prior to instituting a doctor recommended change in therapy and for 4 weeks after the change. After 5 weeks the participants returned to the clinic to discuss their results with their doctor, who made therapy recommendations based on the reports and his clinical judgment. Symptom scores were synchronized with the medication diary and the temporal effects of therapy on weekly and hourly timescales were calculated. Results: Thirteen participants successfully completed the study and averaged 4.9 assessments per day for 3 days per week during the study. The doctor instructed 8 participants to continue their new regimens and 5 to revert to their previous regimens. The smartwatch-based assessments successfully captured intraday fluctuations and short- and long-term responses to therapies, including detecting significant improvements (p < 0.05) in at least one symptom in 7 participants. Conclusions: The smartwatch-based app successfully captured temporal trends in symptom scores following application of new therapy on hourly, daily, and weekly timescales. These results suggest that validated smartwatch-based PD monitoring can provide clinically relevant information and may reduce the need for traditional office visits for therapy adjustment.

Introduction
Parkinson’s disease (PD) affects the motor system and is characterized by tremor (most commonly in the upper limbs), bradykinesia (i.e., slowed movements), and rigidity of musculature. Currently in the USA, there are approximately 1.5 million patients living with PD and 60,000 new cases reported each year [1]. Medication therapy must be customized for each patient, with optimal quality of life being the most important goal. Under treatment with dopaminergic medications, many patients ex-
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perience “wearing off” (a return of symptoms attributed to declining benefit from the previous dose and prior to the next dose) or delayed “on” (prolonged time to experience improvement in symptoms after a treatment dose) [2, 3]. In addition, involuntary movements known as dyskinesias can occur when dopamine stimulation in the brain is relatively high [3]. Patients work with their health-care provider to manage these motor complications by adjusting medication type, quantity, and timing to maintain continuous clinical benefit. Dopaminergic medication adjustments are typically advanced slowly to minimize side effects and utilize the smallest dose that provides adequate symptomatic control. This gradual titration of medication decreases symptom severity but repeated clinical visits for adjustments increase costs [4].

While evidence-based practices for adjusting medication do exist [5], managing fluctuations to maximize “on” times, while minimizing dyskinesias continues to be a daunting task [6]. Optimization of medication places the patient in the middle of a complex system where drug types, dose levels, and dose timing interact to create patterns of motor symptoms and side effects fluctuating throughout the day. Clinical rating scales, most commonly the Unified Parkinson’s Disease Rating Scale [7], are used by physicians to track disease progression during routine clinical management but they require time for observation and the presence of a clinician, which prohibits monitoring symptom fluctuation patterns throughout the day or outside the clinic. Obtaining only a snapshot of symptoms during a single clinical office visit does not provide enough time resolution to determine how to optimize symptomatic benefit. To supplement these clinical evaluations, patients are often asked to keep a diary of their symptoms throughout the day [8]. Paper diaries, however, can be burdensome to complete, leading to poor compliance and inaccuracies [9]. These limitations can make decisions about medication adjustments particularly challenging and require costly trial and error to determine what works best.

Patients’ understanding of their disease state and treatment options is a critical element of health-care engagement. Studies have shown that patients want to know more about their health [10] and participate more effectively in the treatment of their illnesses when they are better informed [11]. This can result in improved outcomes [12] and an improved sense of health, as well as increased optimism about the efficacy of therapy [13]. Patients were found to be more likely to continue their therapy when shown a graphical printout of results [11]. Despite the clear impact of education and empowerment on health outcomes, there is still an unmet need in PD since patients are often unable to recognize when they are not responding optimally and are unaware of what changes they can make themselves to improve treatment [14–16].

The movement disorders community has been looking into applications of novel technology for PD monitoring outside the clinic with the goals of tailoring symptomatic therapy and enhancing health outcomes [17–19]. Wearable technology has shown great promise for providing an objective evidence base for clinical decision-making in PD [12, 20–24]. Smartphone-based systems have been used to collect and process motion data along with manually entered records of medications, nonmotor symptoms, and exercise, as well as perform additional recording tasks [23, 25]. With the advancement and availability of smartwatchs, high fidelity wrist-worn sensor platforms can be easily obtained off the shelf at a cost reasonable to a patient and clinician. This study aims to evaluate the clinical utility of one such system in patients undergoing therapy changes.

Materials and Methods

This work was approved by the Advarra institutional review board and completed in accordance with the Declaration of Helsinki. All participants provided signed informed consent prior to participation. All participants were required to be ambulatory individuals with a clinical diagnosis of PD and capable of using the smartphone-based KinesiaU™ motor assessment system (Great Lakes NeuroTechnologies Inc., Cleveland, OH, USA) either independently or with the help of a caregiver. Enrollment occurred during a routine clinical visit during which the clinician prescribed a change in medication regimen (i.e., change in medication type, dosage, or frequency) or recommended changing an activity (e.g., increasing exercise).

Clinical and Participant Use

Participants were provided a smartphone (Samsung Galaxy J3 or A10E) and smartwatch (Mobvoi TicWatch E) with the KinesiaU app installed (shown in online suppl. Fig. 1; for all online suppl. material, see www.karger.com/doi/10.1159/000518571) to use over the course of 5 weeks. The app instructs the participant to perform 2 brief motor tasks (arms resting and wrist rotation) while wearing the smartwatch on the more affected side. The smartwatch records the motion data, which are then automatically scored for tremor, slowness, and dyskinesia on a 0–4 scale using previously validated algorithms shown to be highly correlated with clinical ratings [26–28] and responsive to therapy changes [21, 29, 30]. Medication and exercise events can be recorded for tracking in graphical reports.

The participants were instructed to use the system prior to and after initiating the prescribed therapy change to allow for the new therapy’s effect on symptoms to be measured and reviewed by the participant and clinician. Recommended use of the system included any 3 days during week 1 (before making the change) and then for at least 3 days during each of weeks 3 and 5 (after implementing

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the new therapy). This use included performing the brief smartwatch-based assessments at least 5 times per day and recording in the electronic diary when medication was taken and exercise was performed. Participants were able to view reports on the smartphone detailing symptom severities within the day and across days as color-coded graphs corresponding to good/none, mild, moderate, and severe (shown in Fig. 1). After 5 weeks, participants returned the KinesiaU systems to their doctor, who then reviewed the KinesiaU reports with the participant and made a therapy recommendation based on the reports and his clinical judgment. No specific instructions were given to the doctor on how he was to use the data in the KinesiaU reports in his clinical decision-making. At the conclusion of the study, participants completed a survey asking subjective questions on a 5-point Likert scale how they felt about the ease of use of the system, comfort, and whether they would continue using a similar system.

Post-Study Analysis
After data collection was complete, the symptom and medication data were further analyzed to identify temporal relationships that may provide additional useful clinical information. Because medications were taken at different times throughout the days and recording sessions occurred both in on and off states, analysis was performed by either aggregating large periods of time or synchronizing to the duration since medication. Recorded symptom scores, medication doses, and exercise performances over the course of the 5-week study for each participant were aggregated in reports by week, day, and hour. The data from each of the three 1-week periods (weeks 1, 3, and 5) were binned and averaged for each symptom to demonstrate the impact of the therapy initiated during week 2 upon the participant’s symptom scores. Two sample t-tests with unequal variances were utilized to determine if any of the symptoms changed significantly after the initiation of therapy.

Collected scores and events for each participant were synchronized and binned into 1 h periods corresponding to each hour of the day. Averaging of this binned data was used to create a representation of an average day’s temporal pattern, a method that assumes that sufficient data have been collected to balance pre- and post-medication effects and that medication is taken at approximately the same time every day.

Timestamps of each recorded event (assessment, medication, and exercise) were synchronized to measure the temporal relationship between symptoms and therapy. Each motor symptom score was aligned in relationship to the nearest medication doses. For each participant, these recordings were binned within the 1 h prior to a dose or within one of the 4 h following a dose.

Results
Sixteen adults with PD (7 male, 9 female; age 59–87 years; 7.7 ± 4.0 [mean ± standard deviation] years since diagnosis; 15 at Hoehn and Yahr stage 2, one Hoehn and Yahr stage 3) were enrolled during an office visit, in which...
### Table 1. Prescribed therapy regimens and clinical outcomes

| Participant | Prescribed therapy | Clinician post-study observation and recommendation | Tremor | Slowness | Dyskinesia |
|-------------|--------------------|--------------------------------------------------|--------|---------|-----------|
|             |                    |                                                  | Baseline | New therapy | Change (95% CI) | Baseline | New therapy | Change (95% CI) | Baseline | New therapy | Change (95% CI) |
| 1           | Levodopa inhalation powder | Improved: continue medication as needed | 0.18±0.49 | 0.26±0.65 | 0.08 (−0.18, 0.34) | 0.54±0.72 | 0.57±0.83 | 0.03 (−0.18, 0.24) | 0.06±0.22 | 0.08±0.27 | 0.02 (−0.18, 0.24) |
| 2           | Levodopa inhalation powder | Improved: continue medication as needed | 0.02±0.08 | 0.01±0.16 | −0.01 (−0.18, 0.07) | 0.15±0.24 | 0.16±0.31 | −0.11 (−0.28, 0.06) | 0.48±0.85 | 0.31±0.49 | −0.17 (−0.68, 0.35) |
| 3           | Levodopa inhalation powder | Discontinue due to lack of benefit | 0.15±0.37 | 0.01±0.04 | −0.14 (−0.37, 0.09) | 0.65±0.25 | 0.49±0.25 | −0.16 (−0.28, 0.05) | 0.62±0.12 | 0.05±0.15 | −0.57 (−1.1, −0.07) |
| 4           | Trihexyphenidyl | Discontinue due to side effect (rash) | 0.13±0.16 | 0.02±0.08 | −0.11 (−0.22, 0.00) | 2.3±0.24 | 2.3±0.4 | 1 (−0.08, 0.28) | 0.23±0.87 | 0.11±0.52 | −0.12 (−0.61, 0.37) |
| 5           | Istradefylline | Discontinue due to lack of benefit | 0.01±0.03 | 0.05±0.04 | 0.04 (−0.07, 0.15) | 0.36±0.27 | 0.78±0.33 | 0.42 (0.05, 0.79) | 0.01±0.03 | 0.02±0.06 | 0.01 (−0.01, 0.04) |
| 6           | Increase melatonin dose | Improved: continue with higher dose | 0.11±0.25 | 0.46±0.88 | 0.35 (−0.4, 0.11) | 1.4±0.83 | 0.98±0.27 | −0.4 (−0.97, 0.16) | 0.15±0.34 | 0.13±0.15 | −0.02 (−0.35, 0.21) |
| 7           | Add exercise | Improved: continue with exercise | 0.16±0.16 | 0.02±0.04 | −0.04 (−0.13, 0.05) | 0.42±0.28 | 0.28±0.15 | −0.14 (−0.28, 0) | 0±0 | 0.01±0.03 | 0.01 (0, 0.02) |
| 8           | Istradefylline | Improved: continue with Istradefylline | 0.07±0.09 | 0.03±0.06 | −0.04 (−0.09, 0.01) | 0.31±0.3 | 0.58±0.31 | 0.27 (0.09, 0.54) | 0±0 | 0±0 | 0 (0, 0) |
| 9           | Change C-L schedule | Unable to return for 6-week visit | 0.10 | 0.01±0.04 | 0.01 (0.0, 0.02) | 0.94±0.35 | 1.3±0.32 | 0.32* (0.08, 0.54) | 0.23±0.38 | 0.42±0.51 | 0.19 (−0.05, 0.41) |
| 10          | Increase C-L dose | Improved: continue with higher doses | 0.17±0.38 | 0.01±0.05 | −0.16 (−0.32, 0) | 0.41±0.36 | 0.19±0.17 | −0.22 (−0.38, −0.06) | 0.11±0.17 | 0.23±0.32 | 0.12* (0.01, 0.24) |
| 11          | Increase C-L dose | Discontinue: resume original dose | 1.2±0.34 | 0.66±0.41 | −0.36* (−0.76, −0.36) | 0.86±0.19 | 1.1±0.1 | 0.22* (0.13, 0.3) | 0±0 | 0.02±0.12 | 0.02 (−0.02, 0.07) |
| 12          | Reduce C-L dose | Did not complete due to technical difficulties | 0.3±0.03 | 0.03±0.09 | 0.02 (−0.01, 0.05) | 0.26±0.13 | 0.02±0.05 | −0.24* (−0.38, −0.1) | 0.11±0.22 | 0.08±0.12 | −0.03 (−0.11, 0.06) |
| 13          | Increase exercise | Improved: continue with additional exercise | 0.01±0.03 | 0.03±0.09 | 0.02 (−0.01, 0.05) | 0.26±0.13 | 0.02±0.05 | −0.24* (−0.38, −0.1) | 0.11±0.22 | 0.08±0.12 | −0.03 (−0.11, 0.06) |
| 14          | Istradefylline | Discontinue due to lack of benefit | 0.28±0.29 | 0.25±0.26 | −0.03 (−0.17, 0.11) | 0.74±0.5 | 0.69±0.45 | −0.05 (−0.28, 0.17) | 0±0 | 0±0 | −0.01 (−0.03, 0) |
| 15          | Increase exercise | Did not complete due to technical difficulties | 0.82±0.56 | 0.34±0.28 | −0.48* (−0.8, −0.15) | 0.35±0.24 | 0.16±0.12 | −0.19* (−0.33, −0.05) | 0±0 | 0±0 | −0.77 (−1.7, 0.15) |
| 16          | Increase doses of C-L and trihexyphenidyl | Improved: continue with higher doses | 0.12±0.25 | 0.03±0.09 | −0.09 (−0.22, 0.05) | 0.22±0.13 | 0.02±0.05 | −0.2 (−0.38, 0) | 0±0 | 0±0 | −0.2 (−0.38, 0) |

As measured by KinesiaU, mean symptom scores ± standard deviation are listed for baseline (week 1) and after initiation of the new therapy regimen (weeks 3 and 5) along with the mean change and 95% confidence interval (negative change indicates improvement). C-L, carbidopa-levodopa. * Indicates a significant change (p < 0.05) between baseline and weeks 3 and 5.
the doctor (DE Riley) prescribed a change in medication type, dosage, or frequency or change in activity such as increasing exercise (Table 1).

User Compliance
The KinesiaU system was successfully used for the 5-week duration of the study by 14 out of the 16 participants. Two participants did not complete the recordings due to user difficulty or technical issues with the smartwatch that were unable to be corrected over the phone with the clinician. The 14 participants that completed the recording study averaged 4.9 ± 1.4 smartwatch-based assessments per day during the requested weeks, demonstrating participants were complying with device use. Despite being requested to use the device for a minimum of 3 days in the desired weeks (9 total days), the median usage was 12.5 days, with eleven participants continuing to use the system beyond the minimum use and one participant using the system thirty unique days.

Clinical Impact of Therapy Change
Thirteen out of the fourteen participants who successfully used the hardware returned for the follow-up clinician visit, while one was unable to return due to COVID-19 travel difficulties. The clinician reviewed the KinesiaU reports with each participant and made a therapy recommendation based on the reports and his clinical judgment (Table 1). For example, participant 10’s tremor was helped by the additional medication as demonstrated by the KinesiaU reports, which allowed the clinician to persuade the patient to continue with a higher dose of medication. The clinician determined eight participants demonstrated improvements from their therapy and were instructed to continue, while five participants were instructed to discontinue the new therapy. There were no specific trends regarding specific therapies found relating to the demographics of the participants with different symptoms and medical histories but the efficacy of the wearable system for quantifying these varied participants demonstrates the utility of this monitoring system across symptoms, disease state, and therapies used.

Participant Approval of the System
All 16 participants, including those who experienced technical difficulties, completed the patient survey. A representative selection of questions and participant responses are presented in Table 2. Most users who completed the survey found the system easy to use and the tasks easy to perform but the perceived utility of the reports varied. Review of survey responses and KinesiaU usage for participants who completed the study revealed some trends. Participants who reported viewing the reports more often and found them to be more useful were often those who performed more recordings per day. Specifically, the more recordings per day on an average a participant performed, the more they agreed with the statement “The KinesiaU reports made me more aware of changes in my symptoms” (R = 0.52, p = 0.05).

Temporal Post-Analysis
Weekly Averages and Motor Fluctuations
Each participant’s data were aggregated by week as shown in Figure 2 for participant 11. Eleven of the fourteen participants who completed the recording study had a significant change (p < 0.05) in at least one motor symptom (as measured by KinesiaU, either an improvement or worsening (shown in Table 1). Of the eight participants who were deemed by the clinician to have improved, five demonstrated significant improvements in at least one symptom measured by KinesiaU from week 1 to weeks 3 and 5. Of the five participants whom the clinician decided to return to previous therapy, one showed significant improvements in at least one symptom, two showed worsening, and two showed no change.
Daily Averages and Motor Fluctuations

Hourly binning to create an average day allows for automatic aggregation of data to demonstrate quantitatively the temporal patterns of motor symptoms. Participants with motor fluctuations demonstrated a general pattern of cyclical high and low scores throughout the average day (shown in Fig. 3, participant 14). The plotted data showed similar fluctuations prior to initiation of therapy, and a lack of improvement was found by the clinician.

**Fig. 2.** Boxplot of symptom scores over the course of the 5 weeks (aggregated into weeks 1, 3, and 5) are shown for participant 16. Significant ($p < 0.05$) week-to-week changes are marked with an asterisk. This participant demonstrated a decrease in tremor and slowness severity following the change in therapy regimen (increased carbidopa-levodopa).

**Fig. 3.** Hourly average symptom severities (mean ± standard deviation) after initiating therapy are plotted for participant 14, demonstrating regular fluctuations. The mean medication times are vertical dashed lines.
Pre- and Post-Dose: Delayed on, Wearing off, and Dyskinesia

Synchronization of scores with medication and exercise events allowed for measurement of the temporal effect of each therapy on individual symptom scores for each participant. In some participants, symptoms of tremor or slowness demonstrated an improvement following medication that lasted for 3–4 h, while others would demonstrate brief periods of improved symptoms (shown in Fig. 4, participants 6 and 14). Levodopa-induced dyskinesia could be found in some participants, peaking in the second hour after taking their regular medication dosage (e.g., Fig. 4, participant 2).

Discussion/Conclusion

The smartwatch-based motor assessment system successfully enabled remote quantification of motor symptoms in response to therapy and was well received by patients with PD. The clinician’s responses to the patient’s therapies were often reflected in the statistically significant outputs of the change in symptoms following novel therapy found in post-analysis, signifying those changes in symptoms due to the initiation of the therapy are being observed by both wearable and clinician. Every therapeutic decision is based on many factors, and the procedures in this study did not include a prescribed algorithm or formula on how the recorded data should be used to influence the ultimate call for each individual participant. The study supports the premise that relying on patient recollection of their symptoms and clinical status, even within a short time period as in our study, can be misleading and result in errors of judgment, such as abandoning therapies that are, in fact, useful or persisting with therapies that have no objective utility and may only lead to side effects. Additional analyses demonstrated temporal relationships between medication doses and symptoms.

Patient Acceptance

The system was successfully used by fourteen of the sixteen participants, all performing the requested recordings throughout the day and recording medication events. Two participants had technical difficulties that were not solved through a phone call with the clinician but they may have been solved with additional training or support. This study provided the Android smartphones and smart-
watches as a kit to use only for this study. However, if participants had been using the system on their personal devices, with which they are more familiar, they may have been more able to troubleshoot and remedy the technical issues themselves. This suggests that remote monitoring systems should support multiple platforms and that users be well-trained to avoid technical issues and abandonment. Patient-facing apps should be designed for the most common operating systems, enabling installation into the individual’s own hardware in a way that increases comfort, wear time, and compliance.

For those who completed the study, the graphic reporting method onboard the smartphone was sufficiently expressive of the data to assist in clinical decision-making on the efficacy of the introduced therapy. As mentioned, studies have shown that patients provided with printouts of their results are more likely to continue their therapy, and patients who feel informed about their progress have an improved sense of health and optimism about their therapy [11, 13]. This group was mixed on the effectiveness of the current design of the reports but had positive feelings about the device and recordings. As described in the results, participants who performed more recordings per day were more likely to find the reports useful, highlighting the importance of frequent assessment. Current commercially available systems only provide offline feedback through post-analysis, meaning this provision of visual reports directly to the users is unique and should be replicated for improving patient care.

Therapy Management

The simple aggregation reporting method on the app that binned recorded scores into varying resolutions of time demonstrated short- and long-term trends which, when combined with participant subjective description of their symptom state, led to eight participants being instructed to continue their therapy and five to modify it. Five of the eight participants that the clinician determined had improved showed statistically significant improvements in at least one symptom score after initiating therapy, confirming that a wearable system can collect the necessary quantitative information to assist in clinical care. In post-analysis, the system successfully detected changes in PD symptoms on a variety of time scales. Observation of changes in symptom scores over weeks (shown in ) allows for long-term quantification of symptom effects. Binning and averaging symptom scores in hour long periods across days (shown in Fig. 3) allow tracking of motor fluctuations, which could lead to treatment recommendations such as changes in medication dose frequency or adjustment to extended-release medications. Quantifying the relationship between symptom scores and the time since last medication dose (shown in Fig. 4) can help clinicians identify medication side effects and determine how quickly medication wears off. This type of reporting can demonstrate when patients are likely in need of an adjustment to therapy that will reduce dyskinesia such as lowering levodopa dose, addition of an anti-dyskinesia medication, or switching to advanced therapies like deep brain stimulation or drug pumps. This would be particularly beneficial for a subgroup of patients who have difficulty differentiating their motor status. In the future, an algorithm could guide a personalized therapy regimen that provides automated dose notifications and detects when a therapy change could be advantageous.

Some limitations of this study must be noted. Of the week-to-week changes that were statistically significant (Table 1), some were so small that may not be clinically meaningful. For example, participant 7’s mean dyskinesia score worsened from 0 to 0.015, which, while statistically significant (p = 0.0437), would not likely indicate a meaningful clinical change in function or be noticed by the patient or a clinician. Further research with additional clinician and patient-reported responses to therapies will be necessary to determine what is a minimal clinically important change in symptom severities.

It is also important to note the average symptom severity in the weeks before and after a change in therapy regimen may not always be the best metric. For example, participant 3 demonstrated statistically significant improvements in slowness and dyskinesia after week 1 (Table 1) but the levodopa inhalation powder was discontinued. Inhaled levodopa is designed to be an as-needed medication, and clinical review of the smartphone app reports may have shown that the participant was not demonstrating the desired immediate response to the medication, though they may have had small positive long-term effects.

Telemedicine Implications

One participant in this study was unable to return to the clinic at the time of the follow-up visit because of COVID-19 travel restrictions though he did complete the 5 weeks of in-home recording and discussed results with his physician via the phone. When implemented in a telemedicine program, the ability for medical apps to automatically transmit data to clinicians over the internet will enable remote monitoring so patients need not travel back to the clinic for routine therapy adjustments. Reducing office visits has become increasingly necessary in light of the COVID-19 pandemic and will likely remain an important part of patient care in the years to come.
Wearable systems are growing in popularity and their onboard sensors allow for easy recording and processing for clinical applications. For widespread use in PD patient care, the collected data must be presented in a manner that is easily interpreted by the clinician (and patient, if a patient-facing app) and integrated with existing telehealth platforms and electronic health records system so that the barrier to practical application of the recorded data is minimized. Reporting may include color-coded plots as incorporated in this system, graphs from advanced processing that analyzes the large data set automatically on different time scales, or even a text recommendation for therapy change to the user based on algorithmic analysis of the scores. Future updates to clinical reporting software will allow for more processed reports using temporal analysis with regards to medication dosing, and possibly automated detection that a medication regimen is not meeting desired therapy goals. Further wearable research and development will continue to increase availability of the optimized therapies for patients at lower cost and with reduced in-office clinical time.

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Statement of Ethics

This work was approved by the Advarra institutional review board (Protocol NR018128-01) and completed in accordance with the Declaration of Helsinki. All participants provided signed informed consent prior to participation.

Conflict of Interest Statement

A.J. Hadley and D.A. Heldman are employees of and own stock in Great Lakes NeuroTechnologies. D.E. Riley has received grant support from Great Lakes NeuroTechnologies.

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Author Contributions

Aaron J. Hadley contributed to methodology, investigation, formal analysis, visualization, data curation, and writing – original draft. Dustin A. Heldman contributed to conceptualization, methodology, writing–review and critique, project administration, and funding acquisition. David E. Riley contributed to methodology, investigation, resources, writing–review and critique.

Data Availability Statement

The data that support the findings of this study are not publicly available due to their containing information that could compromise the privacy of research participants but are available from the corresponding author [A.J.H.] upon reasonable request.

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