Spotlight

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Processing Wearable Sensor Data to Optimize Deep-Brain Stimulation

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Recent advances in miniature-sensor technology have enabled the development of wearable systems[1] that physicians could use to monitor motor behavior in individuals with Parkinson's disease. Parkinson's disease occurs when neurons in a part of the midbrain referred to as *substantia nigra pars compacta* degenerate and stop producing dopamine, a neurotransmitter involved in motor and cognitive functions. Symptoms include tremors, bradykinesia (slowed movement), rigidity, and impaired balance. Therapy is based on augmenting or replacing dopamine using drugs that activate dopamine receptors. These therapies are often successful for some time, but patients eventually develop motor complications such as *wearing off* (that is, the benefits wear off within a few hours of taking the medication) and *dyskinesias* (involuntary and sometimes violent writhing movements).

When pharmacological interventions can't sufficiently manage symptoms, stimulating the subthalamic nucleus—or *deep-brain stimulation*—can help. Physicians determine the optimal settings for deep-brain stimulation by clinically testing different combinations of various stimulation parameters. However, target symptoms respond to parameter changes at different times—some within seconds, others not for days or weeks. Another complication is how various medications work when combined with deep-brain stimulation. Choosing optimal stimulator parameters is thus very challenging.

This is a first step toward implementing advanced strategies for optimizing clinical outcomes using systematic data capture and analysis.

Gathering accelerometer data from patient-worn sensors following the adjustment of stimulation settings could be key in optimizing deep-brain stimulation. Here, we present the results of a pilot study we conducted to evaluate this approach. Our work is a first step toward implementing advanced strategies for optimizing clinical outcomes using systematic data capture and analysis.

DATA COLLECTION AND ANALYSIS

Deep-brain stimulation requires quadripolar electrodes, extension cables, and an internal pulse generator. Stimulators deliver pulses through cylindrical electrode contacts that are 1.27 mm in diameter and 1.5 mm long. The relevant stimulation parameters, which the physicians control using an external console, are electrode polarity, contact location, and the pulse amplitude, duration, and frequency. Generally, the pulse amplitude ranges from 1 to 3.5 volts, the pulse width from 60 to 90 μs, and the frequency from 110 to 150 Hz. The stimulation across the quadripolar electrode can be either monopolar or bipolar.[2] Clearly, numerous combinations of stimulation parameter values exist.

Our goal was to determine whether accelerometer data could help physicians

- predict clinical scores for the severity of tremor, bradykinesia, and dyskinesia;
- identify distinct movement patterns that mark transitory behaviors once stimulation has stopped; and
- estimate the rate of change in the

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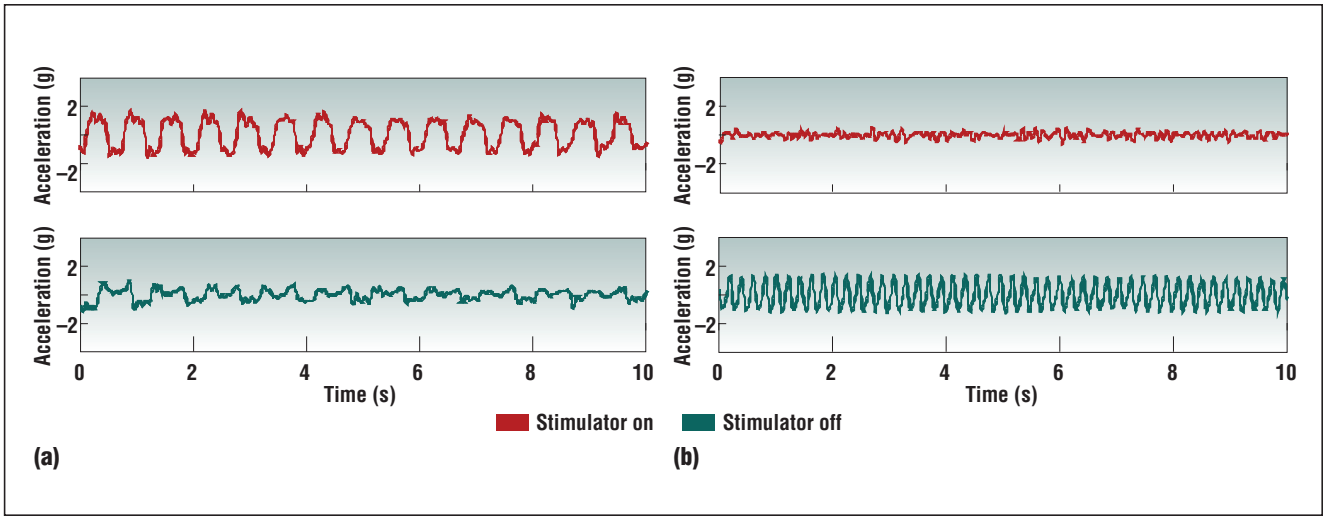

Figure 1. A subject undergoing deep-brain stimulation with the stimulators on and off: accelerometer data recorded while the subject (a) moved her forearm and (b) sat quietly.

severity of the tremor, bradykinesia, and dyskinesia.

We recruited five subjects, ages 60 to 67, with late stage Parkinson's disease. They all had previously implanted deep-brain stimulators, and their neurologists had adjusted the stimulation parameters during clinical evaluations.

The subjects performed a series of motor tasks, adapted from standardized clinical tests, several times over several hours. This helped us assess the severity of symptoms associated with certain motor tasks. We conducted the first trial (pretest) while the deep-brain stimulator was on. When we turned the stimulator off, we performed three more trials, 30 minutes apart. (If the subject was fatigued or experiencing discomfort, we performed fewer trials.) Then, we turned the stimulator back on and conducted one or two more trials, again 30 minutes apart. We videotaped each session.

We placed single-axis accelerometers bilaterally on the forearm and upper arm, the shank, and the thigh. To capture movements of the upper extremities, we oriented the accelerometer axes in the anteroposterior direction (for subjects standing with their arms at their side, palms touching their thighs, the axes of the accelerometers pointed forward). For the lower extremities, we oriented the axes distally ("down," when subjects were standing). We sampled the data at 128 Hz using an ambulatory system, and we used a high-pass elliptic filter with a 1-Hz cut-off frequency to attenuate components associated with gross postural adjustments.[3]

The accelerometer data in figure 1 shows the effect of bradykinesia and tremor on the recordings. We collected the data while the subject performed repetitive pronation-supination movements of the forearms (figure 1a) and while the subject sat quietly (figure 1b). The data is from two trials—one with the stimulator on and one with it off. We recorded the data in figure 1a from an accelerometer on the right forearm. These accelerometer time series demonstrated a larger range of motion and higher frequency of movement when the stimulator was on. We expected this, because bradykinesia typically increases when the stimulator is off.

Figure 1b shows an accelerometer's output on the right upper arm. The output was low-level noise (essentially flat) when the stimulator was on, but we observed fast oscillations (approximately 5 Hz) when the stimulator was off.

Predicting clinical scores

We inspected each session's video recordings, processed the accelerometer data, extracted features from the data segments, and built clinical-score predictors. We filtered the accelerometer time series to isolate the frequency components of interest. We applied a band-pass filter of 3 to 8 Hz for tremor analysis and a low-pass filter with a cut-off 3 Hz for bradykinesia and dyskinesia analysis (we used elliptic filters). Subsequently, we segmented the accelerometer time series using a window randomly positioned throughout the recordings.[4]

We extracted 30 data segments (or *epochs*) for each motor task.[4] We used different combinations of accelerometer data to predict the severity of different symptoms. Table 1 summarizes the body segments from which we extracted features for different symptoms. Certain features from accelerometer sensors effectively capture the main characteristics of movement patterns associated with Parkinson's symptoms.[4] Such features include

- the root mean square value,
- the data range (that is, the time series' peak-to-peak amplitude),
- the dominant frequency,
- the ratio of the energy associated

SPOTLIGHT

TABLE 1
The motor tasks used to derive data features for predicting tremors, bradykinesia, and dyskinesia.

Task	Tremor	Bradykinesia	Dyskinesia
Alternating hand movement	Both legs	Both arms	Both legs
Right-hand finger to nose	Both legs and left arm	Right arm	Both legs
Left-hand finger to nose	Both legs and right arm	Left arm	Both legs
Right-hand finger tapping	Both legs and left arm	Right arm	Both legs
Left-hand finger tapping	Both legs and right arm	Left arm	Both legs
Sitting	Both arms and legs	NA	Both legs
Right-hand movement	Both legs and left arm	Right arm	Both legs
Left-hand movement	Both legs and right arm	Left arm	Both legs
Right-leg agility	Both arms and left leg	Right leg	N/A
Left-leg agility	Both arms and right leg	Left leg	N/A

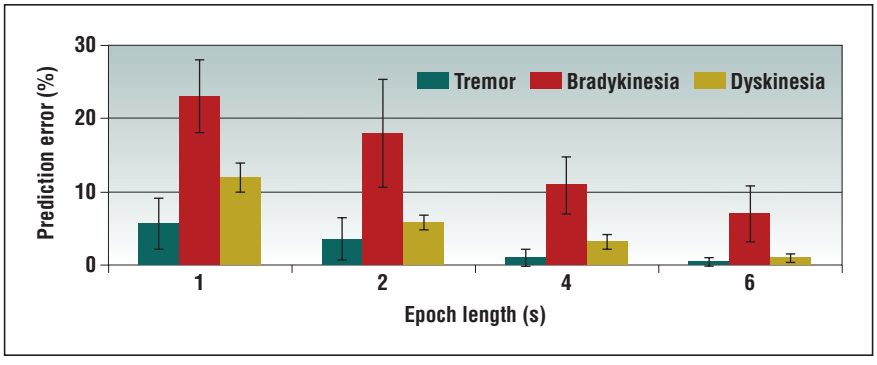

Figure 2. Prediction errors derived using a linear-discriminant classifier for different epoch lengths and symptoms.

with the dominant frequency and the total energy of the accelerometer time series,
- the correlation coefficient among pairs of accelerometer time series,
- the time lag corresponding to the peak of the cross-correlation function among pairs of accelerometer time series, and
- the approximate entropy.

We implemented the clinical-scores predictor using a linear discriminant classifier[5] with tenfold cross validation. We fed the algorithm values derived from windows of different duration ranging from 1 to 6 s (that is, the duration of the epochs we used to extract features). We derived results on a subject-by-subject basis, separately for tremor, bradykinesia, and dyskinesia. We averaged the results across the tasks and presented them as a function of the duration of the window used to extract segments from the accelerometer data. We aimed for an average prediction error (across all symptoms) of 5 percent, because this value approximates how much scores vary when you ask different clinicians to examine the same patient.[6]

Capturing on-off behaviors

We considered whether accelerometer features could capture changes corresponding to the transitory behaviors triggered by switching the stimulator off and on. We visually examined the data-feature structure using Sammons mapping, a nonlinear transformation technique that reduces data dimensionality by preserving the distance between points in lower dimensions. We used this technique to derive 2D projections of the feature space for tremors, bradykinesia, and dyskinesia. Subsequent observations revealed whether distinct clusters were associated with accelerometer feature sets derived from different trials performed in each individual.

Estimating symptom changes

We derived measures to determine how quickly feature sets associated with different symptoms changed from trial to trial. We estimated distance values among feature sets pertaining to the pretest trial and to trials with the stimulator off by taking the centroid as the reference point for each trial's feature set. We added all the distance values to normalize the estimated distance measures. We derived the distance values by considering all pairs of consecutive trials (the pretest versus the first "off" trial, the first "off" trial versus the second "off" trial, and so on).

This provided us with a measure of the change in feature values from pretest trial to trials performed with the stimulator turned off. We visually compared these distance values with the clinical-score time series. We hypothesized that distance measures would demonstrate that the accelerometer-based method could interpolate between discrete changes in the clinical scores observed during "off" trials. If so, accelerometer data might

better capture changes in motor symptoms than traditional, observational clinical tests.

RESULTS

Figure 2 shows results achieved using a linear discriminant classifier to predict clinical scores provided by trained clinicians who visually inspected the video recordings. We derived predictions based on features estimated from the accelerometer data using different epoch lengths. We averaged our results across subjects and across motor tasks for tremor, bradykinesia, and dyskinesia. Average prediction errors ranged from approximately 5 percent (for tremor) to 23 percent (for bradykinesia) for one-second epochs.

As we anticipated, the prediction errors decreased when the epoch duration increased. We used four-second epochs for the rest of our analyses, because they satisfied our prediction error goal. The average error when using a four-second epoch (across all symptoms) was approximately 5 percent (ranging from 3 to 11 percent).

Figure 3 shows results for one subject, representative of the group results, using Sammons mapping. We derived the feature sets from recordings gathered while the subject performed the finger-to-nose motor task with the left arm. We derived the 2D projection (figure 3a) from features selected to predict clinical scores of bradykinesia throughout the recording session.

This subject performed six trials: a pretest trial, three trials with the stimulator off, and two trials with the stimulator on (see figure 3b). We can identify distinct clusters in the 2D Sammons map, each cluster corresponding to a different trial. The projection plane is divided into two sections, based on whether the stimulator was on or off. Clinical scores (the 1 and 2 values next to each cluster) also seem to correspond to different portions of the projection plane, thus supporting the feasibility of predicting clinical scores from accelerometer data features.

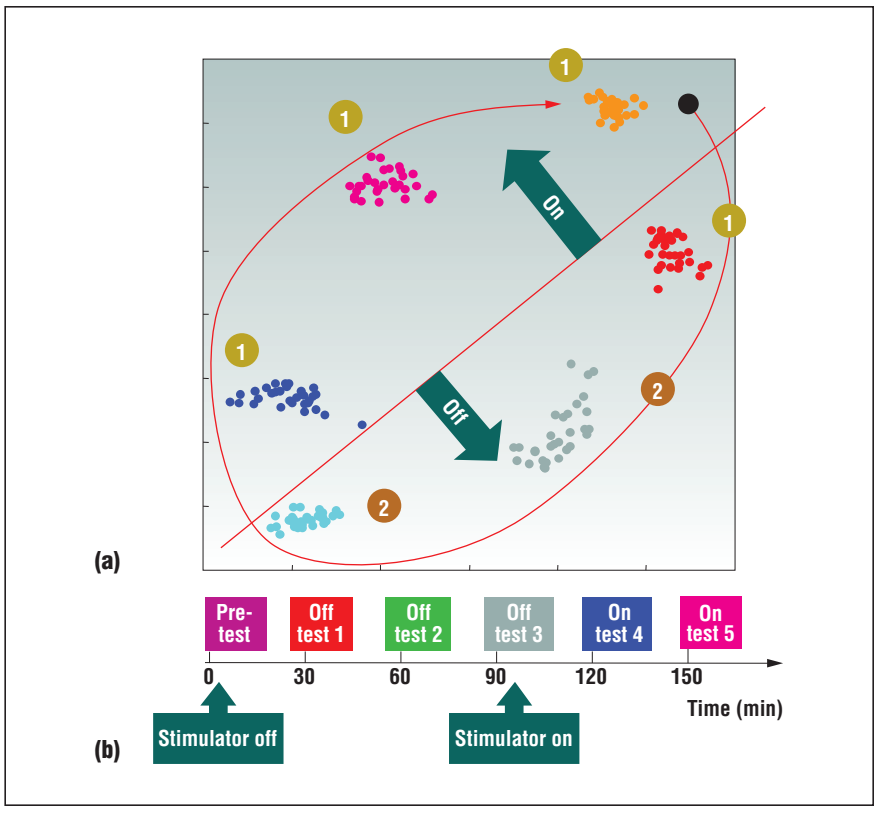

Figure 3. Results for one subject: (a) A 2D Sammons projection of the feature set for bradykinesia. The numbers are the clinical scores achieved, and the colored clusters correspond to the different tests. (The axes are arbitrary, so the map doesn't represent numerical values in a given measurement unit.) (b) The experimental procedure: the pretest (baseline) trial, with the stimulator on, followed by three trials with the stimulator off and two with it on.

The clockwise displacement in the relative position of feature sets (clusters) derived from consecutive trials suggests a well-defined pattern of changes in feature values. This pattern indicates that changes in feature values that occurred when we turned off the stimulator are reversed when the stimulator is switched back on. Accelerometer data appears adequate to capture transitory responses to switching the stimulator off and on. We can identify distinct clusters that correspond to data sets associated with the same clinical scores. So, using accelerometer features might enhance clinical techniques based on visually inspecting the patient.

We also explored whether the accelerometer-based technique could measure the rate of change in the severity of symptoms that follows modifications in the stimulator settings. We studied the association between cluster distance measures for different trials with the stimulator turned off and the corresponding clinical scores.

Figure 4a demonstrates the relationship between cluster distance measures and clinical scores of tremor in one subject. Tremor occurred immediately after switching the stimulator off. The corresponding clinical score jumped from 0 to 4, the maximum value on the clinical scale. The cluster distance measure showed a significant increase between the pretest cluster and the first trial with the stimulator off. However, the cluster distance measure also showed a pattern of continuous change after the first "off" trial.

Figure 4b also supports the hypoth-

SPOTLIGHT

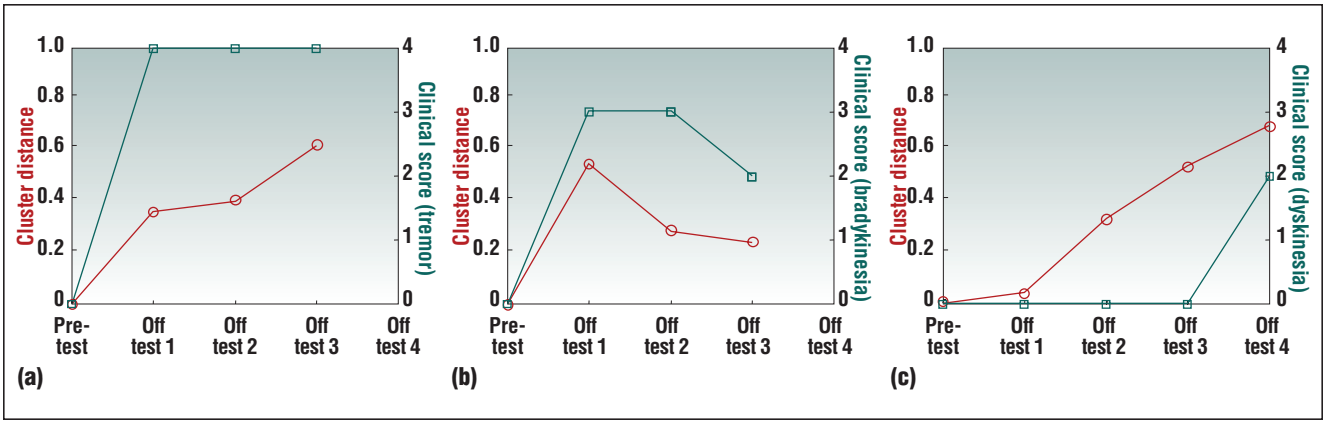

Figure 4. Measures of changes in motor symptoms based on the centroids of clusters associated with trials in which the stimulator was off, compared to the pretest trial. We provide examples for different subjects, so a different number of trials appears for different symptoms, according to how many trials we performed with the stimulator turned off. (a) Tremor results derived from data recorded when the subject sat quietly; (b) bradykinesia results recorded when the subject performed the leg agility task; (c) dyskinesia results recorded when the subjected performed the finger-to-nose task.

esis that accelerometer features might lead to greater sensitivity to changes in motor patterns than clinical measures. We observed a change in the bradykinesia clinical score from 0 to 3 when the stimulator was off. Correspondingly, the cluster distance measure changed noticeably. Eventually, the bradykinesia clinical score decreased to 2 (in the third trial with the stimulator off). The cluster distance measure also decreased, indicating that the accelerometer features were moving closer to those of the pretest condition. Interestingly, the clinical score stayed at 3 during the second "off" trial, whereas the cluster distance measure changed from the first to the second "off" trial in the direction of the observations gathered during the third "off" trial.

Figure 4c further supports our hypothesis. We observed a change in the clinical score only during the fourth trial with the stimulator off. This isn't unexpected, because dyskinesia responds to changes in stimulator settings with a longer time constant than tremor and bradykinesia. However, the cluster distance measure demonstrated changes after the first "off" trial, with an increase of the distance between "off" trial data and pretest data over time.

Our study suggests that a sensor-based technique might be an important adjunct to existing clinical measures to improve the management of patients undergoing Parkinson's control therapy via deep-brain stimulation. In the future, clinicians could gather accelerometer data for approximately one week before and after outpatient visits for deep-brain stimulation adjustments. An expert system

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could then merge clinical observations and results of the accelerometer data analyses to recommend optimal settings. Physicians would decide how to apply these recommendations as one option for the clinical management of motor symptoms, including adjustments in medication intake as well as changes in settings for deep-brain stimulation.

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