Emerging Wearable Technologies Enhance Multisystem Monitoring and Treatment of Parkinson's Disease

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Parkinson's disease (PD) is the second most common neurodegenerative disease and most common movement disorder; almost 90,000 people are diagnosed with PD in the U.S. each year. PD is extremely difficult to diagnose and treat early, as it shows wide variability in clinical presentation. The most common clinical manifestation of PD is motor dysfunction, including slowing of movements, freezing of gait (FOG), and tremor. Standard of care PD diagnosis is based on the severity of these motor symptoms, as quantified in the clinic.

Wearable technologies have emerged as promising tools to characterize PD symptoms. Wearables track symptom progression better than conventionally used rating scales and present a portable, non-invasive means to monitor co-existing symptoms in real-time. Using wearables to monitor symptoms outside the clinic can lead to earlier detection of disease onset and more accurate tracking of symptoms, which are crucial for improving assessments during clinical trials and optimizing treatment regimens with less time needed in the clinic.

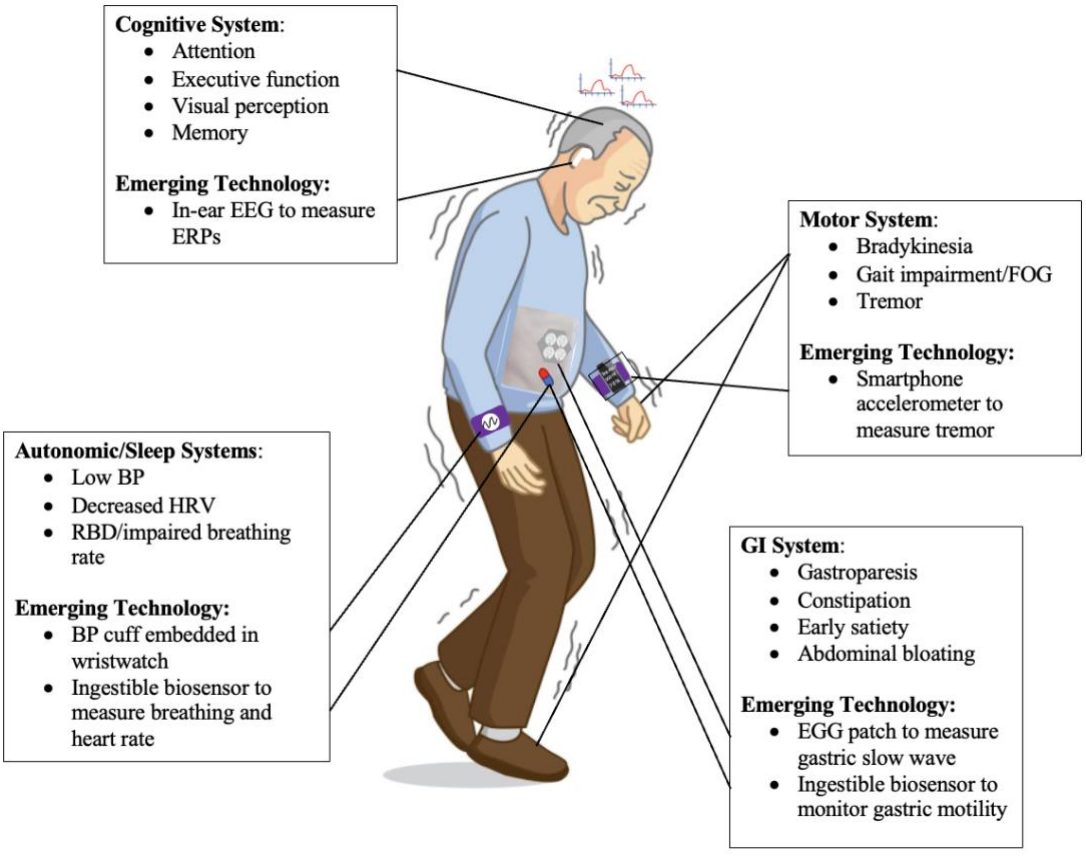


Figure 1. **Motor System:** IMUs built into a smartphone can monitor personalized kinematics of PD motor symptoms such as tremor. **Cognitive System:** One can frequently track cognitive and psychomotor functioning by measuring ERPs using in-ear EEG. **GI System:** It is now possible to assess one's GI function and diagnose GI conditions using EGG sensors placed on the abdomen. **Autonomic/Sleep Systems**: Wearable technologies, including a wristwatch embedded with BP monitoring, can measure real-time autonomic state of PD individuals.

While increases in motor dysfunction indicate progression of the disease, there is growing evidence of nonmotor issues that may begin decades before motor symptoms are present. Cognitive, gastrointestinal (GI), and autonomic dysfunction are hard to manage and significantly affect the quality of life of PD individuals. Tracking of motor and nonmotor symptoms is performed using rating scales, which introduces the subjectivity of clinician interpretation and a lack of fine-grained specificity in symptom characterization. Additionally, measuring this wide array of coexisting symptoms in the clinic becomes difficult because symptoms come and go and can fluctuate in different settings and environments. Wearables enable wholistic disease management using objective measures for a variety of symptoms continuously monitored inside and out of the clinic. Thus, wearables create opportunities to view PD as a multisystem disorder, which includes assessment and treatment of both motor and nonmotor symptoms, Figure 1.

Motor Function

Common motor deficits in PD include loss of voluntary movement and the slowing of movements. People with PD also can have difficulty executing repetitive movements and have gait impairment and tremor. Wearable sensors have emerged as valuable tools to monitor motor symptom progression over time. Wearable motion sensors can capture personalized, continuous kinematics both in and outside the clinic. Typically, inertial measurement units (IMUs) are placed on the limbs of subjects, such as the shanks and wrists, and their built-in accelerometers, gyroscopes, and magnetometers can record features of PD movement. A recent study using IMUs coupled with convolutional neural network modeling to track FOG in PD subjects explored sensor locations that maximized patient adherence for personalized at-home motor symptom monitoring. Additionally, smartphones can measure spatiotemporal features of rest tremor using a three-dimensional, built-in accelerometer and robust software packages. For instance, a 2010 study successfully used an iPhone strapped to the back of the hand to characterize the magnitude and frequency in Hertz a of PD tremor.

Cognitive Function

The development of wearable technologies to assess cognitive impairment presents an emerging opportunity to track subtleties in cognitive decline. This allows for more frequent but targeted cognitive assessments and neuropsychiatric tests that patients can take at home, thus not requiring extensive time and expense for a clinical visit. Smartwatch and smartphone-based cognitive assessments can measure cognition in real-time outside of the clinic environment, as cognition may fluctuate with exercise, sleep, stress, and social settings. A twelve-month longitudinal study explored monitoring of cognitive and psychomotor functioning in PD via smartphone app, *BrainBaseline*. PD subjects and healthy controls performed cognitive tests to assess complex attention and psychomotor speed. Of note, lower performance on the standard cognitive battery of tests correlated with worsened performance on these smartphone cognitive assessments. Along with the ability to synchronously collect other digital biomarkers, such as step information under cognitive load, results are promising for frequently monitoring cognitive and psychomotor functioning throughout daily life.

Gastrointestinal (GI) Function

GI dysfunction often remains untreated and increases in severity over time. GI symptoms for PD can include swallowing and esophageal motility abnormalities, constipation, nausea, vomiting,

early satiety, excessive fullness, bloating, and abdominal distension. GI symptoms are left untreated in part because it is difficult to know what organ(s) in the GI tract are responsible for the dysfunction. A 2021 finding noninvasively assessed irregular electrical patterns pertaining to stomach neuromuscular function using a four-channel electrogastrogram (EGG) placed on the surface of the abdomen in early-stage PD subjects and healthy controls. Irregular gastric slow wave activity was found in the PD patients prior to eating a meal, suggesting gastric dysmotility in PD.

Prof. Todd Coleman of Stanford U. recently developed high-resolution EGG (HR-EGG) that enables the tracking of spatial slow-wave abnormalities from cutaneous multi-electrode recordings. The HR-EGG device includes a patch with stretchable electrodes that is adhered to skin on the abdomen, Figure 2. Approximately half of PD patients have gastroparesis; constipation, colonic dysmotility, and vagal atrophy are also quite common co-occurrences. The HR-EGG patches, which have recently shown to be deployable in an ambulatory setting, could be key to understanding spatial gastric slow wave abnormalities and their triggers and in differentiating them from other causes of GI symptoms in PD individuals.

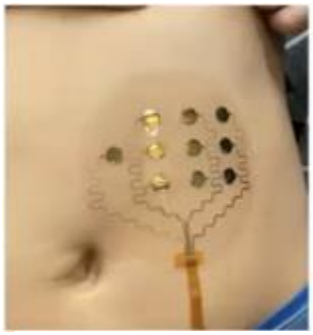


Figure 2. Electrogastrography device, Image credit: Coleman Lab, Stanford U.

Autonomic Function

Monitoring cardiovascular dysregulation is crucial for tracking disease progression in PD but has proven quite difficult thus far. Autonomic symptoms, for example, dizziness (due to postural hypotension) and heart arrhythmia vary throughout the day based on activity and circadian patterns in addition to changing over the long-term course of the disease. Regular blood pressure (BP) monitoring in PD individuals is crucial to detect irregular fluctuations, inform disease management, and reduce cardiovascular risks and falls. As such, technologies such as cuff-less BP monitors on the wrist are entering the market. In 2021, the first smartwatch that monitors real-time BP using photoplethysmography in PD subjects had initial successful tests in both clinical and ambulatory settings.

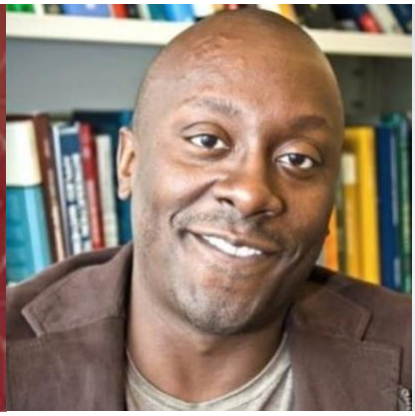
Ingestible devices have been shown to measure gastric motility, and recent prototypes demonstrate the ability to monitor breathing rate and heart rate. Ingestible devices function continuously in the body, even during sleep. Embedded temperature sensors and IMUs in ingestible devices could measure changes in core temperature and sleep quality. Thus, future ingestible devices may be useful for a variety of diagnoses involving irregular autonomic function and respiratory function.

Emerging Wearables Enable Better PD Treatments and Improved Quality of Life

Wearable technologies have unique potential to track and monitor objective measures of motor and nonmotor symptoms of PD. These allow for better understanding of mechanisms of PD, assessing their physiologic fluctuations during clinical trials, and monitoring both disease progression over time and wholistic treatment efficacy. As novel wearable sensors and form-factors emerge, they should be validated for accuracy using clinical standards and rating scales for both motor and nonmotor symptoms of PD. Wearables will enable new understanding of the disease and its complex symptoms with the goal of improving treatments and quality of life for people with PD.

Reference

Kehnemouyi, Y. M., Coleman, T. P., Tass, P. A., "Emerging wearable technologies for multisystem monitoring and treatment of Parkinson's disease: a narrative review." *Frontiers in Network Physiology*, V.4 2024, https://www.frontiersin.org/articles/10.3389/fnetp.2024.1354211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