Technology at the Edge: Emerging Use of Actigraphy as an Outcome Measure

PEER REVIEWED

Wearable devices incorporating actigraphic technologies are transforming the way researchers aggregate, display and interpret health-related data. These devices and the mobile software applications built to work with them enable researchers to monitor and capture data on a wide range of physiological functions – including cardiovascular parameters and movement, temperature, galvanic skin response, blood and oxygen saturation. The devices can collect data passively or actively, which can be used to collect data at random times, at all times, on a set schedule, or in response to specific prompts. They can capture data while the patient is at home or at work, awake or asleep, active or at rest. Among wearable devices, the use of accelerometers has gained ascendancy because of the rich portfolio of information that can be derived.

Actigraphy has long been used to measure clinical sleep parameters, but the evolution of wearable technologies suggests a far wider range of applications such as safety monitoring, patient phenotyping and medication adherence monitoring. However, evolving capabilities raise questions about new methods of data acquisition, analysis and interpretation. They prompt discussion regarding data ownership, data sharing and informed consent. These are questions that are accentuated by geographical differences in regulatory and societal endorsement, adding an element of complexity when it comes to incorporating wearables within the context of international clinical research.[1]

Nevertheless, both patients and developers are increasingly interested in using technology that facilitates ecologically meaningful assessments, while promoting more participatory activity on the part of patients and families. This interest ripples through almost every element of protocol design and study operations today, partially eclipsing the historical dominance of clinical measures with the capture of remote assessments. Correspondingly, patients and advocacy groups are increasingly well-informed about emerging technologies in research and development and aware of potential benefits as well as possible liabilities.[2]

Actigraphy in Observational and Interventional Studies

Wearable devices based on actigraphic technologies have proven to be useful for measures of sleep parameters such as total sleep time, wake after sleep onset, number of awakenings and sleep efficiency. There is an abundance of literature on the utility of actigraphy for this application and searching the terms "actigraphy" and "sleep" can retrieve over 3600 publications. More recently published data indicate that actigraphy can provide a moderately accurate way to identify levels of mobility in adults across a range of indications.

For example, a variety of accelerometer-based motion sensor devices with indirect calorimetry have been used successfully to measure physical activity intensity in youth with cerebral palsy.[3–5] The data within this indication as well as others suggest that most instrumentation would have comparable performance characteristics in the context of controlled activity movements. With inter-instrument reliability (ICC=.94–.99) and good concurrent validity, all of these accelerometers discriminated physical activity intensity across most activity trials.[6] Numerous studies have examined actigraphy tracking of motion in dementia patients and found that it was possible to acquire objective data on individual motor behaviour of patients using actigraphy and that sensor-derived analyses were consistent with clinical observations and symptoms.[7–10] Thus, concordance between clinical measures of activity and those obtained through instrumentation generally are supported within different environments, although exceptions and potential confounders have been reported.

A study by Straiton *et al.* (2020) on the validity and reliability of consumer-grade activity trackers in older adults found that while wearables accurately measured step count and activity duration, slower walking pace and impaired ambulation reduced the levels of agreement.[11] A paper by Verceles and Hager (2015) reviewed several studies that used accelerometry to measure physical activity in the care of mechanically ventilated adult ICU patients. It found that while accelerometry correlated well with direct observation in reporting the frequency and duration of various physical activities (rolling, sitting up, transferring, walking), it could not differentiate intensities of activity or whether movements were voluntary or involuntary.[12] Likewise, a case study by Lauritzen *et al.* (2013) examined activity trackers in walker-dependent elderly with reduced mobility. Their findings indicated that slow walking speed and gait disorders hampered the utility of these devices for physical activity measurement, a finding that is clinically intuitive.[13]

A 2017 study by Mitchell *et al.* found that activity patterns vary across lifespan and differ by race, sex, and education – potentially identifying additional sources of variability.[14] A 2019 meta-analysis of actigraphy found that daily activity tracking is effective in evaluating mood disorders and treatment effects, but the study also identified confounding factors, including the type of actigraphy device used, patients' illness severity, hospitalisation versus outpatient status and the influence of medications.[15] As studies move to use consumer-grade actigraphy devices for data collection in real-world settings, new parameters influence decisions for the use within protocol, including technical issues such as disconnection and syncing challenges, practical considerations such as loss of the device, and the logistics required to ensure smooth data collection across sites, regions and phases of protocol.[16]

Controlled Activity Versus Spontaneous Movement

Measuring how accelerometers perform in tracking and permitting quantitative analysis of freestanding, spontaneous movements, remains to be established, although promising results have been reported.

A home study using accelerometers to evaluate upper-limb activity in non-disabled adults and adults with chronic stroke produced results that were consistent with findings from patients in the more controlled setting of an inpatient rehabilitation

centre.[17,18] Another study found that accelerometer-produced data on upper limb daily performance was highly consistent across neurologically intact, community-dwelling adults. Yet another study proved the validity of accelerometry to assess bilateral upper extremity activity during the performance of set, everyday tasks in neurologically intact adults.[19,20]

These findings indicate that accelerometers can produce clinically meaningful data in both clinical and non-clinical settings when the framework for the movement is defined. However, the small number of data sets as well as device limitations suggests improvements are needed. Wearable devices have been of questionable and inconsistent utility for measurement of movement, unless that movement is within a protocol with choreographed procedures. When manoeuvres have been codified and highly regimented, accelerometers have produced data that correlates well with clinical measures of interest. However, movement that is not orchestrated can also be informative, particularly when coupled with machine learning.[21,22]

An Emerging Opportunity: Extracting the Signal from the Noise

As of February 2020, actigraphy is currently being used as an outcome measure in 762 trials on clinicaltrials.gov in a wide range of disparate indications, including arthritis, Alzheimer's disease, cancer, multiple sclerosis, pregnancy, chronic pain and heart failure.

Although studies suggest that the data collected through actigraphy correlates with functionally important outcomes, there remain open questions about how actigraphy might be used to maximally inform study sensitivity. Specifically, should it measure overall activity, overall activity minus sedentary activity, or moderate to severe activity only? Parameters include the number of days per week during which actigraphy will be used, the number of weeks during which the measurements will be captured, the number of hours within the week that need to be recorded, as well as the methods of aggregating the data and managing missing data for purposes of analyses.

Actigraphy focuses on measurable parameters, such as capturing daily time spent in non-sedentary activity and total daily life physical activity. In some studies, a mean value from the previous week of study treatment is proposed to determine the change from baseline conditions in interventional trials. Others will simply collect activity data over a period of weeks without limitations in structure. Maximal use of accelerometers enjoys utility in observational studies to help define the range of assessments and sampling times that might be employed in a subsequent interventional study.

Proof of Concept or Potential Registration Study?

Actigraphy has ecological validity in a post-approval setting because it correlates well with quality of life, is easy for patients to use and can potentially monitor the effectiveness of clinical care. For example, activity monitoring was shown to be an acceptable means of measuring functional status in idiopathic pulmonary fibrosis patients. The mean daily activity level correlated with quality of life (QoL) measures and forced vital capacity (FVC).[23]

Recent clinical trial announcements also suggest a growing acceptance of accelerometer data as an addition to traditional end points beyond the anticipated acceptability of this methodology within proof of concept or post-approval studies. In one example, the federal drug administration regulatory authorities (FDA) agreed to a Phase II/III study in patients with pulmonary hypertension (PH) associated with interstitial lung disease (PH-ILD), which includes physical activity data captured by wearable actigraphy monitors.[24]

Ultimately, the granularity of data that might be obtained using an accelerometer offers an exciting prospect for innovative trial design. Actigraphy would provide an exceptionally attractive and clinically intuitive option, demonstrating a larger effect size with possibly fewer patients and a shorter duration of treatment to demonstrate other clinically relevant effects. Correlations with assessments based upon quality-of-life and patient-reported outcomes are also potentially demonstrated[25–28], while assessment of key clinical sleep parameters is well established.[29–32] For patient activity, structured data acquisition by time of day, day of week, and week of study has ascendancy, including sampling activity from orchestrated as opposed to spontaneous movement as a study end point.

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