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Review

With life there is motion. Activity biomarkers signal important health and performance outcomes☆

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ABSTRACT

Measures of human motion provide a rich source of health and physiological status information. This paper provides examples of motion-based biomarkers in the form of patterns of movement, quantified physical activity, and characteristic gaits that can now be assessed with practical measurement technologies and rapidly evolving physiological models and algorithms, with research advances fed by the increasing access to motion data and associated contextual information. Quantification of physical activity has progressed from step counts to good estimates of energy expenditure, useful to weight management and to activity-based health outcomes. Activity types and intensity durations are important to health outcomes and can be accurately classified even from carried smart phone data. Specific gaits may predict injury risk, including some re-trainable injurious running or modifiable load carriage gaits. Mood status is reflected in specific types of human movement, with slumped posture and shuffling gait signaling depression. Increased variability in body sway combined with contextual information may signify heat strain, physical fatigue associated with heavy load carriage, or specific neuropsychological conditions. Movement disorders might be identified earlier and chronic diseases such as Parkinson's can be better medically managed with automatically quantified information from wearable systems. Increased path tortuosity suggests head injury and dementia. Rapidly emerging wear-and-forget systems involving global positioning system and inertial navigation, triaxial accelerometry, smart shoes, and functional fiber-based clothing are making it easier to make important health and performance outcome associations, and further refine predictive models and algorithms that will improve quality of life, protect health, and enhance performance.

Practical implications

- Human movement patterns are biomarkers that signal a wide range of important information including health and physiological status
- Triaxial accelerometry is becoming a ubiquitous human movement sensor and applied to the trunk, wrist, or feet provides useful data for physiological predictions
- Example biomarker predictions include activity patterns and energy expenditure, musculoskeletal injury risk, mood status, movement disorders, and head injury and dementia
- Use case examples of predictions from accelerometry include monitoring physical workload of new trainees to prevent musculoskeletal injury; detection of movement patterns signaling impending injury that can facilitate "pre-habilitation" and injury prevention; assessment of the adequacy of sleep-rest periods to permit musculoskeletal remodeling and neurophysiological recovery; assessing progression of movement disorders to improve clinical management; and monitoring progression of rehabilitation and gait retraining.

1. Introduction

Human motion is a fundamental biomarker of behavior and physiology. If one is alive, there is detectable motion. Even a patient in deep coma exhibits motion activity representing cardioballistic pulsations.[1] When we move, our gross movement patterns of ambulation signal much about our physiology, reflecting health, mood, and physical performance. Ambulatory activity patterns are biomarkers of head injury, dementia, and depression as well as musculoskeletal injury or impending injury. Ambulatory activity also summarizes energy expenditure, mental and physical activation, and specific metrics of performance. At a higher organizational level, the analysis of human movement can go further to explain behavior and performance of

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teams. Patterns of movement in a team summarize interactions of team members as well as socially influenced performance of the team, be this a sports team on the field or a squad of soldiers in a military operation.

Within the past decade, the combination of rapid improvements in sensor technology and wearable physiological monitoring and increased computing power has made it easy to acquire and analyze huge amounts of information about human motion. The "quantified self" interest from the public in commercially available wearable systems that can produce reams of data has exploded, but none of this sensing is particularly useful without physiological models to interpret data.[2] Just as with the human genome, we now need physiological model "phenomics" to explain what the data means to health and performance. This is where many of the current generation of wearable monitoring devices fall short. One can obtain personal data on number of footsteps, hours in apparent sleep, and categories of daily activity, but these data can be further interpreted to provide far more useful and actionable information using predictive physiological models. Human physiology should not be the last entry into the current artificial intelligence revolution that is taking place in society and in the military.

Ground breaking efforts in modeling human biomarkers are taking place as highlighted by other presenters in this symposium on military biomarkers. This symposium will advance collective efforts to describe motion and other physiologically-relevant biomarkers through predictive models that provide important information. This overview is presented from the perspective of a physiologist looking for useful biomarkers based on new sensors and algorithms that can be applied to practical warfighter problems.

2. Quantifying physical activity and energy expenditure

2.1. Step counting

Simple waist-worn pedometers provided early technology to help individuals quantify their physical activity for general health and weight management. Customers of these devices wanted guidance on how many footsteps might be a good daily health behavior goal; 10,000 footsteps was randomly proposed as a reasonable achievable daily goal.[3] Subsequent research has demonstrated a remarkably tight association between daily ambulatory activity and health outcomes, and confirming ~10,000 steps as a suitable health goal from an extensive literature review of pedometry and accelerometry studies.[3] As an example at the upper end of daily activity, Amish farmers wearing a simple waist-worn step counter were shown to average about 20,000 steps/day (except on Sundays), with at least 50 h/week of self-reported moderate-to-vigorous physical activity (MVPA).[4] Cadence and intensity using modern microelectromechanical systems (MEMS) provides objective information about time spent in MVPA, an important metric in physical activity guidelines that is not obtainable from simple pedometry.[5] Tudor-Locke et al. point out that the 2018 US physical activity guidelines can be reasonably met walking at a rate of 100 steps/min (~MVPA, 3–6 Mets) for 30 min/day (~3000 steps).[3] A very striking relationship between step counts and all-cause mortality was demonstrated in an analysis of death outcomes of 4840 NHANES participants (age > 40 years) with one week step counts obtained at least a decade earlier using hip-worn accelerometers.[6] Compared to individuals averaging 4000 steps/day, death rates were 50% lower for individuals averaging 8000 steps/day, and the risk flattened out beyond ~10,000 steps/day.

2.2. Estimating physical activity energy expenditure (PAEE)

Converting accelerometry data to estimated physical activity energy expenditure (PAEE) has improved with greater computing power and more sophisticated math modeling tools such as machine learning. Early attempts to estimate activity-based energy costs were based on first principle models of body movement during walking and running, estimating energy costs of body movements in each axis of a body-worn triaxial accelerometer but subsequent empirical models have used regressions or machine learning analyses.[7] Nonlinear modeling of hip-worn triaxial accelerometry data provided good estimates of PAEE obtained from metabolic chamber measurements of energy expenditure.[7] Use of more than one sensor, such as those used in the Intelligent Device for Energy Expenditure and Activity system (IDEEA, with feet, thigh, trunk accelerometers) provided additional information with high resolution of duration and intensity of types of activity.[8] The IDEEA was a bold early concept of a comprehensive wearable biomechanics monitor, but limited by the computing power and analytical tools of 20 years ago. The IDEEA system overestimated energy expenditure when compared to calorimeter data and free-living doubly labeled water estimates, however, a significant portion of this error came from the non-activity estimates of energy expenditure.[9] This highlights a key limitation to activity-based estimation of total daily energy expenditure, specifically, the significant portion of error from estimation, rather than direct measurement, of individual resting metabolic rate, sitting and standing energy costs.

Wrist-worn accelerometry-based predictions of PAEE have converged with hip-worn prediction but now, even smart phones carried somewhere on the body, provide reasonable activity estimates that are accurate enough to inform individual activity-based health behaviors.[10] The contribution to energy expenditure from nonessential activity thermogenesis (NEAT) is also measureable. Actigraphs worn on the right hip in two different studies successfully quantified activity from "dynamic sitting" (NEAT) and these data demonstrated an inverse correlation between activity levels and BMI, suggesting additional PAEE beneficial to weight management.[11] The triaxial accelerometer technology has also evolved, with good accuracy for raw data output to the point of interchangeability between commonly used research devices.

Further improvements on energy expenditure from accelerometry may be possible with additional sensor data. Before accelerometry, monitoring heart rate alone provided useful estimates of PAEE, such as the classic studies by Spurr that demonstrated an energy expenditure "ceiling" for free-living malnourished Columbian school children.[12] Heart rate and activity together might be expected to provide complementary workload data that could provide even more accurate PAEE information. Soren Brage combined heart rate information with accelerometry using branched equation modeling to improve PAEE estimates compared to chamber calorimetry.[13] PAEE is significantly improved in combined activity and heart rate models such as that used by the Actiheart system.[14] The combined model estimates held up well in free living subjects compared to doubly labeled water estimates over 14 days, but the precision is better if heart rate data is individually calibrated.[13] Unfortunately, commercially available wearable sensors still provide poor PAEE estimates. A recent assessment of popular wearable monitors revealed relatively poor validity of PAEE from their respective proprietary algorithms, although the raw heart rate data was excellent.[15]

Sensing at the foot provides another approach to activity-based energy expenditure prediction. From comparative physiology studies, Taylor et al. demonstrated a biological principle across species that supported weight and ground contact time explained energy costs for locomotion.[16] Reed Hoyt applied this finding to humans walking and running on the treadmill, deriving a predictive equation using body weight and foot contact time against conventional lab energy expenditure.[17] This was followed by Army-led development of a boot-worn sensor that could provide PAEE as well as distinguish and classify types of locomotor activity (e.g., run, walk, slow walk, shuffle/non-exercise activity thermogenesis).[18] This effort was integrated into an Army dead reckoning module (DRM4000L), providing inertial navigation inside buildings or under tree canopies when GPS access is denied, in addition to classifying motion and estimating energy costs.

PAEE estimation has a variety of applications in workload estimation studies in field workers, military trainees, and even as a component of thermoregulatory models. Monitoring training load is useful in preventing injury and other adverse health outcomes associated with inappropriate loading strategies.[19] Thomas Wyss developed an accelerometry-based system to monitor workload during training of Swiss recruits, identifying and correcting a serious problem of high musculoskeletal overuse injuries from excessive physical demands and distance traveled on foot in the early part of recruit training; the correction was to institute and enforce an appropriate progressive training plan.[20]

2.3. Public health applications

More recent studies with triaxial accelerometry have characterized activity patterns and energy expenditure in association with public health outcomes.[21] This provides important insights into health associations that were not previously possible by activity observation or self report. For example, individuals might report walking for several hours per day but cannot accurately quantify 30 minute bouts of moderate intensity activity in their normal routines.[21] The 2003–2006 NHANES obtained 7 days of nonsleeping waist worn triaxial accelerometry data for a large sample of Americans, successfully characterizing activity levels and patterns associated with health and disease.[21] A subsequent sampling in the 2011–2014 NHANES obtained continuous data for 7 days using wrist worn accelerometers, with even greater volunteer compliance because of the convenience and user acceptability of a wrist-worn activity monitor.[21] Other very large informative datasets have been collected and reported such as the UK Biobank data with a subset of over 90,000 adults with wrist-worn accelerometry to estimate physical activity patterns and health associations.[22]

Sleep duration is another aspect of health behavior which is notoriously inaccurate in self report but can be better estimated with wrist worn accelerometry. The greatest error in activity-based sleep monitoring is the failure to adequately distinguish between sleep and awake inactivity, while there is greater specificity compared to polysomnography because periods of non-sleep activity are reliably recorded.[23,24] When Patricia Horoho assumed the role of the US Army Surgeon General in 2011, she directed the use of a commercially available system to assess and provide individual feedback to soldiers about their daily sleep and activity patterns in a first ever soldier health readiness effort that included digital activity biomarkers (the Performance Triad initiative). Subsequent efforts to acquire and digest these data from large groups of military personnel are beginning to establish an early foundation for “internet of soldier things.”[25] The US Navy has established a prototype system for personnel watch standing scheduling that is informed by sleep and activity data from currently available commercial wearable monitors.[26]

3. Activity pattern predictions of musculoskeletal injury risk

Gait monitoring provides a rich source of information on musculoskeletal injury risk. Davis et al. have promoted “altering the fingerprint of gait” with gait retraining to prevent injury or re-injury for individuals who have adopted suboptimal movement patterns.[27] Injurious gaits are defined as those with sudden large impact transient, especially high vertical impact peak load rates.[27] A key goal is to reduce the magnitude of these repetitive impacts by transitioning individuals from rear foot strike to fore foot strike gaits. In one study, Crowell and Davis, demonstrated an effective gait retraining program using real time feedback from a tibial accelerometer.[28] They accomplished nearly 50% reduction in tibial accelerations and reductions in vertical force loading rates that were still present in retesting a month later.[28] This research offers potential promise in injury reduction but requires more longitudinal study. Previous injury is one of the key risk factors for musculoskeletal injury in military studies and this may be explained, at least in part, in terms of an unresolved underlying injurious gait.[27] This gait retraining differs from other types of gait training that would improve efficiency and performance such as attempts to decrease vertical oscillation, over-striding, and excessive arm movement. A variety of malalignments are commonly noted in injured runners, with the most common abnormal movement pattern as a combination of excessive hip adduction, internal rotation, and contralateral pelvic drop.[27] Training optimal running gait is significant for the military, where injuries such as stress fracture still represent a major cause of recruit attrition and cost millions of dollars per year in training and medical costs.[29] A prospective study on gait and musculoskeletal injury in Army recruits is currently underway as part of the Army Research Institute of Environmental Medicine Reduction in Musculoskeletal Injury (ARMI) study.

Heavy load carriage is another aspect of military performance for which distinctive adaptive gait patterns have been described. Harman et al. noted a forward lean of the trunk and specific gait changes as carried load increased from 6 to 44 kg.[30] At the heaviest load, stride frequency increased and double support as percent of stride increased with the load.[30] Birrell and Haslam also noted the increase in double support and decrease in preferred stride length as load carried increased, and a decreased range of motion around the knee and pelvic rotation.[31] Qu and Yeo, found that increased load increased gait width variability, hip range of motion, and trunk range of motion along with fatigue and heavy load.[32] Thus, carrying heavy loads tends to shift individuals to adaptive movement with shorter stride length and widening gait pattern that reduce braking and propulsive ground reaction forces (reduced injury risk) and increase the base of support and stability.[33] In a review of 20 military load carriage studies, Walsh and Low observed that studies of experienced soldiers tested outside of the constraints of a laboratory treadmill tended to show a greater resilience with increasing load carriage, with fewer changes in gait.[34] More studies conducted in naturalistic conditions may improve our understanding of these movement biomarkers, perhaps eventually providing individual feedback for safer and more efficient load carriage (e.g., better load balancing, movement strategies, reduced forces on the knees and ankles). Fatigue during load carriage (defined by RPE rating > 17) produces a more variable gait width and trunk sway, increasing the risk of falls.[32]

Similar to dysfunctional gait analyses, faulty movement patterns in a scripted biomechanical task such as a jump-landing test can be used to identify modifiable lower extremity injury risks.[35] The Landing Error Scoring System (LESS) is a validated clinical assessment tool that assesses seventeen lower extremity biomechanical risk factors during jump landings.[36] The LESS is effective for identifying motor control impairments related to hypohydration and hyperthermia,[37] neuromuscular control changes during competitive athletics,[38] residual functional impairments from serious injuries such as anterior cruciate ligament (ACL) tears,[39] as well as training-induced improvements in movement quality and technique.[40]

4. Fatigue and other neurophysiological states reflected in patterns of motion

4.1. Physical and mental fatigue

Reductions in muscular force, power output, and movement velocity are early detectable signs of muscle fatigue.[41] In addition, peak strength capabilities can be inferred from the velocity at which an individual can displace external resistance. One repetition maximum (1RM) predictions, determined by measuring velocity loss during submaximal exercise, are accurate and eliminate the challenges of conducting a maximal assessment.[42] By contrast, mental fatigue is associated primarily with higher than normal perceived exertion, with reduced time to exhaustion as the main alteration in physical performance.[43] No clear movement signals have yet been associated with mental fatigue.

4.2. Depression and sadness

Neurologists and psychiatrists have long noted the characteristic patterns of patient movement associated with specific categories of clinical disorders. Depression is typically accompanied by observable slow gait and slumped posture. Patients with major depression compared to never-depressed individuals demonstrated lower gait velocity arm swing, and vertical head movements, as well as larger lateral swaying movements of the upper body[44] and reduced stride length and double limb support.[45] College students with sad or happy moods induced by music demonstrated similar gait characteristics when they were in a sad mood.[44] Depression results in reduced activity including little time spent in moderate to vigorous activity.[46] While low activity is a marker of depression, deliberate increase in exercise activity can reduce depression symptoms.[47] Simply replacing 60 min of sedentary time with moderate to vigorous physical activity reduces a range of depression symptoms.[48]

5. Predicting and managing disease from digital biomarkers

5.1. Chronic neurodegenerative diseases

Chronic diseases characterized by movement disorders such as Parkinson's disease (PD) have provided models of normal and abnormal gait. For PD, this is useful for earliest detection of the disease, especially where earlier interventions including regular intense exercise, may provide the greatest benefits in the delay of disease progression. The abnormal gait that first defined the disease actually signifies late stage disease when a large number of striatal dopaminergic neurons have already been damaged. Earlier (prodromal) movement-related biomarkers include arm swing asymmetry and a unique REM sleep behavior disorder characterized by reenactment of dreams. Even after abnormal gait becomes a feature, PD is a chronic disease that individuals may live with for many years. Practical automatic monitoring of PD progression becomes important to effective disease management and quality of life.[49] This includes monitoring and management of other disease features that may be reflected in abnormal movement such as apathy, depression, and PD-related dementia. Originally, movement disorders were diagnosed simply by skilled observation but clinical scales were then devised to more objectively classify disease stage and symptom severity. The Hoehn and Yahr (H&Y) scale developed in the 1960s describes the severity of a patient's disease, largely based on observed mobility. For at least the past 20 years, the unified Parkinson's disease rating scale (UPDRS) has provided a more detailed scaling of disease effects on gait and mobility, but requiring a skilled observer to score patients in a standard series of movements. More recently, using accelerometers and gyroscope sensors attached to each shoe, Klucken and Eskofier used modern AI tools to empirically determine a set of movement characteristics that could automatically classify day-to-day disease status.[50] Continuous motion-based objective monitoring of Parkinson's has been demonstrated in the Validating DIGItal biomarkers for better personalized treatment of Parkinson's Disease (DIGI-PD) European initiative and a variety of other patient centric wearable monitoring programs, with machine learning analyses to develop a biomarker signature and quantify features of Parkinson's.[51] Characteristic features include short steps, shuffling gait, and postural instability (with fall risk) and the defining measures such as stride length, gait velocity, stride time, swing phase time, and stance phase time correspond to H&Y and UPDRS scores.[52,53] Parkinson's disease is a model for useful wearable monitoring based on activity patterns and it is relevant to soldiers and veterans with increased disease risk as a consequence of hazardous military chemical exposures, head injury, and trauma.[54]

Other diseases with important movement disorder features can be assessed through their own characteristic movement digital biomarkers. For example, multiple sclerosis includes significant balance control issues.[55]

5.2. Head injury and dementia

Wildlife biologists use the global positioning system (GPS) to study the factors that influence animal movement patterns. A key metric from these patterns is described by fractal d, a measure of path tortuosity. High fractal d values reflect greater tortuosity and might be associated with factors such as increased local foraging behavior or scent tracing by species under study. William Kearns applied this tool to aging veterans restricted to a discrete area that could be monitored for movement patterns and demonstrated strong associations with dementia and with head injury.[56] One study used wrist worn transponders to track dementia patient movement in an assistive living facility for 30 days and compared fractal d scores to Mini Mental State Exam (MMSE) scores. There was a strong relationship to geographic orientation subscale.[56] This also corresponded to observer classification of a tendency to aimless locomotion ("wanderers"). Increased variability in stride time was also inversely correlated with MMSE scores and predicted increased fall risk in elderly patients in another study.[57] Kearns and his colleagues have also applied movement path monitoring to objectively track progress in rehabilitation of patients with traumatic brain injury, demonstrating improved functional status with a linear decline in fractal d in the patients responding favorably to their treatment.[58] Thus, movement path tortuosity is a useful digital biomarker of motor impairment in various contexts including the wandering of dementia, the inability to walk as straight line due to alcohol impairment, and traumatic brain injury.[56,58]

6. Activity biomarker assessment technologies

The explosion of wearable technologies has led to the invention of many new applications in sports and military performance monitoring. Systems like Catapult make real time monitoring of individual player performance possible, using GPS, accelerometers, and camera systems to track players within the circumscribed area of a playing field.[59] Useful variables of player behavior include playing time, position, distance, repeated high intensity efforts, accelerations, and collisions.[59,60] Coaches and trainers are finding such digital biomarkers of player performance useful in guiding individual strength and conditioning programs.[59] For example, knowledge about specific physical demands by player position can support enhanced specific training and assessment of those characteristics.[59] From this experience with athletes, it will be possible to expand beyond a limited arena to free field exercises and monitoring of individual soldier performance in a large training area or operational site.

Even better information about health and performance will come from the development of better sensing tools. Ambitious efforts by military researchers have included instrumented insoles such as the MOBILE system developed between the US Marine Corps and MIT Lincoln Laboratory to produce large amounts of information about biodynamic forces acting on the foot and gait patterns.[61] Complex research solutions typically yield to simpler solutions as the essential data becomes better defined and new algorithms are developed from the observed relationships between activity and relevant outcomes. Inertial measurement units (IMUs) attached to shoes as piloted by Hoyt et al. in prediction of PAEE from foot contact time,[18] by Eskofier and Klucken with empirical classification of Parkinson's disease progression,[50] and in prediction of performance and injury risk.[59] Computational improvements have increased the accuracy of shoe-worn IMUs for inertial navigation and may also move gait monitoring capabilities to handheld smartphones.[62,63] Lightweight ear-worn sensors have been shown to match treadmill parameters (gait cycle and step period asymmetry) and may be particularly useful where the movement associated with imbalanced foot movement is accentuated at the level of the head.[64]

Future ubiquitous movement monitoring will involve wear-and-forget systems simply built into shoes and clothing fabric.[65] With greater predictive reliability, some of these systems will automatically respond to the user needs, providing feedback and alerts such as Parkinson's motion assist systems[66] or smart shoes responding to user fatigue state (or running surfaces) and automatically changing shoe stiffness to optimize conditions.[67]

7. Conclusions

Activity biomarkers are central to monitoring and optimizing human health and performance through automatic longitudinal classification and quantification of motion interpreted by predictive models and algorithms. These digital biomarkers and sophisticated models and algorithms will influence health behaviors, prevent overuse injuries, enhance training for specific types of performance, and can contribute to early identification of disease and contribute to its effective management.

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Declaration of interest statement

The authors state that they have no conflicts of interest involving this manuscript.

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