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Digital biomarkers of spine and musculoskeletal disease from accelerometers: Defining phenotypes of free-living physical activity in knee osteoarthritis and lumbar spinal stenosis

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Abstract

BACKGROUND CONTEXT: Lumbar spinal stenosis (LSS) and knee osteoarthritis (OA) are 2 of the leading causes of disability worldwide. In order to provide disease-specific prescriptions for physical activity, there is a clear need to better understand physical activity in daily life (performance) in these populations.

PURPOSE: To discover performance phenotypes for LSS and OA by applying novel analytical methods to accelerometry data. Specific objectives include the following: (1) to identify characteristic features (phenotypes) of free-living physical activity unique to individuals with LSS and OA, and (2) to determine which features can best differentiate between these conditions.

STUDY DESIGN AND SETTING: Leveraging data from 3 existing cross-sectional cohorts, accelerometry signal feature characterization and selection were performed in a computational laboratory.

PATIENT SAMPLE: Data from a total of 4,028 individuals were analyzed from the following 3 datasets: LSS Accelerometry Database (n=75); OA Initiative (n=1950); and the 2003 to 2004 National Health and Nutrition Examination Survey (pain-free controls, n=2003).

METHODS: In order to characterize the accelerometry signals, data were examined using (1) standard intervals for counts/minute from Freedson et al. and (2) the physical performance intervals for mobility-limited pain populations. From this, 42 novel accelerometry features were defined and evaluated for significance in discriminating between the groups (LSS, OA, and controls) in order to then determine which sparse set of features best differentiates between the groups. These sparse sets of features defined the performance phenotypes.

OUTCOME MEASURES: Accelerometry features and their ability to differentiate between individuals with LSS, OA, and controls.

RESULTS: Given age and gender, classification rates were at least 80% accurate (pairwise) between diseased and pain-free populations (LSS vs. controls and OA vs. controls). The most important features to distinguish between disease groups corresponded to measures in the light and sedentary activity intervals. The more subtle classification between diseased populations (LSS vs. OA) was 72% accurate, with light and moderate activity providing the prominent distinguishing features.

FDA device/drug status: Not applicable.

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CONCLUSIONS: We describe the discovery of performance phenotypes of LSS and OA from accelerometry data, revealed through a novel set of features that characterize daily patterns of movement in people with LSS and OA. These performance phenotypes provide a new method for analyzing free-living physical activity (performance) in LSS and OA, and provide the groundwork for more personalized approaches to measuring and improving function.

Keywords: Accelerometry; Biomarkers; Knee osteoarthritis; Lumbar spinal stenosis; Performance phenotypes; Physical activity.

Introduction

Lumbar spinal stenosis (LSS) and knee osteoarthritis (OA) are two of the leading causes of disability worldwide [1–3], and are associated with significant economic burden [4–6]. It is of particular concern that most individuals with LSS and OA do not meet physical activity guidelines for maintenance of good health [7–11], and are at risk for diseases of inactivity as a result (eg, diabetes, heart disease, and obesity) [12,13]. Current guidelines focusing on moderate-vigorous physical activity are not realistic or useful for LSS and OA populations [9,10]. There is a clear need for disease-specific and personalized interventions aimed at increasing function and mobility in LSS and OA. However, one barrier to identifying new therapies is a lack of objective, disease-specific measures of function.

Recent advances in sensor technology have allowed researchers to begin measuring daily physical function using accelerometers (activity monitors). Accelerometers provide a method to examine the intensity, volume, and duration of activity. This free-living physical activity is known as *performance*. Examining performance provides a snapshot into someone's functional limitations and patterns of behavior. This objective measurement also delivers the opportunity to better understand physical activity and its relationship to disease. In particular, objective measures of performance promise to improve our understanding functional deficits in these populations, and, therefore, guide development of targeted interventions.

Sensors alone are not sufficient to provide deep understanding of physical performance. Rather, intelligent and disease specific methods for analysis are required. Traditional analysis of accelerometry data is conducted using the variable of "counts/minute" and stratifies physical activity as it relates to energy expenditure into the following intensity categories: sedentary, light, moderate, and vigorous [14]. Methods to date have been driven by fitness and cardiovascular research, and, therefore, have focused on measures of energy expenditure dominated by measurements of the moderate-vigorous activity intervals. Although these methods are appropriate for studies of cardiovascular disease, they are not designed to measure the impact of mobility-limiting disorders on a person's performance. It is likely that analysis focusing on moderate-vigorous activity will miss important details about the light activity range, where clinical experience and recent research demonstrates greater impacts of LSS and OA [9,10,15,16].

To solve this problem, our group empirically derived the physical performance intervals that were developed to analyze counts/minute accelerometry data from individuals with pain and mobility limitations [17,18]. These new accelerometry intervals provide a model for objective measurement of free-living physical performance in people with LSS and knee OA. In particular, these new methods provide the capability to examine data from the light intensity range with increased granularity. Using this methodology we were able to describe the complex relationships between physical activity and low back pain [19], and derive new insights about function in LSS [19–23].

Here, we leverage the opportunity to apply these new analytical methods to existing accelerometry datasets in an attempt to discover digital phenotypes of performance in LSS and OA, and to better understand physical function in people with these conditions. Our goal in this study was to use these new methods to develop objective digital profiles of physical performance or "*performance phenotypes*" of LSS and OA. We anticipate that defining unique physical performance phenotypes will be an important first step toward developing disease-specific physical activity recommendations and other precision health interventions for OA and LSS. Therefore, with this study we aim to (1) characterize accelerometry features of physical performance in people with LSS, knee OA, and controls; and from this (2) discover a sparse set of predictive features (performance phenotypes) that best differentiate between people with LSS, OA, and controls.

Materials and methods

Data sources

All analyses were conducted in 3 distinct populations: LSS, OA, and pain-free controls. Data for these 3 populations were obtained, respectively, from the following existing datasets: the LSS Accelerometry Database (LSSAD), the OA Initiative (OAI) database, and the US National Health and Nutrition Examination Survey (NHANES).

Ethics approval for this study was obtained from the Stanford University and University of Calgary human research ethics boards.

Accelerometry details

All individuals in the 3-source datasets were instructed to wear an ActiGraph accelerometer on a belt, at the natural waistline on the right hip in line with the right axilla, upon rising in the morning and continuously until going to bed at night, for 7 consecutive days. The ActiGraph, Florida is the industry standard accelerometer for research, and has been validated extensively for measurement of performance [15,21,24–28]. All OA and LSS data were collected before any recommended treatment.

The LSSAD

In an effort to improve the understanding of performance in LSS, our group has created the largest known database of accelerometry data from people with LSS, the LSSAD. This database is an aggregate of data from multiple LSS intervention studies, including lifestyle intervention [29], epidural steroid injections [22], and surgery [20,30,31].

Inclusion criteria for source LSS studies: all individuals included in the source studies, and, therefore, the database had LSS diagnosed clinically, and confirmed on imaging by a physician spine specialist (neurosurgeon, orthopedic spine surgeon, or spine physiatrist). All participants were required to be 45 years or older. All individuals were tested with accelerometers 1 week before undergoing treatment as part of the aforementioned source studies. This database represents a heterogeneous population of individuals with LSS, both in terms of age (range of 49–85), symptoms (visual analog pain range 2–10), and disability (Oswestry Index range 21–97).

Inclusion criteria for current study: according to the standards established for accelerometry-based physical activity research, we included only individuals who qualify based on accepted wear-time algorithms that require at least 4 valid days with at least 10 hours of accelerometry data [32,33]. We defined nonwear periods as at least 90 minutes with 0 activity counts, allowing for 2 consecutive interrupted minutes with counts <100 [15]. Based on the accelerometry inclusion criteria, 75 of the 125 individuals were eligible for analysis. There were no statistically significant differences in demographics or clinical details between these 75 included and those who were excluded.

The OAI

The OAI is a longitudinal study of knee OA in the United States. Of the 4,796 participants in the OAI, 2,127 were included in an accelerometry substudy at the 48-month follow-up visit (2008–2010) [34]. Data were obtained from the OAI website.

Inclusion criteria for the OAI: all participants in the OAI were 45 to 79 years of age and considered at risk for knee OA. They were required to meet one of the following criteria: overweight, previous knee injury or surgery, knee pain during the past year, or with a parent or sibling who has had a knee replacement [34].

Inclusion criteria for the current study

Following the methodology of Lee et al. [34], we included patients with radiographic knee OA defined as a Kellgren Lawrence (KL) grade of ≥ 2 in at least 1 knee. According to the standards established for accelerometry-based physical activity research, we included only individuals who qualify based on accepted wear-time algorithms that requires at least 4 valid days with at least 10 hours of accelerometry data [32,33]. We defined nonwear periods as at least 90 minutes with 0 activity counts, allowing for 2 consecutive interrupted minutes with counts <100 [15]. Of these source participants in the OAI accelerometry substudy, 1,950 were eligible for accelerometry analysis based on the inclusion criteria. We conducted an analysis comparing the 1,950 included participants to those exclude and found no statistically significant differences in the key accelerometry variables, or in demographic variables.

The NHANES

The NHANES is a continuous study designed to assess the health the US population. NHANES provides samples that are representative of the US population. Data were obtained from the National Center for Health Statistics website.

NHANES inclusion criteria: NHANES is a large cross–sectional study, which uses a complex, multistage probability design to obtain a representative sample of the US civilian noninstitutionalized population. Full details of the methods can be found at http://www.cdc.gov/nchs/nhanes.htm.

Inclusion criteria for current study: the present analysis used data from NHANES 2003 to 2004, which included self-reported pain and accelerometry. We only included data from individuals who provided negative responses to all trunk and lower body-pain questions. According to the standards established for accelerometry-based physical activity research, we included only individuals who qualify based on accepted wear-time algorithms that requires at least 4 valid days with at least 10 hours of accelerometry data [32,33]. We defined nonwear periods as at least 90 minutes with 0 activity counts, allowing for 2 consecutive interrupted minutes with counts <100 [15]. Of the 10,020 individuals aged ≥ 20 years who participated in the NHANES 2003 to 2004, 2003 individuals met inclusion criteria and were included in this analysis.

Aim 1: Characterizing features of performance in OA, LSS, and NHANES

In order to describe the accelerometry features characteristic of OA and LSS, we applied traditional interval analyses from Freedson et al. [14] as well as the physical performance interval analysis [18] to accelerometry data from the OAI and LSSAD. A feature is a variable derived from the accelerometry data (eg, average number of continuous minutes in the moderate intensity interval). In order to

determine the accelerometry features that are unique to OA and LSS, we compared data from OAI (OA) and from LSSAD (LSS) with the pain-free individuals from the NHANES dataset (controls).

Intervals using counts/minute

For all 3 groups, accelerometry data were interrogated using the recently described physical performance intervals that were developed to analyze counts/minute accelerometry data from individuals with pain and mobility limitations [18]. Specifically, this includes the following continuous intervals: performance sedentary = 1 to 99, performance light 1 (PL1) = 100 to 349, performance light 2 (PL2) = 350 to 799, performance light 3 (PL3) = 800 to 2499, and performance moderate and vigorous (PMV) = 2500 to 29999. We included analyses of total daily time spent within each interval, and duration of sustained activity above each interval threshold ("bouts"). Additionally, we developed a new methodology to incorporate the component of change over time, called change-point analysis. We repeated all of the above analyses using the traditional counts/minute intervals based on energy expenditure, defined by Freedson et al. as sedentary (0–99), light (100–1952), moderate (1955–5723), and vigorous (>5724) activity [14].

Advanced intervals: Change points and capacity

Change points capture time dependent patterns of activity. We measured change points by counting the changes between intervals throughout the course of each day. Every minute of activity throughout the day was coded as one of the change points. For example, change points could include a change from 1 interval to a different interval (eg, PL1 to PL2 coded as X12 in Table 3) or from 1 interval to the same interval (PL1 to PL1 coded as X11).

Capacity indicates an individual's maximum ability. We measured capacity by determining the maximum number of continuous minutes of any physical activity. This is defined as the maximum bout of activity above sedentary (100 counts/min) with no more than 1 intervening minute of counts below 100 (to allow for expected stop and start variability of real-life continuous activity) [35]. We also calculated maximum continuous activity without this 1-minute break allowed. Maximum bouts were also measured for activity at different levels of intensity. Maximum bouts capture each day's longest recorded period of continuous activity within a certain interval (eg, PL1). This was calculated by the number of consecutive minutes within the interval, and then taking the maximum bout from each day.

Aim 2: Discovery of performance phenotypes with a sparse set of predictive features

The measurements defined above comprise 42 accelerometry features, in total, for each individual on every day of valid accelerometry data. To determine which of these 42 accelerometry features is able to distinguish significantly between the 3 groups, we employed logistic regression pairwise between the groups (LSS vs. controls, OA vs. controls, LSS vs. OA). Specifically, separate logistic regressions were performed for each individual accelerometry feature. To control for the effects of age and sex, each logistic regression also included age and sex along with the 42 accelerometry features. We corrected the p values of the multiple hypotheses using the standard false discovery rate (FDR) procedures [36].

To determine a sparse set of predictive features, we used L1-regularized logistic regression. A sparse predictive set is a small group of features that, as a whole, discriminates between groups. Specifically, we regressed on 44 variables, including all 42 accelerometry features identified in Aim 1 along with age and sex. The L1 regularization penalizes the sum of the magnitudes of the coefficients associated with the features, which acts to induce sparsity in the predictive set. We used tenfold cross-validation to choose the relative trade-off between discriminatory power and sparsity. As opposed to choosing an arbitrary number of features a priori, this approach yields a different number of features for each of the 3 pairwise comparisons. After a trade-off value was chosen (from the cross-validation procedure), the final model coefficients were obtained by training on the full dataset.

Results

Table 1 describes the demographic characteristics, and between-group differences for the 3 populations (LSS, OAI, and NHANES).

Table 2 provides the values in minutes/day in each of the Freedson and physical performance intervals. Table 3 describes the p values for discriminatory power, based on

Table 1
Demographic information and p values (by a *t* test) for between-group differences

	Demographics			p values		
	LSS	OA	Controls	LSS versus controls	LSS versus OA	OA versus controls
Age	69 (60–75)	65 (57–73)	48 (32–67)	1.21E−29	5.83E−03	1.63E−187
BMI	28 (26–33)	28 (25–32)	26 (23–30)	1.39E−02	2.38E−01	1.48E−06
Sex (percentage of male)	38%	45%	52%	7.58E−04	1.44E−01	6.57E−21

BMI, body mass index; LSS, lumbar spinal stenosis; OA, knee osteoarthritis; controls, pain-free controls.

Table 2
Minutes/day spent in the defined intensity ranges using the Freedson intervals [14] and physical performance [18]; median (first quartile–third quartile) for Freedson and physical performance interval analysis features

	Cutpoints		
Freedson cutpoints	LSS	OA	Controls
Sedentary (1–99)	1186 (1134–1249)	1149 (1092–1202)	1095 (1017–1170)
Light (100–1952)	220 (164–266)	271 (223–324)	323 (253–393)
Moderate (1953–5723)	3 (1–11)	12 (4–27)	16 (6–31)
Vigorous (5724+)	0 (0–0)	0 (0–0)	0 (0–0.3)
Physical performance cutpoints			
PSE_1.99	1186 (1134–1249)	1149 (1092–1202)	1095 (1017–1170)
PL1_100.349	114 (86–130)	123 (103–144)	149 (121–177)
PL2_350.799	69 (42–88)	88 (69–108)	101 (75–127)
PL3_800.2499	32 (17–61)	63 (42–90)	73 (44–107)
PMV_2500	0.8 (0.2–4.0)	5 (1–17)	7 (2–19)

LSS, lumbar spinal stenosis; OA = knee osteoarthritis; controls, pain-free controls; PSE, performance sedentary; PL, performance light; PMV, performance moderate and vigorous.

between-group comparisons of time spent in the various Freedson and physical performance intervals. When comparing LSS to controls, all features were statistically different between groups, with the exception of Freedson moderate and heavy intervals, as well as the physical PMV interval. When comparing LSS to OA, all features were significantly different, with the exception of the Freedson heavy interval.

In Table 4, all but the maximum bout interval of 2500+ counts/minute (PMV) and maximum continuous activity above 800 counts/min (PL3) were significantly different between LSS and controls. All maximum bout and maximum continuous activity features were significant for OA vs. controls. Between LSS and OA, all but maximum bout intervals 100 to 349 (PL1) were significant.

Table 5 demonstrates that most change-point features were able to distinguish between the groups. The Figure is a visual representation of the between-group differences for change points.

Table 6 presents the sparse sets of predictive features that best differentiate pairwise between the groups. The sparse sets were as follows: LSS vs. controls had a classification accuracy of 0.80 (from 4 features); OA vs. controls had a classification accuracy of 0.83 (from 9 features); and LSS vs. OA had a classification accuracy of 0.72 (from 10 features).

Discussion

These analyses have uncovered performance phenotypes for LSS and OA from count/minute accelerometry signals. The distinct performance phenotypes for LSS and OA, as defined by the sparse set of features that we discovered, were at least 80% accurate in differentiating between the controls and either LSS or OA, and 72% accurate in differentiating between the 2 diseased populations. The majority of features identified in the sparse sets were related to sedentary and light activity,

Table 3
The p value for discriminatory power of Freedson intervals [14] and physical performance intervals [18] given age and sex

Cutpoints	p values for discriminatory power		
Freedson cutpoints	LSS versus controls	LSS versus OA	OA versus controls
Sedentary (1–99)	2.15E–04	5.67E–04	7.64E–08
Light (100–1952)	2.67E–08	2.78E–08	2.32E–13
Moderate (1953–5723)	1.42E–01	2.04E–03	1.56E–10
Vigorous (5724+)	4.62E–01	1.72E–01	1.59E–06
Physical performance cutpoints			
PSE_1.99	2.15E–04	5.67E–04	7.64E–08
PL1_100.349	1.23E–10	2.08E–04	2.66E–72
PL2_350.799	6.26E–05	4.57E–07	5.00E–04
PL3_800.2499	3.26E–03	1.52E–07	1.70E–07
PMV_2500	2.18E–01	5.93E–03	1.35E–12

LSS, lumbar spinal stenosis; OA, knee osteoarthritis; controls, pain-free controls; PSE, performance sedentary; PL, performance light; PMV, performance moderate and vigorous.

Rather than stratifying patients into groups by age and sex and conduct pairwise *t* tests, we conduct logistic regressions with age, sex, and one of the features (sedentary, moderate, etc.) to directly condition on age and sex. The p values are reported for the logistic regression coefficient associated to the feature (sedentary, moderate, etc.).

Table 4
Maximum bouts and maximum continuous activity (minutes)

Maximum bouts and maximum continuous activity				p values for discriminatory power		
Maximum bouts	LSS	OA	Controls	LSS versus controls	LSS versus OA	OA versus controls
mxbPSE_1.99	360 (202–472)	394 (349-440)	448 (398-504)	1.23E−10	1.51E−06	9.11E−48
mxbPSE_100.349	5.1 (4.6–5.9)	5.1 (4.6–5.7)	6.3 (5.4–7.2)	1.23E−10	6.36E−01	5.60E−132
mxbPSE_350.799	4.4 (3.5–5.1)	4.4 (3.9–5)	4.7 (4.1–5.6)	2.41E−03	4.48E−02	8.74E−17
mxbPSE_800.2499	4.0 (2.6–5.7)	5.7 (4.3–7.9)	5.7 (4.3–7.6)	1.62E−02	2.19E−05	5.71E−06
mxbPSE_2500	0.6 (0.2–1.3)	1.9 (0.7–6)	2.0 (1–4.6)	3.78E−01	1.15E−02	2.12E−16
Maximum continuous activity						
mca100	28 (19–40)	39 (29–53)	45 (33–64)	6.40E−05	1.21E−05	2.25E−03
mca350	15 (10–23)	23 (16–34)	23 (16–34)	5.20E−03	1.79E−06	1.20E−08
mca800	6.3 (3.8–13)	13 (7.9–21)	13 (7.9–19)	1.16E−01	6.86E−05	1.15E−19

mxb, maximum bout; mca, maximum continuous activity; LSS, lumbar spinal stenosis; OA, knee osteoarthritis; controls, pain-free controls.

confirming the need for an increased focus on the light range of physical performance when examining physical activity for LSS and OA (vs. the traditional focus on moderate-vigorous physical activity). Most important, we anticipate that performance phenotypes such as these can serve as objective disease-specific metrics for future LSS and OA research. Defining unique performance phenotypes will be an important first step toward developing disease-specific physical activity recommendations and other precision health interventions for OA and LSS.

With disease-specific physical activity recommendations in mind, it is important to recognize that discriminating between the pain-free controls (from NHANES) and the 2 mobility-limited populations, LSS and OA (from LSSAD and OAI, respectively), features of light activity were the most discriminatory and comprise the majority of the features in the sparse sets. The importance of examining light intensity activity is confirmed by other recent work in LSS and OA. For example, a recent study demonstrated that a focus on light activity is most appropriate for people with LSS [10], and several recent studies from the OAI showed

Table 5
Change points: Number of times in a day a person changed between intensity ranges

Change points				p values for discriminatory power		
	LSS	OA	Controls	LSS versus controls	LSS versus OA	OAI versus controls
X11	1111 (1052–1184)	1061 (997–1126)	1002 (918–1086)	1.03E−04	1.02E−04	8.39E−07
X12	48 (40–58)	52 (43–60)	54 (45–64)	1.03E−04	2.01E−02	1.86E−23
X13	18 (13–23)	23 (19–26)	22 (18–26)	2.42E−01	7.57E−08	8.57E−31
X14	6.2 (3.3–10)	9.7 (6.9–13)	10 (6.7–14)	7.74E−01	9.41E−07	5.62E−51
X15	0.1 (0–0.3)	0.2 (0–0.4)	0.5 (0.2–1)	6.81E−03	4.05E−01	8.48E−08
X21	50 (41–57)	52 (44–60)	55 (46–65)	7.82E−05	1.43E−02	1.20E−23
X22	35 (26–44)	37 (29–46)	52 (39–65)	5.22E−12	5.78E−02	1.84E−122
X23	18 (13–24)	22 (17–28)	26 (20–34)	2.26E−06	4.92E−05	1.02E−26
X24	6.5 (3.7–11)	10 (7.4–13)	12 (7.8–17)	1.07E−03	9.73E−09	3.13E−06
X25	0 (0–0.2)	0.2 (0–0.6)	0.4 (0.1–1)	3.33E−03	1.45E−02	1.11E−02
X31	19 (14–23)	23 (19–26)	22 (18–26)	5.28E−01	8.03E−07	7.48E−34
X32	18 (14–24)	22 (18–28)	27 (20–34)	1.28E−06	2.19E−05	1.12E−28
X33	20 (11–29)	25 (18–33)	30 (21–41)	7.82E−05	2.23E−04	5.95E−15
X34	8.4 (3.9–15)	16 (10–22)	18 (11–27)	5.95E−04	1.02E−07	2.49E−03
X35	0.1 (0–0.3)	0.4 (0.2–0.9)	0.7 (0.3–1.6)	6.81E−03	7.94E−03	3.77E−01
X41	6.2 (3.3–9.7)	9.4 (6.7–12)	10 (6.5–13)	4.43E−01	1.26E−07	2.92E−51
X42	6.2 (3.8–11)	11 (7.7–14)	12 (7.9–17)	1.33E−03	9.73E−09	4.32E−07
X43	8.0 (3.8–15)	16 (10–22)	18 (11–27)	1.15E−03	2.45E−07	3.15E−03
X44	11 (4.2–20)	23 (14–39)	27 (15–46)	6.81E−03	8.84E−06	2.64E−04
X45	0.3 (0–1.4)	1.7 (0.5–4.0)	2.5 (0.8–5.7)	3.01E−01	2.01E−02	2.24E−04
X51	0 (0–0.3)	0.2 (0–0.4)	0.5 (0.2–1.1)	4.16E−04	6.04E−01	9.40E−19
X52	0 (0–0.2)	0.2 (0–0.6)	0.5 (0.1–1.0)	6.92E−03	1.43E−02	9.49E−02
X53	0.1 (0–0.3)	0.4 (0.1–1)	0.8 (0.3–1.7)	9.01E−03	6.24E−03	3.67E−01
X54	0.3 (0–1.3)	1.7 (0.5–4.1)	2.4 (0.8–5.5)	3.22E−01	2.01E−02	6.68E−05
X55	0 (0–0.7)	1.9 (0.2–10)	1.9 (0.3–8.5)	4.40E−01	1.15E−02	3.25E−16

LSS, lumbar spinal stenosis; OA, knee osteoarthritis; controls, pain-free controls.
For example, X21, change from PL2 to PL1; 1, PL1; 2, PL2; 3, PL3; 4, PMV; 5, PSE.

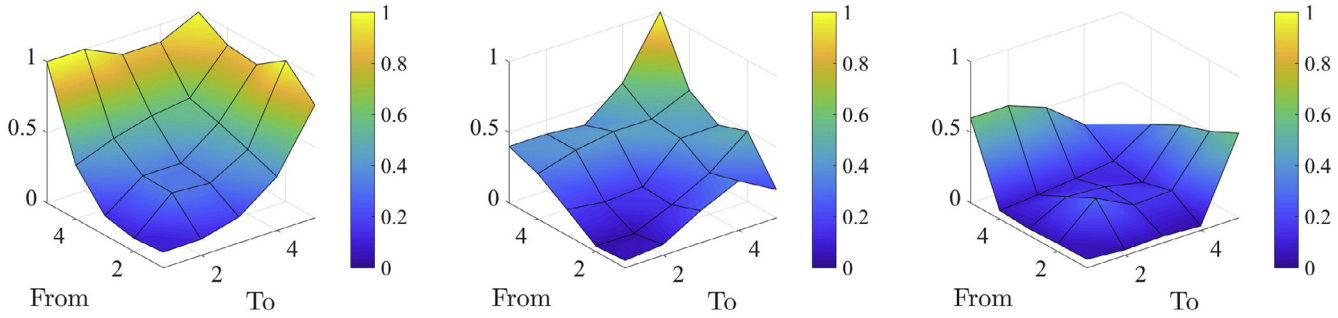

Fig. Between-group differences for change points. (Left) LSS-NHANES; (Middle) LSS-OA; (Right) OA-NHANES. (To, from) pairs correspond to change points. For example, (1, 2) corresponds to X12. Heights at each location represent the absolute differences between groups for each change point. The higher the point, the larger the difference between groups for that change point.

that time spent in light activity and sedentary behavior are related to disability and function, independent of moderate-to-vigorous activity [9,15,16,34]. Combined, these findings highlight an opportunity for new recommendations for OA and LSS aimed at decreasing sedentary time and increasing physical activity, starting with the light range.

Performance phenotype for LSS

Individuals with LSS were shown to be the least active, spending the majority of their time in the sedentary ranges. In particular, the maximum bouts in light activity were notably smaller in LSS compared with both OA and controls. These results suggest that people with LSS are not maintaining comparative levels of continuous movement, even in the light range of activity. When comparing LSS to controls, all features were statistically different between groups, with the exception of the moderate-to-vigorous activity intervals. Similarly, when comparing LSS to OA, all features were different between groups, with the exception of the Freedson vigorous activity interval. These findings highlight the importance of focusing on light activity in people with LSS. This is corroborated by an earlier LSS study that found 99.6% of nonsedentary time was spent in light activity, with just over half of that in PL1 (the lowest of light intensities) [10]. Based on these findings, 1 practical implication is that physical activity interventions in LSS are likely to be more successful and appropriate when focused on decreasing sedentary time with increases in the volume of light intensity physical activity before considering the increases in moderate-to-vigorous intensity activity (which is the traditional starting point for physical activity recommendations).

Performance phenotype for OA

People with knee OA participate in less activity compared with healthy individuals, but are more active than people with LSS. Similar to LSS, people with OA appear to spend the majority of their time in the sedentary range. However, the OA individuals participated in significantly more light activity compared with LSS, including all ranges of light activity. In particular, these results suggest that people with OA are more likely than those with LSS to

Table 6
Sparse sets of selected features, coefficients, and classification accuracy for differentiating between the 3 populations: LSS, OA, and controls

LSS versus controls			OA versus controls			LSS versus OA		
	Coefficients			Coefficients			Coefficients	
	Standardized	Actual		Standardized	Actual		Standardized	Actual
X22	0.949	0.0424	X22	0.786	0.0390	mxbPSE_1.99	0.233	0.0031
mxbPSE_1.99	0.505	0.00499	mxbPL1_100.349	0.611	0.3873	X42	0.232	0.0504
mxbPL1_100.349	0.308	0.1743	mxbPSE_1.99	0.393	0.0044	mxbPL3_800.2499	0.173	0.0473
X51	0.0016	0.0023	X51	0.252	0.4089	mca350	0.145	0.0094
			mxbPSE_2500	−0.013	−0.0020	X13	0.126	0.0219
			mca800	−0.018	−0.0015	mxbPSE_2500	0.113	0.0154
			X55	−0.025	−0.0022	X41	0.108	0.0253
			X41	−0.086	−0.0185	X12	0.101	0.0082
			X31	−0.368	−0.0610	X34	0.053	0.0057
						X24	0.034	0.0076
Classification accuracy with age and gender								
		80%			83%			72%

LSS, lumbar spinal stenosis; OA, knee osteoarthritis; controls, pain-free controls; mxb, maximum bout; mca, maximum continuous activity; X31, change-point performance from PL3 to PL1.

participate in greater volumes, and longer bouts of activity in the higher ranges of light intensity activity, given the average time in PL3 (63 minutes) was almost double that of LSS (32 minutes). People with OA were also significantly more active in the moderate range compared with LSS (5 minutes vs. 0.8 minutes), although still not close to recommended amounts of moderate activity for nonpain populations. A practical implication of these findings is that the optimal place to begin when designing physical activity recommendations for people with OA is to focus on physical activity in the higher end of the light activity intensity range in combination with some increases in moderate activity.

Measurement implications

Results of this study highlight the utility of accelerometers in spine and musculoskeletal disease research. Although many previous studies using activity monitors showed no or little differences between populations with painful spine and musculoskeletal populations and controls using traditional methods [18], this study reveals that analyses that are tuned for the specific population are better able to produce new insights. In fact, in this study the traditional methods of activity stratification based on energy expenditure (Freedson intervals) did not perform as well as the newer activity stratification that was designed for people with mobility limitations from musculoskeletal pain (physical performance intervals). The best evidence of this comes from the predictive sparse sets that only include features from physical performance intervals, and none from the Freedson intervals. Most likely, the physical performance intervals were superior to the traditional methods because they provide more discrimination in light activity range, where real-life daily disability from musculoskeletal pain is manifested. Additionally, the introduction of change-point analysis proved very useful. This analysis introduces the component of time and helped effectively differentiate between the groups with LSS and OA. This is most likely caused by different patterns of physical limitations caused by the 2 different conditions.

Limitations

This analysis was limited to the variables available from the datasets that were used: OAI, LSSAD, and NHANES. As a result, results can only be generalized to individuals who meet the inclusion criteria for these studies. However, the LSSAD included a heterogeneous group of individuals with LSS in terms of age and disease impact. Similarly, the selection criteria that we used for the OAI ensured that this study includes people with a range of knee OA severity. Also, the pain-free controls come from the NHANES study that is representative of the US population. However, given that not all participants in the source studies were included in this analysis, there is potential for selection bias and confounding. We did provide a comparison of available variables between those included and those not and found no statistically significant differences. However, this does not preclude recruitment bias or confounding by other clinical or demographic variables not reported in the sources studies. Although all 3 datasets provide rigorously obtained and validated accelerometry data, this data exists in the counts/minute form, and thus these results apply only to count/minute accelerometry signals and not to accelerometry data at lower or higher sampling rates. Finally, we recognize that this is the first step in defining clinically valid performance phenotypes for these populations. Further validation including comparison against prospectively collected external cohorts is necessary before definitive clinical implications can be drawn.

Conclusions

Using accelerometry data from 3 large existing datasets, and novel analytical methods, we discovered disease-specific performance phenotypes for LSS and OA. These performance phenotypes, representing signatures of free-living physical activity, were revealed using novel data-driven features. The sparse set of features that represent these performance phenotypes is able to differentiate clearly between LSS, OA, and healthy controls. The distinct performance phenotypes for LSS and OA were at least 80% accurate in differentiating between the controls and either LSS or OA, and 72% accurate in differentiating between the 2 diseased populations. Our results indicate that, contrary to existing general activity guidelines that focus on moderate and vigorous activity, focusing on increasing light activity may be more appropriate for mobility-limited populations. This study provides disease-specific performance phenotypes for future LSS and OA research, and a much-needed framework for a personalized approach to improving function in OA and LSS.

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