Ambulatory Stride Variability Measured by a Wearable Device is a Biomarker for Chronic Pain Severity

Shai N. Gozani, MD, PhD and Xuan Kong, PhD; NeuroMetrix Inc., Waltham, MA, USA

PURPOSE

A biomarker is a measurable indicator of the severity or presence of a disease. Chronic pain is a complex biopsychosocial phenomenon that is difficult to manage, partially due to the lack of practical biomarkers to individualize treatment. Biomarkers for chronic pain based on brain imaging and genetics have been explored with some success. Other physiologic functions such as sleep, autonomic regulation and gait can be quantitatively and more easily measured. They are altered by chronic pain, and therefore represent potential biomarkers. However, single measurements at clinic visits are inadequate for this purpose due to lack of specificity and high variability.

Wearable technology has emerged over the past decade to provide convenient tracking of fitness and health parameters, primarily in the form of pedometers worn on the wrist. Recently, monitoring capabilities have expanded to include more complex functions such as sleep time and quality, heart rate variability and gait characteristics such as stride variability. By providing nearly continuous physiologic tracking, these wearable technologies may have a role as practical chronic pain biomarkers. However, the clinical utility of real-world biometric measurements, as opposed to their traditional acquisition in research settings, is still an open question.

In this study, we evaluated the utility of stride variability, obtained in a real-world setting with a wearable device, as a biomarker for chronic pain severity.

METHODS

Study Design and Subject Selection. De-identified data were collected from users of a wearable device to treat chronic pain (Quell®, NeuroMetrix, Waltham, MA) during an 8-month period (1/2017-8/2017). The device delivers high-frequency TENS and monitors physiologic functions. The device and its smartphone app collect and store demographic data, clinical information, and biometrics. Subjects rated 24-hour pain intensity and interference with activity, sleep and mood on an 11-point (0—10) scale using the app. Interference was analyzed as a composite average of the three. Inclusion criteria were devices users who (i) provided demographic and clinical information, (ii) had 5 or more days of gait and pain data, and (iii) consented to use of their anonymized data for clinical research purposes.

Stride Variability Measurements. The device is worn on the upper calf and has an accelerometer that monitors leg movement. Stride time is the interval between sequential toe-off events and stride variability is the ratio between the standard-deviation and mean of stride time, expressed as percentage. Stride variability is calculated for each walk segment of ≥30 consecutive strides and is defined per 24-hour period as the minimum among all segments. Users with low mobility or who use the device only while resting do not generate gait data.

Data Analysis. For each subject, pain intensity, pain interference and stride variability were defined as the median over the study period. Subjects were stratified into low (≤3%), intermediate (3-5%) and high (≥5%) stride variability groups. Differences among the group distributions of gender, age, body mass index (BMI), pain duration, number of health conditions, and pain sites, pain intensity, and pain interference, were evaluated by one-way ANOVA and two-sample t-test for post-hoc analyses. The effect size for low versus high variability was quantified by Cohen's d.

Table 1. Demographic and Pain Characteristics of Device Users (N=1422)

Female: N (%)	787 (55%)
Age (yrs):	57 ± 14 [19-96]
BMI (kg/m^2)	30 ± 6
Pain Duration ≥ 3 Years: N (%)	975 (69%)
No. Painful Health Conditions	3.5 ± 2.0
No. Pain Sites	4.7 ± 2.4
Pain Intensity	5.4 ± 2.1
Composite Pain Interference	4.7 ± 2.4

Mean and standard deviation are shown unless indicated otherwise.

Table 2. Analysis Results Grouped by Stride Variability

	Stride Variability		
	Low	Intermediate	High
User Count: N (%)	620 (44%)	736 (52%)	66 (5%)
Female: N (%)*	272 (44%)	471 (64%)	44 (67%)
Age (yrs)*	55 ± 13	58 ± 14	62 ± 14
BMI	30 ± 6	30 ± 6	30 ± 7
Pain Duration ≥ 3 Years (%)	65%	71%	74%
No. Painful Health Condition*	3.2 ± 1.9	3.7 ± 2.1	4.2 ± 2.4
No. Pain Site*	4.5 ± 2.3	4.9 ± 2.5	5.4 ± 3.0
Pain Intensity*	5.3 ± 2.0	5.5 ± 2.0	6.0 ± 2.2
Composite Pain Interference*	4.6 ± 2.4	4.8 ± 2.4	5.4 ± 2.5

* Group means or percentage are statistically different (p<0.01).

RESULTS

Table 1 gives summary statistics for all study subjects. Approximately equal number of subjects reported a pain duration of <3 years, 3-10 years, and >10 years. The most frequently reported painful health conditions were arthritis (62%) and back injury (41%). The most common pain sites were low back (79%), legs (72%), and hips (57%). The stride variability was 3.3%±0.9% (range 1.6-7.6%).

Table 2 summarizes demographic and pain characteristics of study subjects by stride variability. There were no statistically significant differences in BMI or pain duration among groups. Subjects with high stride variability were older, more likely to be female, and had more painful health conditions and pain sites than subjects with low stride variability.

One-way ANOVA shows that group means are different between low, intermediate, high stride variability groups for pain intensity (p=0.0031) and for composite pain interference (p=0.0226). In post-hoc analyses, statistically significant differences for pain intensity were identified between the low and intermediate groups (p=0.0234) and low and high groups (p=0.0049). Statistically significant differences in pain interference were identified between the low and high groups (p=0.0159). Cohen's d was 0.39 and 0.33 between low and high groups for pain intensity and pain interference, respectively.

CONCLUSIONS

Gait is a complex neurological phenomenon mediated by automated control circuits and high level cognitive processes, particularly executive functions. Chronic pain interferes with both automated and cognitive aspects of gait. This study demonstrated that stride variability, measured with a wearable device in a real-world setting, is a potential biomarker for chronic pain severity in a heterogenous population. High stride variability (≥5%) identified subjects with statistically and clinically significant increases in the number of painful health conditions, number of pain sites, pain intensity and pain interference compared to subjects with low stride variability (≤3%).

While the underlying stride variability definition is the same as that used in laboratory settings, ambulatory measurements cannot control environmental factors which may impact gait. The daily minimum stride variability was used to reduce environmental influences, and the median of all available daily minima was used to estimate the true stride variability for each subject. More active users generally yielded more walk segments, allowing the daily minimum to approach the best achievable stride variability level for the subject. Therefore, higher activity levels may be a confounding factor in the observed relationship between stride variability and chronic pain severity.

Poster #94, Presented at PAINWeek 2017, Sep 5-9, Las Vegas, NV, USA