Poster

Sleep Phenotypes in Chronic Pain Sufferers: Application of Machine Learning to a Large Database

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Abstract

Background: Chronic pain affects over 100 million American adults. There is a negative reciprocal relationship between chronic pain and sleep. As many as 80% of chronic pain patients report poor sleep quality and daytime fatigue. We have recently reported on the clinical benefits of fixed-site high-frequency transcutaneous electrical nerve stimulation (Quell, NeuroMetrix, Inc) in a chronic pain cohort. In addition to delivering therapeutic neurostimulation, this device collects health data including utilization, sleep measures, and activity metrics. The data is communicated to the patient through a smartphone app and aggregated in a cloud server. This digital health database presents a novel opportunity to study population characteristics in a large cohort of chronic pain sufferers.

Objective: Our primary objective was to use machine learning techniques on a large database of sleep data in chronic pain sufferers to determine “sleep phenotypes.” The long-term goal of this research is to develop personalized therapeutic profiles that optimize sleep in chronic pain patients.

Methods: De-identified data from device users consenting to have their data uploaded to a cloud server was analyzed. Individual users were characterized by their median sleep data. The analyzed sleep parameters included total sleep time (TST, hours), sleep efficiency (SE, %), periodic leg movement index (PLMI, events/hour), position change rate (PCR, events/hour), and time out of bed (OOB, minutes). K-means clustering was used to partition the data set into 3 mutually exclusive clusters based on TST, PLMI, PCR, and OOB. The optimal number of clusters was determined by the Silhouette value. Clustering was based on the correlation metric. One-way ANOVA was used to test whether the 3 cluster groups had a common mean for each sleep parameter. For parameters with differences in group means, *t* test was used to identify which pairs of means were different.

Results: A total of 389 users with 5 or more nights of TST between 4 and 12 hours were included in the analysis. The sizes of the 3 clusters were 161 (41.4%), 147 (37.8%), and 81. None of the sleep parameters had the same mean among three clusters (P<.001). The 3 clusters represented 3 sleep phenotypes. The largest group (n=161) was a “good sleeper” phenotype characterized by a mean TST of 7.3, SE of 95.2, and low PLMI (2.1), PCR (1.3), and OOB (1.4). The second largest cluster was a “moderate sleeper” phenotype characterized by a mean TST of 7.4, SE of 92.4, low PLMI (3.9) and PCR (0.9), but relatively high OOB of 12.7. The third cluster was a “poor sleeper” phenotype characterized by TST of 6.6, SE of 91.2, and a high PLMI of 11.7. All pair-wise cluster means were different (P<.025), except for TST between good and moderate sleepers (P=.452).

Conclusions: We identified 3 sleep phenotypes in a large cohort of chronic pain sufferers. The phenotypes reflected a progression from good to poor sleepers. The poorer sleepers were characterized by either a large amount of time out of bed during the night or a high rate of periodic leg movements.

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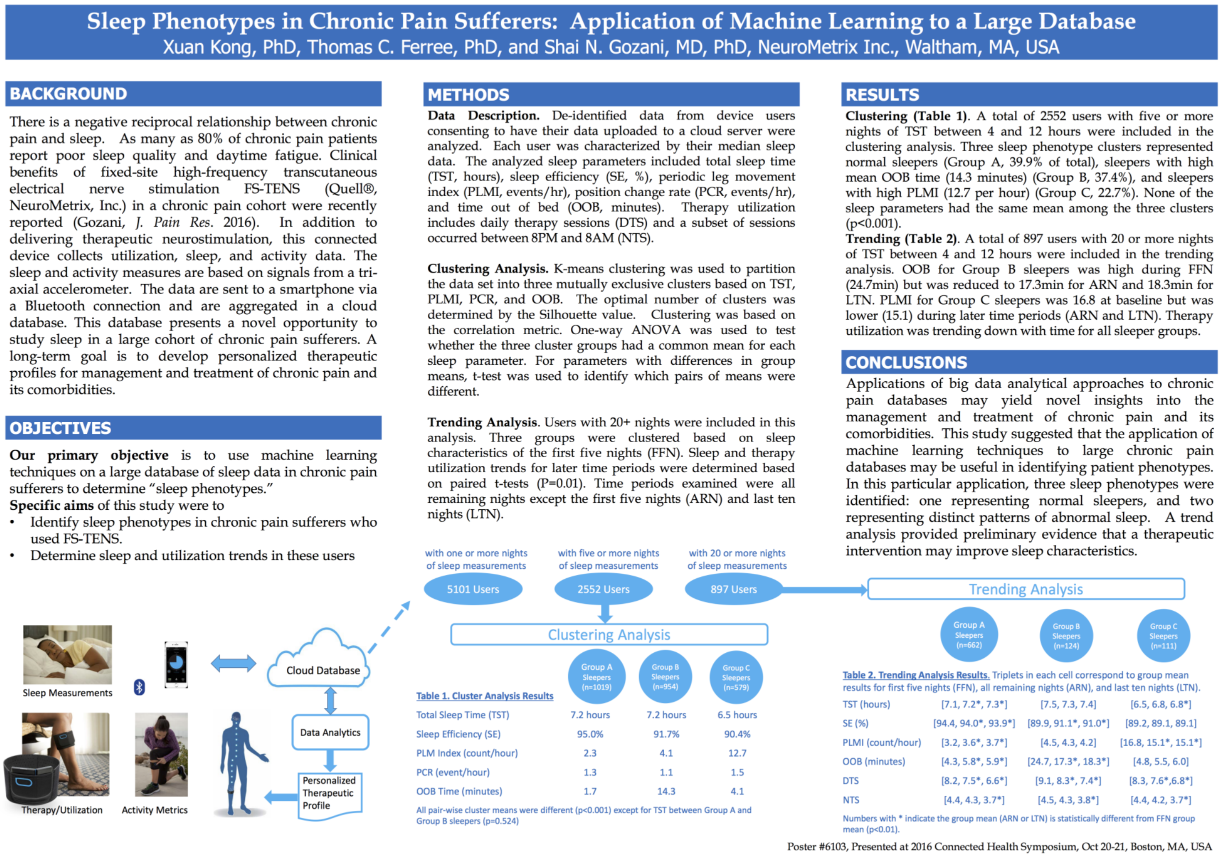
KEYWORDS

sleep phenotype; chronic pain; machine learning; clustering analysis

This poster was presented at the Connected Health Symposium 2016, October 20-21, Boston, MA, United States. The poster is displayed as an image in Figure 1 and as a PDF in Multimedia Appendix 1.

Figure 1. Poster.



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BACKGROUND

There is a negative reciprocal relationship between chronic pain and sleep. As many as 80% of chronic pain patients report poor sleep quality and daytime fatigue. Clinical benefits of fixed-site high-frequency transcutaneous electrical nerve stimulation FS-TENS (Quell®, NeuroMetrix, Inc.) in a chronic pain cohort were recently reported (Gozani, *J. Pain Res*. 2016). In addition to delivering therapeutic neurostimulation, this connected device collects utilization, sleep, and activity data. The sleep and activity measures are based on signals from a tri-axial accelerometer. The data are sent to a smartphone via a Bluetooth connection and are aggregated in a cloud database. This database presents a novel opportunity to study sleep in a large cohort of chronic pain sufferers. A long-term goal is to develop personalized therapeutic profiles for management and treatment of chronic pain and its comorbidities.

OBJECTIVES

Our primary objective is to use machine learning techniques on a large database of sleep data in chronic pain sufferers to determine "sleep phenotypes."

Specific aims of this study were to

- Identify sleep phenotypes in chronic pain sufferers who used FS-TENS.
- Determine sleep and utilization trends in these users

METHODS

Data Description. De-identified data from device users consenting to have their data uploaded to a cloud server were analyzed. Each user was characterized by their median sleep data. The analyzed sleep parameters included total sleep time (TST, hours), sleep efficiency (SE, %), periodic leg movement index (PLMI, events/hr), position change rate (PCR, events/hr), and time out of bed (OOB, minutes). Therapy utilization includes daily therapy sessions (DTS) and a subset of sessions occurred between 8PM and 8AM (NTS).

Clustering Analysis. K-means clustering was used to partition the data set into three mutually exclusive clusters based on TST, PLMI, PCR, and OOB. The optimal number of clusters was determined by the Silhouette value. Clustering was based on the correlation metric. One-way ANOVA was used to test whether the three cluster groups had a common mean for each sleep parameter. For parameters with differences in group means, t-test was used to identify which pairs of means were different.

Trending Analysis. Users with 20+ nights were included in this analysis. Three groups were clustered based on sleep characteristics of the first five nights (FFN). Sleep and therapy utilization trends for later time periods were determined based on paired t-tests (P=0.01). Time periods examined were all remaining nights except the first five nights (ARN) and last ten nights (LTN).

RESULTS

Clustering (Table 1). A total of 2552 users with five or more nights of TST between 4 and 12 hours were included in the clustering analysis. Three sleep phenotype clusters represented normal sleepers (Group A, 39.9% of total), sleepers with high mean OOB time (14.3 minutes) (Group B, 37.4%), and sleepers with high PLMI (12.7 per hour) (Group C, 22.7%). None of the sleep parameters had the same mean among the three clusters ($p<0.001$).

Trending (Table 2). A total of 897 users with 20 or more nights of TST between 4 and 12 hours were included in the trending analysis. OOB for Group B sleepers was high during FFN (24.7min) but was reduced to 17.3min for ARN and 18.3min for LTN. PLMI for Group C sleepers was 16.8 at baseline but was lower (15.1) during later time periods (ARN and LTN). Therapy utilization was trending down with time for all sleeper groups.

CONCLUSIONS

Applications of big data analytical approaches to chronic pain databases may yield novel insights into the management and treatment of chronic pain and its comorbidities. This study suggested that the application of machine learning techniques to large chronic pain databases may be useful in identifying patient phenotypes. In this particular application, three sleep phenotypes were identified: one representing normal sleepers, and two representing distinct patterns of abnormal sleep. A trend analysis provided preliminary evidence that a therapeutic intervention may improve sleep characteristics.

Table 1. Cluster Analysis Results

	Group A Sleepers (n=1019)	Group B Sleepers (n=954)	Group C Sleepers (n=579)
Total Sleep Time (TST)	7.2 hours	7.2 hours	6.5 hours
Sleep Efficiency (SE)	95.0%	91.7%	90.4%
PLM Index (count/hour)	2.3	4.1	12.7
PCR (event/hour)	1.3	1.1	1.5
OOB Time (minutes)	1.7	14.3	4.1

All pair-wise cluster means were different ($p<0.001$) except for TST between Group A and Group B sleepers ($p=0.524$)

Table 2. Trending Analysis Results. Triplets in each cell correspond to group mean results for first five nights (FFN), all remaining nights (ARN), and last ten nights (LTN).

	Group A	Group B	Group C
TST (hours)	[7.1, 7.2*, 7.3*]	[7.5, 7.3, 7.4]	[6.5, 6.8, 6.8*]
SE (%)	[94.4, 94.0*, 93.9*]	[89.9, 91.1*, 91.0*]	[89.2, 89.1, 89.1]
PLMI (count/hour)	[3.2, 3.6*, 3.7*]	[4.5, 4.3, 4.2]	[16.8, 15.1*, 15.1*]
OOB (minutes)	[4.3, 5.8*, 5.9*]	[24.7, 17.3*, 18.3*]	[4.8, 5.5, 6.0]
DTS	[8.2, 7.5*, 6.6*]	[9.1, 8.3*, 7.4*]	[8.3, 7.6*,6.8*]
NTS	[4.4, 4.3, 3.7*]	[4.5, 4.3, 3.8*]	[4.4, 4.2, 3.7*]

Numbers with * indicate the group mean (ARN or LTN) is statistically different from FFN group mean ($p<0.01$).

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Multimedia Appendix 1

Poster.

[PDF File (Adobe PDF File), 226KB-Multimedia Appendix 1]

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