Detecting clinically significant depressive burden in sleep clinics through physiological parameters: Preliminary data as to sleep stages and heart rate

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INTRODUCTION

Due to the powerful link between sleep and mood regulation, polysomnography (PSG) research has largely contributed to investigating psychobiological mechanisms of depression. Studies have focused on the imbalanced sleep architecture which is considered a hallmark of major depressive episode (MDE)[1], and autonomic nervous system function, reporting a reduced parasympathetic activity, stronger under conditions of sleep[2–4].

In this brief report, we present preliminary data from our ongoing clinical study, designed to develop MEB-001, a software medical device based on a machine learning algorithm used to aid in identifying a clinically significant burden of depressive symptoms (CDB) in individuals referred to sleep clinics (SCs) for a full-night sleep study. MEB-001 processing includes the calculation of sleep stages, resting heart rate (HR), and heart rate variability (HRV) indexes.

These preliminary analyses aimed to compare sleep features and HR/HRV between subjects with (CDB+) and without CDB (CDB-) to identify those physiological parameters able to discriminate between the two groups.

MATERIALS AND METHODS

We are carrying out a single-arm, prospective, multicenter study conducted under a common protocol in SCs across the United States. Inclusion criteria: subject 1) aged ≥22 years and ≤75 years; 2) undergoing a PSG due to suspected primary or secondary sleep disorders; 3) willing and able to provide the informed consent; 4) able to read and understand the instructions for the study; 4) willing to adhere to study procedures; 5) willing to undergo a full night PSG study, as prescribed by the referring physician. Exclusion criteria: subject 1) with a pacemaker; 2) has undergone heart transplant; 3) is undergoing a C-PAP titration study.

CDB was defined through the Patient Health Questionnaire – 9 items (PHQ9)[5] at the cut-point score of ≥ 10, corresponding to moderate to severe depressive symptoms, and considered the cut-off for the likelihood of a current major depressive episode (sensitivity and specificity ranging from 0.64 to 0.85 and from 0.85 to 0.89, respectively[6]).

Statistical analysis: analysis of covariance was applied to test mean differences in the HR/HRV and sleep parameters between the two groups (CDB+ vs CDB-). Significance level was set at 0.05. The R programming language version 3.6.2[7] was used to perform the statistical analyses.

RESULTS

243 subjects (153 CDB- and 90 CDB+) referring to the different SCs for sleep complaints were consecutively recruited and analyzed.

Differences between the two groups in demographic and clinical features, and PSG, HR/HRV parameters are described in Table 1 and Table 2, respectively.

CONCLUSION

Our preliminary results suggest a greater brain activity during early sleep stages in subjects with CDB, as shown by the increased sleep deepening latency and brain excitability during light sleep, and earlier awakening onset. These findings are in line with the observed decrease of deep sleep and the increased sleep fragmentation revealed by previous studies[1,8].

In addition, subjects with CDB showed a general increase in sympathetic activity, and decreased parasympathetic activity in N2 and N3 stages, as previously reported[2–4]. The main limitation of our preliminary analyses is the small sample size, which reduces the statistical power to detect differences between groups (Type II error) and does not allow considering multiple potential confounding variables. However, our data shed light on the possibility to optimize the use of PSG to identify through objective parameters the CDB among individuals referred to SCs for sleep disturbances.

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Table 1. Demographic and clinical features of the sample

	Subjects CBD * (n 153)	Subjects CBD+ ** (n 90)	t-test/Fisher's exact test; p-value
age, years; m±sd	50.93±13.73	38.83±13.90	6.58; < .001
gender, female; n (%)	68 (44.4)	60 (66.7)	< .001
education, years; m±sd	14.6±2.16	13.39±1.72	-4.49; < 0.01
BMI; m±sd	33.09±8.45	35.49±10.67	1.92; 0.28
antidepressant medications, yes; n (%)	39 (25.5)	52 (57.8)	< .001
current cardiac diseases, yes; n (%)	41 (26.8)	9 (10)	< .001

BMI, body mass index; CDB-, subjects with clinically significant burden of depressive symptoms; CDB+, subjects without clinically significant burden of depressive symptoms; m, mean; n, number; sd, standard deviation; %, percentage; * PHQ9<10; **PHQ9≥10 (from moderate to severe depressive symptoms)

Table 2. PSG, HR and HRV parameter comparison between subjects with and without CDB

	Subjects CBD * (n 153)	Subjects CBD+ ** (n 90)	p-value
Sleep architecture removing (m±sd)			
N2 latency, seconds; m±sd	28.97±24.07	37.13±30.03	.02
WASO, minutes; m±sd	58.81±40.54	48.2±36.52	.04
alpha/beta 1 ratio, relative power***	3.02±1.37	2.44±1.08	.02
alpha/beta 2 ratio, relative power***	4.62±2.63	3.66±2.05	.02
HR-HRV (m±sd)			
N3 stage			
HR, beats/minute	66.73±11.63	73.3±10.98	.02
SDNN, ms	32.87±15.81	31.35±15.25	.04
RMSSD, ms	31.11±21.26	29.29±19.84	.02
pNN20, %	39.23±25.93	35.88±25.82	.02
REM stage			
HR, beats/minute	67.29±10.96	73.09±10.36	.02
N2 stage			
HR, beats/minute	65.3±10.7	71.47±10.47	<.01
SDNN, ms	42.22±15.4	40.3±15.47	.02
RMSSD, ms	32.16±18.54	30.82±16.46	.01
pNN20, %	40.93±22.45	39.93±22.72	.02
pNN50, %	14.17±16.45	13.54±15.17	.03
HF power, ms²	593.73±741.96	531.02±576.9	.01
WAKE			
HR, beats/minute	69.61±12.1	75.75±10.37	.01

CDB-, subjects with clinically significant burden of depressive symptoms; CDB+, subjects without clinically significant burden of depressive symptoms; m, mean; ms, milliseconds; n, number; HF, absolute power of the high-frequency band (0.15–0.4 Hz); HR, heart rate; HRV, heart rate variability; pNN20, percentage of successive RR † intervals that differ by more than 20 ms; pNN50, percentage of successive RR † intervals that differ by more than 50 ms; PSG, polysomnography; REM, rapid eye movement; RMSSD, root mean square of successive RR † interval differences; sd, standard deviation; SDNN, standard deviation of NN ◊ intervals;

WASO, wakefulness after sleep onset; %, percentage. * PHQ9<10; **PHQ9≥10 (from moderate to severe depressive symptoms); ***calculated from 'light off' to N2 stage. ◊ NN intervals, interbeat intervals from which artifacts have been removed; † RR intervals, interbeat intervals between all successive heartbeats.