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Depressive symptoms and sleep: A population-based polysomnographic study

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ABSTRACT

The goals of the present study were to determine the prevalence of depression in the adult population of Sao Paulo, Brazil and to explore the relationship among sociodemographic, physical and psychological factors, sleep-related symptoms and polysomnography parameters. Participants of a cross-sectional study ($N=1101$) were administered questionnaires and submitted to polysomnography. A score >20 in the Beck Depression Inventory was used to describe depression. Results revealed that the prevalence of depression was 10.9%. Estimates were higher in women and were significantly higher among housewives, non-workers and individuals with lower education and income. A combination of sleep-related symptoms and impaired quality of life was 2.5 times more frequent among depressed than non-depressed. Co-morbid insomnia and anxiety were positively associated to depressive symptomatology. There were no alterations in the polysomnography parameters, in either group. The occurrence of sleep apnea with values on the apnea-hypopnea index ≥ 5 was similar and frequent in both groups (around 30%). The findings suggest that depressive symptoms were associated with low education, low income, severe comorbid symptomatology, and impaired quality of life. Considering the high prevalence of sleep apnea, these results point to potential social and financial burdens associated with the depressive symptomatology and various sleep diagnoses.

1. Introduction

Depression has an estimated 12-month prevalence of 6.6% and lifetime prevalence of 16.2% (Kessler et al., 2003, 2005a, 2005b), it is a significant cause of disability and places a burden on society from both economic and social perspectives (Kessler et al., 2005b).

Comorbid depression is related to significant worsening of existing medical conditions, resulting, for example, in an eight-fold increase in mortality among congestive heart failure patients (Barth et al., 2004, Yates et al., 2004) and a 2.3-fold increase in mortality among type-2 diabetes patients (Katon et al., 2005). On the other hand, sleep-related breathing disorder (SRBD) was shown to increase the risk of developing depression (Peppard et al., 2006, Wheaton et al., 2012).

Common symptoms in depression and general medical conditions are obstacles to establish one diagnosis in the presence of the other. Among the most challenging overlapping complaints are sleep disturbances, such as insomnia or hypersomnia (Ong et al., 2009, Harris et al., 2009). The greater part of depressed individuals report dysfunctional sleep, and sleep disturbance is particularly often the issue that makes patients seek medical help (Mendlewicz, 2009).

Despite the fact that the symptoms of SRBD are similar to the neuro-vegetative features of depression (Ohayon, 2003), sleep problems in depressed individuals are rarely followed by objective sleep evaluations using an overnight polysomnography (PSG). In this regard, PSG evaluations may help to identify sleep issues in depressed patients from a positive history of SRBD (Kushida et al., 2005).

Some symptoms, such as fatigue and sleepiness, usually thought of as indicative of SRBD, may be more likely caused by depression (Harris et al., 2009). Indeed, previous studies have not observed strong associations between SRBD and fatigue or sleepiness (Gottlieb et al., 1999, Kapur et al., 2005). Only a few PSG studies examining the relationship between depression and sleep disorders have been performed, and these studies were usually based on small samples of patients with major depressive disorder (MDD) (Ong et al., 2009,

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Reynolds et al., 1982, Reynolds et al., 1985). There was only one large population-based study, but that did not employ PSG evaluation (Ohayon, 2003).

The Sao Paulo Epidemiologic Sleep Study (Santos-Silva et al., 2009) was implemented to establish the profile of sleep disorders in the adult population of the city of Sao Paulo, Brazil and to examine associations with a vast range of indicators including mood scales. This study examined the frequency of depressive symptoms in the general population, and compared demographic and sleep characteristics, including PSG evaluations, between individuals classified as depressed and non-depressed.

2. Methods

2.1. Setting and participants

A survey was conducted in the adult population of Sao Paulo from July to December of 2007 using a three-stage probabilistic cluster sampling procedure (Korn and Graubard, 1999) to proportionally select a pool of participants according to gender, age (20–80 years) and socioeconomic status. A sample size of 1101 volunteers was determined as allowing for prevalence estimates with 3% precision (Korn and Graubard, 1999). First, 96 districts were proportionally selected from the 1500 that are used to divide Sao Paulo into four homogeneous socioeconomic regions for census purposes (IBGE, 2000). Next, 11 homes from each district were selected. Finally, one individual from each home was randomly selected. If we were unable to contact the individual after three attempts, the home was replaced using the previously established criteria. Pregnant or breastfeeding women and individuals with disabilities who required outside care were excluded. The study protocol was approved by the Ethics Committee for Research of the Universidade Federal de Sao Paulo-UNIFESP (CEP 0593/06) and registered with ClinicalTrials.gov (Identifier NCT00596713). Participants signed written informed consents. The detailed methodology has been previously described (Santos-Silva et al., 2009).

2.2. Procedures

2.2.1. Questionnaires

We used the following questionnaires: the Brazilian Criterion of Economic Classification (ABEP, 2003), the UNIFESP Sleep Questionnaire (Braz et al., 1987), the Pittsburgh Sleep Quality Index (PSQI) (Buysse et al., 1989), the Insomnia Severity Index (ISI) (Bastien et al., 2001), the World Health Organization Quality of Life (WHOQOL-BREF) (Skevington et al., 2004), the Chalder Fatigue Scale (CFS) (Chalder et al., 1993), the Beck Anxiety Inventory (BAI) (Beck et al., 1988) and the Beck Depression Inventory (BDI) (Beck et al., 1961).

2.2.2. PSG

Full in-lab PSG was recorded through a digital system device (EMBLA® S7000, Embla Systems, Inc., Broomfield, CO, USA) during the participants' habitual sleep time. Standard montage and criteria for scoring sleep stages were used (Rechtschaffen and Kales, 1968). Arousals, leg movements and respiratory events were scored according to the guidelines from the *American Academy of Sleep Medicine* (Iber et al., 2007).

2.3. Assessments

2.3.1. Depression criteria

The BDI was used to screen depressive symptoms. Its 21 items relate to symptoms of depression such as sadness and loss of interest, thoughts such as guilt or feelings of being punished, as well as physical symptoms such as fatigue, weight loss, sleep disturbance and lack of interest in sex. Each symptom was rated by the respondents on a 0–3 scale, with 0 representing "absence" and 1–3 representing increasing levels of symptoms severity. The BDI yields a total score ranging from 0 to 63, with higher scores indicating greater levels of depressive symptoms. Subjects scoring below 20 were considered as "non-depressed", whereas those scoring above 20 are considered as "depressed" and included as cases for the estimation of the prevalence of "probable major depression" in Sao Paulo. BDI is the most frequently used instrument to assess depressive symptoms in the psychiatric and sleep literature, and it has been validated in different populations since its first publication in 1961 (Beck et al., 1961, Clark et al., 1983, 1997, Johnson et al., 1996, Campbell et al., 1984, Lisspers et al., 1997, Lasa et al., 2000, Kendall et al., 1987).

2.3.2. Reported symptoms

The definitions of the various symptoms are as follows. *Insomnia*: based on the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* (DSM-IV) general criteria (First et al., 2004), items from the questionnaires were combined for difficulty initiating or maintaining sleep, or early morning awakening that persisted for six months and occurred in the last month, with frequencies of at least three times a week and with extreme interference of daily functioning (First et al., 2004), *Nightmares*: report of waking up anxious after a nightmare in the past 6 months at more than once a week (Braz et al., 1987), *Non-Restorative Sleep*: reports of tiredness upon awakening independently of time slept occurring two or more times a week in the past 6 months (Braz et al., 1987), *Disturbed sleep*: report of agitation as generally present in sleep, in the past 6 months (Braz et al., 1987), *Headache-related awakening* (*HRA*): awakening from a headache more than once a week in the past six months (Braz et al., 1987), *Sleepiness*: excessive daytime somnolence with impairment in performing daytime activities or sleep attacks with sudden fallings asleep, occurring three or more times a week in the past six months (Braz et al., 1987), *Fatigue*: scores equal to or greater than five in the Chalder scale (Chalder et al., 1993), *Sleeping Pills*: taking a medication to promote sleep three or more times a week in the past six months (Braz et al., 1987), *Anxiety*: scores equal to or greater than twenty on the BAI, which indicates moderate to severe symptomatology (Beck et al., 1988), *Poor Quality of Life*: scores lower than fifty for each domain of WHOQOL-BREF (Skevington et al., 2004).

2.3.3. Objective measures

The following variables from the PSG report were compared between groups: sleep onset latency (SOL), total sleep time (TST), sleep efficiency, wake time after sleep onset (WASO), arousal index, stages 1 and 2, slow-wave sleep (SWS), rapid-eye movement (REM) sleep, REM latency, periodic leg movements (PLM) index, percentage of TST with the SpO_2 below 90% ($SpO_2 < 90\%$) and the Apnea and Hypopnea Index (AHI).

2.4. Statistical analysis

The SPSS version 13.0 for Windows was the statistic software used for data analysis. Prevalence estimates were generated using pseudo likelihood maximization. Variability and precision as well as confidence intervals (95% CI) were estimated using Taylor series linearization to avoid underestimation bias (Korn and Graubard, 1999). Descriptive statistics are presented for population and group characteristics. Reliability analysis was used to investigate the internal consistency of the BDI and to calculate Cronbach's alpha coefficient. Cross-tabulations of various factors with depression were examined to evaluate associations. General linear models (GLM) were used for variance analysis of the PSG scores by depression status controlling for age and the AHI (covariates that influence sleep fragmentation and architecture) (Feinberg, 1974). Effect sizes (partial eta squared – η^2) and the power of the multivariate model were also evaluated.

3. Results

From the 1101 selected and interviewed participants, a total of 1042 agreed to visit the Sleep Institute for PSG recordings. There were no significant differences between those not participating ($N=59$) and the participants, indicating no selection bias (Santos-Silva et al., 2009). The mean age was 41.9 ± 14.4 years, and 613 were women, representing 53.5% (95% CI: 48.3–58.7%) of Sao Paulo inhabitants (55.7% before weighing). Most participants were married (66.8%, 62.7%–70.7%), participated in the labor force (75.9%, 71.8–79.6%), belonged to the middle class (65.3%, 59.8–70.3%), and were less than 50 years of age (70.5%, 65.2–75.3%).

3.1. BDI distribution and reliability

Some participants did not complete all of the BDI items. Thus, to avoid selection or measurement bias, they had to be excluded. A total of 917 participants were included in the analysis. The mean BDI score was 9.8 (9.1–10.5), with a median of 8.0, and a mode of 6.0. An acceptable and reliable Cronbach's alpha (87%) was found, with no coefficient corrections when any item was deleted, indicating consistency and good reliability.

3.2. Prevalence and sociodemographic

The prevalence of probable major depression in Sao Paulo was 10.9%. Estimates were slightly higher in women than in men (10.6% versus 7.9%, $p=0.060$), and much lower in the elderly (Table 1). Fig. 1 presents the mean BDI scores according to gender and age (in decades) to illustrate these findings. Among the depressed, there

were significantly higher frequencies of housewives, unemployed people, individuals with lower education and those with lower monthly income than among the non-depressed (Table 1).

3.3. Reported symptoms

Compared to non-depressed individuals, depressed ones presented with significantly higher frequencies of all assessed symptoms. Insomnia and anxiety were found in almost one-third of them. Complaints of non-restorative and disturbed sleep were very much characteristic in depressed individuals as nighttime symptoms, and daytime symptoms included sleepiness and fatigue. Additionally, they presented with much higher frequencies of poor physical, psychological, social and environmental quality of life compared to non-depressed individuals (Table 2).

The co-occurrence of nighttime (insomnia, nightmares, non-restorative and/or disturbed sleep) and daytime symptoms (headache, sleepiness, fatigue, and/or anxiety) and impaired quality of life (physical, psychological, social and/or environmental) was investigated in order to estimate the severity of comorbid symptomatology between the two groups. A diagram was created by crossing the three categories: nighttime symptoms (NtS), daytime symptoms (DtS) and poor quality of life (pQOL). The combination of all three categories was 2.5 times more frequent in the depressed than in the non-depressed individuals (69.3 versus 28.1, $p=0.01$) (Fig. 2).

Table 1
Weighted frequencies of sociodemographic variables by depression groups.

	No depression ($n=815$)			Depression ($n=102$)			χ^2	p
	%	95%	CI	%	95%	CI		
Prevalence	**89.1**	86.6	91.2	**10.9**	8.8	13.4		
Gender								
Women	**52.8**	46.9	58.6	**66.8**	53.5	77.8	6.9	0.06
Men	**47.2**	41.4	53.1	**33.2**	22.2	46.5		
Age (years)								
20–29	**25.7**	21.6	30.4	**25.6**	15.1	39.9	10.9	0.10
30–39	**22.2**	18.3	26.6	**30.6**	20.3	43.3		
40–49	**21.9**	19.0	25.1	**19.0**	10.3	32.4		
50–59	**15.6**	12.2	19.8	**20.3**	12.4	31.4		
60–80	**14.5**	10.5	19.8	**4.5**	2.0	9.8		
Occupational status								
Worker	**76.8**	71.8	81.1	**74.4**	64.4	82.3	**12.8**	**0.03**
House-wives	**7.1**	4.8	10.1	**14.7**	7.3	27.3		
Retired	**11.1**	7.7	15.7	**3.4**	1.3	8.8		
Non-worker	**5.0**	3.7	6.8	**7.5**	3.1	17.4		
Years of scholarship								
Less than 4 years	**15.3**	12.0	19.3	**19.3**	10.7	32.5	**16.9**	**0.01**
5–8 years	**21.4**	17.7	25.6	**26.9**	19.7	35.6		
9–11 years	**28.4**	24.3	32.8	**39.3**	27.7	52.2		
Over 12 years	**35.0**	29.3	41.0	**14.5**	8.8	22.8		
Family monthly income (R$)*								
Less than 1520	**38.4**	33.6	43.5	**69.3**	58.4	78.4	**38.6**	**0.001**
1520–5700	**44.9**	40.3	49.6	**25.3**	17.1	35.8		
Over 5700	**15.0**	11.1	20.0	**2.7**	1.0	7.3		

Abbreviations: 95% CI: confidence interval; χ^2: chi-square.

* 1.00 U$ ≈ 2.00R$ (Brazilian 'reais')

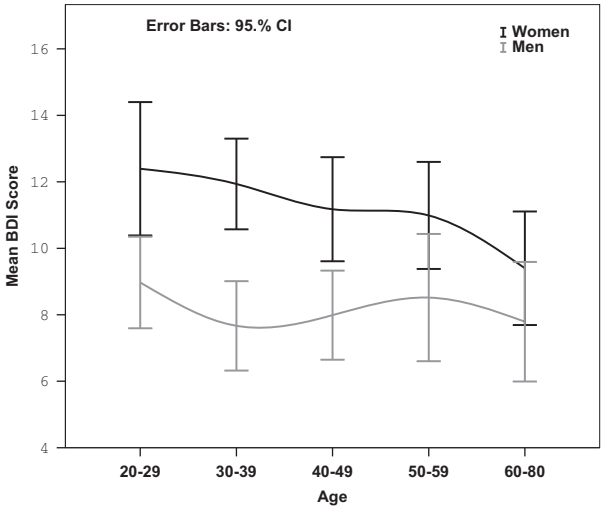

Fig. 1. Means and 95%CIs of BDI scores according to age (years) and gender ($N=917$). Abbreviations: 95% CI: confidence interval, BDI – Beck depression inventory.

3.4. Objective measures

Depressed individuals presented no significant signs of sleep fragmentation compared to non-depressed individuals. They slept a similar amount and had the same sleep efficiency, and interestingly, had a lower number of arousals than non-depressed. They had significantly higher SOL and PLM index values, although the differences were small (Table 3). It is necessary to mention that TST was reasonably low in the total sample (6.0 ± 0.5 h), and so was sleep efficiency ($81.9 \pm 12.7\%$). The distribution of sleep stages was within normal ranges in both groups (AASM, 2005). No differences in REM latency, REM sleep nor SWS were found (Table 3).

Moreover, depressed individuals presented with similar SpO_2 values compared to non-depressed (Table 3), but were found to have a lower frequency of the AHI ≥ 15 (8.1% versus 17.9%, $p=0.01$, data not shown in tables). An analysis to investigate a dose–response relationship between depression and increasing levels of AHI severity found that the frequency of depression actually tended to decrease ($p=0.08$) with AHI severity as shown in Fig. 3.

4. Discussion

The purpose of this study was to investigate the occurrence of depressive symptoms and their relationship to sleep disorders in the general population. To our knowledge, this is the first time a large epidemiologic sleep study has used overnight PSG to establish this relationship.

The point prevalence estimate of moderate to severe depressive symptomatology in Sao Paulo was 10.9%. This is comparable to estimates from other cities in Brazil (Almeida-Filho et al., 1997) and with the prevalence of major depression episode (MDE) in Hong Kong (8.4%), but higher than the 1-month prevalence reported in the National Comorbidity Survey (NCS) (4.9%) in the Unites States (Blazer et al., 1994), which was from a study with a sample of 8098 individuals from 15 to 54 years of age.

The highly frequent co-occurrence of nighttime and daytime symptoms, impaired quality of life (Table 2), and variances in the PSG (Table 3) reinforces the importance of investigating depressive symptoms among patients with sleep complaints (Harris et al., 2009). Moreover, there are studies showing that cognitive-behavioral therapy for insomnia is effective in significantly improving sleep and attenuating depression related endurance (Smith and Perlis, 2006). Moreover, these findings are in accordance with the forthcoming DSM-V sleep-wake disorders nosology, which emphasizes the co-occurrence of sleep and psychiatric disorders as comorbid conditions, rather than making causal attributions (Reynolds and Redline 2010). In addition to mental care support, patients with psychiatric and a separate coexisting sleep disorder may benefit from independent clinical attention.

Table 2
Weighted frequencies of symptoms by depression groups ($N=917$).

	No depression			Depression			χ^2	p
	%	95%	CI	%	95%	CI		
Insomnia	**12.7**	9.7	16.4	**26.3**	16.9	38.6	**22.6**	**0.001**
Nightmares	**6.1**	4.3	8.6	**25.3**	13.5	42.2	**43.4**	**0.001**
Non-restorative Sleep	**44.6**	40.0	49.3	**78.9**	69.2	86.1	**42.1**	**0.001**
Disturbed Sleep	**38.9**	34.7	43.2	**53.6**	39.6	67.0	**7.9**	**0.04**
HRA	**6.1**	4.1	9.1	**20.5**	13.0	30.9	**25.9**	**0.001**
Sleepiness	**24.8**	20.7	29.4	**41.9**	27.6	57.6	**13.3**	**0.02**
Fatigue	**45.3**	40.5	50.1	**79.8**	69.5	87.3	**40.9**	**0.001**
Anxiety	**6.5**	4.7	8.9	**34.0**	24.0	45.5	**76.7**	**0.001**
Poor physical QOL	**13.0**	9.9	16.8	**42.7**	35.2	50.6	**58.1**	**0.001**
Poor psychological QOL	**10.0**	7.8	12.7	**55.4**	45.4	64.9	**143.6**	**0.001**
Poor social QOL	**14.2**	11.2	17.9	**51.9**	39.4	64.1	**84.4**	**0.001**
Poor environmental QOL	**33.0**	27.7	38.8	**69.2**	57.7	78.7	**49.8**	**0.001**
Sleeping pills	**4.2**	2.9	6.0	**9.4**	3.8	21.5	5.3	0.06

Abbreviations: 95% CI: confidence interval; χ^2: chi-square; HRA: headache-related awakening; QOL: quality of life.

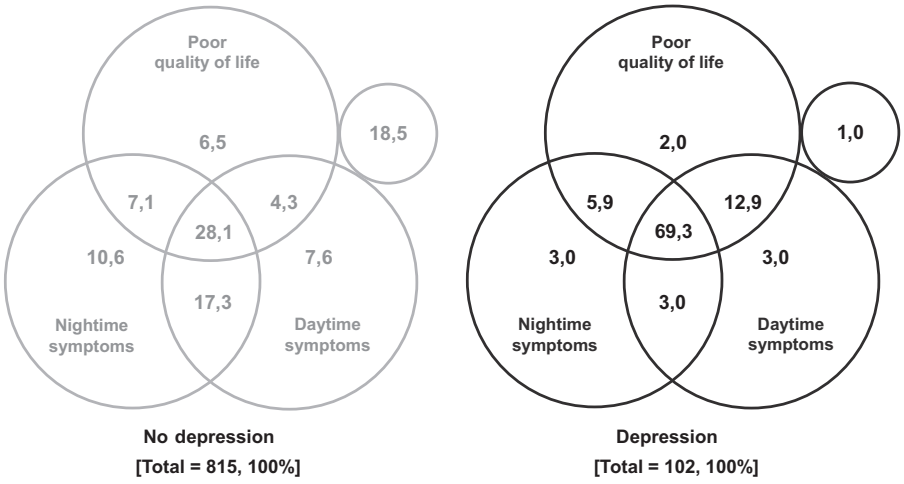

Fig. 2. Diagram with frequency of depression and no depression for the combination of symptoms categories and QOL ($N=917$). Abbreviations: pQOL: poor quality of life, NtS: nighttime symptoms, DtS: daytime symptoms Note: numbers are percentages of the combined complaint categories

Depressed individuals presented with higher SOL and PLM values but lower arousal index values than non-depressed people. Our hypotheses on these findings are that (1) one-third of the depressed individuals presented with the complaints of insomnia or anxiety, and this may explain the increase in SOL, (2) larger numbers of depressed people than non-depressed people reported using sleep promoters, and it is possible that these medications affected the PLM index value as sleeping pills have been demonstrated to cause an increase in PLM events, and (3) finally, an increase in the number of arousals has been associated with aging, and our depressed group was younger than the non-depressed group (Guilleminault and Silvestri, 1982).

Our population study did not replicate the findings of significant alterations in objective sleep parameters in subjects with major depression found by a few researchers (Buysee et al., 1999). Alterations such as decreased sleep continuity, decreased slow-wave sleep, enhanced percentage of REM sleep or a decrease in REM latency were not characteristic in the individuals with "probable" major depression in our study.

Epidemiologic and sleep EEG studies establish a role for sleep disturbances in the pathogenesis of depression (Peppard et al., 2006, Ohayon, 2003), but there are controversial findings related to the specificity of physiological sleep changes as biomarkers of depression (Lustberg and Reynolds, 2000). Benca et al., (1992) attempted to clarify this issue in a meta-analysis of polysomnography findings from 177 studies of 7151 patients to test for the specificity of sleep changes to psychiatric diagnoses. No single sleep variable was found to be a sensitive or specific marker for any particular psychiatric disorder (Benca et al., 1992). Moreover, to our knowledge, there have been no studies that measured a possible effect or role of OSA in the association of depression to sleep architecture.

The relationship between OSA and depression was previously demonstrated in OSA clinical samples (Borak et al., 1994, Derderian et al., 1988, Edinger et al., 1994, Flemons and Tsai, 1997, Kales et al., 1985), in clinical samples of depressed individuals (Ong et al., 2009, Deldin et al., 2006), and only in one population-based cross-sectional telephone survey (Ohayon, 2003). In other study, Wheaton et al. (2012) showed that symptoms of sleep disordered breathing were associated with depression symptomology in a national sample of adults.

Additional research may be needed to determine whether regular screening for these conditions by mental health professionals and sleep specialists should be recommended. In the adult population of Sao Paulo, the prevalence of the AHI ≥ 5 was similar in depressed and non-depressed individuals when assessed by an overnight PSG with a nasal cannula detecting the airflow. It is important to stress that among depressed people, there were more women and younger adults who are less likely to develop OSA (Punjabi, 2008). Moreover, depression and OSA present several overlapping complaints, and it is no surprise that Ohayon (2003)

Table 3
Variances of PSG variables by depression groups ($N=917$).

	No depression			Depression			*F*	*P*
	Mean	95%	CI	Mean	95%	CI		
SOL	**14.5**	13.2	15.7	**19.3**	15.7	22.9	**6.07**	**0.009**
TST	**345.7**	340.6	350.9	**355.5**	340.6	370.4	1.47	0.23
Sleep efficiency	**82.7**	81.9	83.4	**82.4**	80.2	84.7	0.03	0.86
WASO	**58.7**	55.7	61.6	**55.7**	47.1	64.3	0.41	0.52
Arousal index	**14.8**	14.2	15.3	**12.9**	11.3	14.6	**4.45**	**0.03**
% S1	**4.4**	4.2	4.6	**4.5**	3.8	5.2	0.08	0.78
% S2	**54.3**	53.7	55.0	**53.5**	51.7	55.3	0.68	0.41
% SWS	**22.0**	21.4	22.5	**21.9**	20.3	23.5	0.00	0.95
% REM	**19.3**	18.8	19.7	**20.0**	18.8	21.3	1.25	0.26
REM latency	**96.6**	93.1	100.1	**96.1**	86.0	106.2	0.01	0.92
PLM index	**0.9**	0.4	1.4	**2.8**	1.3	4.2	**5.84**	**0.02**
$SpO_2<90\%$	**1.7**	1.3	2.2	**2.1**	0.8	3.4	0.33	0.57

Note: covariates in the model are evaluated at the following values for AHI and age: AHI = 7.9, Age = 41.8.
Abbreviations: 95% CI: confidence interval; *F* statistic: analysis of variance (GLM); SOL: sleep onset latency; TST: total sleep time; WASO: wake time after sleep onset; S1 and S2: sleep stage; SWS: slow-wave sleep; REM: rapid-eye movement; PLM: periodic leg movement; SpO_2: oxyhemoglobin saturation.

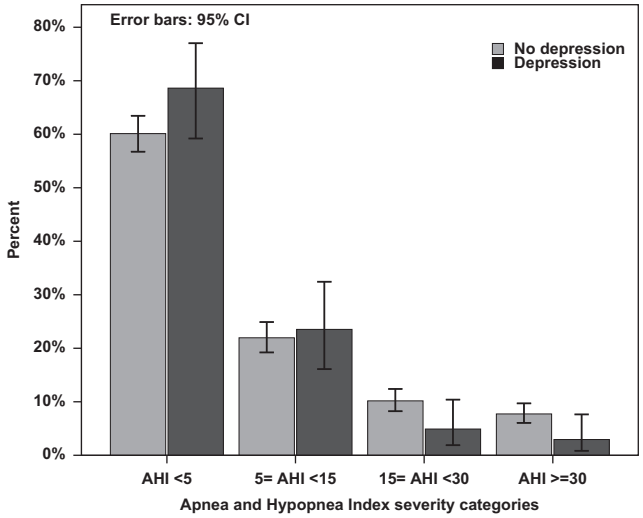

Fig. 3. Frequencies of depression and no depression as a function of OSA severity categories for the studied sample ($N=917$). Abbreviations: 95% CI: confidence interval, AHI: apnea and hypopnea index.

found an odds ratio of 5.26 for SRBD in individuals with major depression, as it was a population-based investigation performed by telephone. The non-depressed individuals were perhaps more prone to underestimate the presence of PSG-defined OSA, and depressed individuals were perhaps more prone to overestimate it as they probably also complained of fatigue and sleepiness.

The estimates of the prevalence of OSA range widely depending on its definition and method of assessment. In the Sleep Heart Health Study, 1824 individuals with a mean age of 65 ± 11 years had an in-home one-night PSG recording, and the prevalence of scores ≥ 5 on the respiratory disturbance index (RDI – apneas plus hypopneas) was 51% (Gottlieb et al., 1999). According to the *DSM-IV*, a diagnosis of OSA is based entirely on clinical symptoms (First et al., 2004). Therefore, many individuals with OSA might not be aware of this sleep disturbance if they do not perceive their symptoms, do not recognize as characteristics of OSA, and consequently do not report to their health care provider (Ong et al., 2009).

Although in our sample, the prevalence of OSA was similar in the depressed and non-depressed individuals, it is worth noting that it was high in both groups, especially when the AHI ≥ 5 was considered (32.2% versus 39.4%, $p=0.22$). Additionally, the OSA and depression comorbidity must be vigorously investigated and should be noted as a predictor of morbidity, mortality and diminished quality of life (Harris et al., 2009).

Importantly, comparing the polysomnographic results presented herein with the existing research in major depression should be done cautiously due to the following reasons: (1) published PSG data have been obtained from psychotropic drug free patients as a rule, who have usually been off prescribed and over the counter agents for two weeks or longer; (2) generally two nights of polysomnography have been recorded, if not more, allowing investigators to adjust for variance related to first night effects; (3) timing of PSG recordings have been aligned with diary based measures of usual sleep wake schedule, and (4) participants have typically been asked to refrain from ingestion of alcohol for 2 weeks in advance of PSG.

It is undeniable that some limitations in our study design might have introduced some methodological biases. The lack of standardized questionnaires for the *DSM-IV* criterion to diagnose major depression may have affected our results. Also, the cross-sectional design does not allow for chronological assumptions between depressive symptoms and sleep abnormalities.

With respect to the lack of association between depressive symptoms and objective sleep parameters, it is possible that the use of data from the one-night PSG evaluation without an adaptation night, as already mentioned above, may have introduced measurement bias, leading to non-statistically significant results. Additionally, in the present study, we did not control for a possible effect of gender in the distribution of sleep stages, especially when there were more women among the depressed. There is evidence that estrogen exerts modulatory effects on the serotoninergic system (Bethea et al., 2002), and that serotonin is a key neurotransmitter implicated in both depression and sleep regulation (Tsuno et al., 2005). Such adjusted analyses will be conducted in a future study.

Moreover, most individuals who reported depressive symptoms belonged to a low income level, and they had a severely impaired quality of life, which may be markedly related to their harsh living environmental conditions. Environmental factors may have interfered with the assessment of their usual quality of sleep because the assessment was done at the Sleep Institute where they may have had a nice, quiet and safe room to sleep for the first time.

Our study population was unique. Living in one of the largest metropolitan areas on earth, with one of the highest frequencies of miscegenation and inequality in income distribution (IBGE, 2000), the population of Sao Paulo city showed characteristics that may not be entirely generalizable. However, these findings can lead to some interesting lines of research.

In our study, individuals presenting with moderate to severe depressive symptomatology had a lower frequency of AHI ≥ 15 compared to the non-depressed, but they had a much higher frequency of insomnia. When AHI was categorized as values ≥ 5, the prevalence increased remarkably in both groups. This increase may point to an overlap of depression, insomnia and mild sleep apnea in younger adults and the overlap presumably impairs their quality of life and worsens symptom severity. Indeed, they had a wide range of highly frequent nighttime and daytime symptoms. Treatments that are more favorable in comorbid depression and OSA are currently unknown, although CBT has been shown to improve depressive symptoms when insomnia is treated (Smith and Perlis, 2006).

A clear causal link between depression and OSA has not yet been established, and the same is true between depression and sleep abnormalities. Our findings found a lack of specificity of objective sleep changes in the context of depression in a stratified sample representing the adult population of a metropolitan area. Additionally, from what our evidence shows, there may be many other factors modulating the association between depression and

sleep, and some may be in the causal pathway of complaints such as nightmares, headache-related awakenings and anxiety, or even others that were not addressed herein.

Depressive symptomatology was found to be associated with a whole set of other sleep and physical symptoms. These findings suggest an important social and economic burden that is not yet completely addressed by public health authorities. Clinical evidence had previously shown the need to investigate depression among individuals with OSA, insomnia and other sleep-related complaints. The present report sought to shed some light in the complex universe of depression through the perspective of sleep medicine and with a public health concern.

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