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Abstract

The current study examined the relationship between plasma orexin-A and sleep in obesity. Concentrations of orexin-A and sleep were evaluated in 26 obese, 40 morbid obese and 32 healthy-weight participants. The sleep monitor Actiwatch AW7 and the Pittsburgh Sleep Quality Index were used to evaluate sleep. The Symptom Checklist-90-Revised was administered to assess symptoms of psychopathology. A higher weight status was associated with elevated orexin-A levels ($p = .050$), greater depression, anxiety and somatization symptoms (all: $p < .001$), and impoverished self-reported sleep quality ($p < .001$). A quadratic trend was found in objective sleep time, being longest in the obese group ($p = .031$). Structural equation modeling showed plasma orexin-A to be related to poor total sleep quality, which in turn was associated with elevated body mass index. Our data confirm an interaction between elevated plasma orexin-A concentrations and poor sleep that contributes to fluctuations in body mass index.

Keywords: Obesity; Body Mass Index; Orexin; Sleep

Introduction

With the steady rise in body mass index (BMI) over the past few decades, the prevalence of obesity (OB) and morbid obesity (MOB) is rapidly rising worldwide (Finucane et al., 2011). The increase in body fat and visceral obesity has been associated with multiple cardiovascular and metabolic illnesses, thus prevention of obesity is becoming a pressing public health issue (Bombak, 2014). Parallel to the increase in the prevalence of obesity, a rapid decline in sleep time has been described (Bixler, 2009).

A meta-analysis of 18 studies examining a total of 604,509 adults, showed a progressive increase in the likelihood of obesity with a decrease in sleep time; odds ratio for obesity being 1.55 for less than 5 hours of sleep and a decrease of one hour/night of sleep yielding an increase of $0.35 kg/m^2$ in BMI (Cappuccio et al., 2008). Later, a meta-analysis of prospective studies concluded that prolonged short sleep duration increased the risk of developing obesity later in life with an odds ratio of 1.45 (Wu, Zhai, & Zhang, 2014). Diminished sleep quality also seems to be present in obesity as well as a greater use of sleep medication (Bidulescu et al., 2010).

Actigraphy has evidenced adiposity and BMI to be associated with reduced sleep duration, inconsistent sleep patterns and poor sleep efficiency (Appelhans et al., 2013; Bailey et al., 2014).

The relationship between poor sleep and weight has also been observed in several sleep and eating disorders. For example, narcolepsy is a chronic, neurodegenerative sleep disorder characterized by recurrent intrusions of REM sleep during the day, sometimes accompanied by cataplexy (sudden muscle weakness). Affected individuals are frequently obese (Tsujino & Sakurai, 2013). Binge eating (the consumption of large quantities of food within a short period of time), as seen in the binge eating disorder, has been associated with sleep problems (Tzischinsky, Latzer, Epstein, & Tov, 2000) and obesity (Bulik & Reichbornkjennerud, 2003). Obesity is also common in the sleep-related eating disorder, consisting in recurrent episodes of eating at the transition from night-time sleep to arousal, and the night eating syndrome, in which a large proportion of daily food intake is consumed at night (Auger, 2006); Meule, Allison, & Platte, 2014).

Sleep regulation can be attributed to a wide range of environmental and biological mechanisms. One of these is the hypocretin (orexin) neuron system (Tsujino & Sakurai, 2009, 2013). Orexin A (hypocretin 1) and orexin B (hypocretin 2) are 33- and 28-amino-acide neuropeptides derived from the protein precursor labeled prepro-orexin primarily synthesized in the lateral-posterior-perifornical hypothalamus, and attach to the orexin receptor-1 and orexin receptor-2 spread across several brain sites. Orexins innervate an extensive number of areas throughout the central nervous system thus playing a role in multiple physiological processes, among which are arousal, behaviour, homeostatic mechanisms, reward seeking and autonomic function (Burdakov, Karnani, & Gonzalez, 2013; Mahler, Smith, Moorman, Sartor, & Aston-Jones, 2012; Sakurai, 2005; Tsujino & Sakurai, 2009, 2013).

It is widely agreed that orexins are involved in the sleep/wake cycle. Orexins innervate aminergic nuclei that promote arousal and inhibit rapid eye movement (REM) sleep (Tsujino & Sakurai, 2009; Sakurai, Mieda and Tsujino, 2010). Extracellular levels of orexin have been found to rise during wakefulness (Yoshida et al., 2001), and electrophysiology has identified wake-active neurons in animals, with firing rates that peak when the animals are active (Alam et al., 2002). Concordant, the administration of orexin receptor antagonists have proven to be effective sleep inducers (Winrow & Renger, 2014). The role of orexin in the sleep/wake system has also been consistently documented in narcolepsy; a chronic, neurodegenerative sleep

disorder characterized by recurrent intrusions of REM sleep during the day, sometimes accompanied by cataplexy (sudden muscle weakness). Orexin knockout mice display extreme sleepiness and frequent motoric arrests during the dark (active) phase (Chemelli et al., 1999). Long-term hypothalamic staining has shown a progressive decrease by 85%-95% in orexin-firing neurons in narcoleptic patients, not found in neurologically healthy controls (Thannickal et al., 2000).

Early studies in narcolepsy also suggested the involvement of orexin-A in energy balance (Tsujino & Sakurai, 2013). Neuronal orexin damage and irregularities in orexin function have been linked to the development of obesity despite hypophasia in both human narcoleptic patients and animal-models of narcolepsy (Tsujino & Sakurai, 2013). Initial reports in obesity have shown a similar pattern. In a study of 15 morbidly obese participants who underwent a surgical intervention, peripherally measured orexin-A was found to be inversely associated with BMI, and weight loss resulted in an increase of orexin-A levels (Adam et al., 2002). Similarly, BMI has been shown to inversely correlate to serum orexin-A in children (Tomasik, Spodaryk, & Sztefko, 2004), and an increase in plasma orexin-A levels has also been observed in children after participating in a weight-loss programme (Bronský et al., 2007)..

Later studies, however, have obtained contrasting results. Heinonen and colleagues (2005) reported elevated plasma orexin-A levels in obese individuals waiting for a gastric band operation compared to lean controls, which remained unchanged at a one-year post-surgery follow-up. Others found inter-individual differences in post-surgery changes in orexin-A; plasma concentrations increased in some obese participants after weight loss, while in others there was a decrease (Gupta et al., 2014). Furthermore, a study conducted in patients with chronic obstructive pulmonary disease, who are frequently malnourished, found that orexin-A did not correlate with BMI, but was only related to greater food intake (Akbulut et al., 2014).

In summary, an exponential increase in the prevalence of obesity has been reported. Evidence points to an interplay between the role of orexin-A in the regulation of sleep/arousal and energy balance to contribute (Nixon et al., 2015), however limited research has been conducted to examine the nature of this relationship in obese humans and studies thus far have obtained conflicting results. Our objective was to analyze plasma orexin-A levels in obese and morbid obese participants in comparison to a healthy-weight comparison group, and to explore the interaction between plasma orexin-A levels, sleep quality and fluctuations in BMI. Based on the

existing literature we were unable to predict possible deviations in the plasma concentrations of orexin-A in the obese groups, but we expected that an interaction between elevated orexin-A levels and poorer sleep would be related to raised BMI.

Materials and methods

Participants

The sample comprised a total of 98 female participants of which 26 were OB (BMI = 30-39.9 kg/m^2), 40 were MOB (BMI > 40 kg/m^2) and 32 were healthy-weight controls (BMI = 18.5-24.9 kg/m^2). Participants were excluded if they were male, younger than 18 years, had a lifetime history of a mental disorder (evaluated by means of the General Health Questionnaire-28; Goldberg, 1978) and/or had a sleep disorder. The possible presence of the obstructive sleep apnea syndrome, along with other sleep disorders, was based on a clinical evaluation from an expert professional and, if necessary, polysomnography. Several centers that belong to our Spanish Research Network (CIBEROBN), participated in this study. The OB and MOB participants were patients continuously referred to these centers, while the control group was a convenience sample recruited via word-of-mouth and advertisements at the local universities from the same catchment areas.

Mean BMI of the healthy-weight controls was 22.6 kg/m² (*SD* = 2.7), of the OB group was 35.5 kg/m² (*SD* = 2.5), and of the MOB was 46.4 kg/m² (*SD* = 4.9) ($p < .001$). Mean age of the controls was 37.3 years (*SD* = 5.6), which was significantly lower to that of the OB (*M* = 47.0 years, *SD* = 11.4) and MOB (*M* = 43.2 years, *SD* = 10.4) groups (controls vs OB: $p < .001$; controls vs MOB: $p = .009$). No difference was found between the OB and MOB participants ($p = .112$). Eating disorder psychopathology (measured with the total score of the Eating Disorder Inventory-2, (Garner, 1991) was highest in the MOB group (*M* = 79.4, *SD* = 30.6), followed by the OB group (*M* = 66, *SD* = 28.7) and lowest in the controls (*M* = 23.6, *SD* = 24.6) (MOB vs controls: $p < .001$; MOB vs OB: $p = .063$; OB vs controls: $p < .001$).

Measures

Sleep quality. The Pittsburgh Sleep Quality Index (PSQI) (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989) was used to evaluate self-reported problematic sleep and sleep time. The questionnaire consists of 19 items scored on a Likert scale ranging from 0 (no difficulty) to 3

(severe difficulties). Seven "components" of sleep are obtained: 1) subjective sleep quality; 2) sleep latency; 3) sleep duration; 4) habitual sleep efficiency; 5) sleep duration; 6) use of sleeping medication; 7) daytime dysfunction. From the sum of the scores of each table, a global sleep quality score is obtained ranging from 0 to 21, with higher scores indicating poorer sleep. Scores above 5 are representative of sleep disturbance. Additionally, the PSQI includes five open questions habitual sleep-wake patterns. Test-retest reliability for the global score was acceptable (.85). Comparison between patients and lean controls using the 5 cut-off score to indicate pathology has shown a sensitivity of 89.6% and a specificity of 86.5% (Buysse et al., 1989). Internal consistency of the Spanish version of the PSQI is of (Chronbach alpha) 0.81 (Royuela & Macías, 1997).

Objective sleep time. The duration of nocturnal sleep was also evaluated using the movement monitor Actiwatch AW7 (Actiwatch AW7; CamNtech Ltd, Cambridge Neurotechnology, Cambridge, UK). This is a small (39×32×9 mm), light-weight (10.5 g), triaxial instrument that records movement intensity in the form of counts in a 1-minute epoch length. It can be utilized as an actigraph, whereby users press a marker button to indicate bed time and get up time and data of actual nocturnal sleep time is extracted. Participants were also asked to keep sleep logs. Sleep time is analyzed using the Actiwatch Sleep Analysis 7 software (CamNtech Ltd). Actigraphy has shown to correlate with polysomnography recording, the gold standard of sleep, with an intra-class correlation co-efficient of .76 for sleep time (Blackwell et al., 2008). The Actiwatch was purposely included in the procedure to avoid the possibility of incorrect estimates of sleep duration due to self-reported misperception.

Orexin A plasma concentrations. Blood samples were collected from all participants between 0800h and 0900h after an overnight fast. Method of analysis has been described elsewhere (Sauchelli et al., 2016).

Body Mass Index. The Tanita Multi-Frequency Body Composition Analyzer MC-180MA (Tanita Corporation, Tokyo, Japan) was used to measure BMI. This is a weighting instrument that provides information on body composition using bioelectrical impedance analysis. The device is repeatedly revised to meet the reference standards dual-energy X-ray absorptiometry (DEXA) (http://www.bl-biologica.es/tanita_tbf.htm) and has been validated against other weighing methods (Strain et al., 2008). Height was obtained by using a stadiometer.

General psychopathology. To examine general psychopathology, the Symptom-Checklist-revised (SCL-90-R) (Degoratis, 1990) was used. This self-administered questionnaire comprises 90 items answered on a 5-point Likert scale, from which scores on 9 dimensions are obtained: 1) somatization; 2) obsession-compulsion; 3) interpersonal sensitivity; 4) depression; 5) anxiety; 6) hostility; 7) phobic anxiety; 8) paranoid ideation; 9) psychoticism. Scores on three global indexes are also obtained: 1) the Global severity index (GSI) to appraise overall distress; 2) the positive-symptom total (PST), which indicates self-reported symptoms; 3) the positive symptom distress index (PSDI) to assess symptom intensity. The Spanish validation of this questionnaire (Derogatis, 2002) has revealed a mean internal consistency of .75 (coefficient alpha). The depression, anxiety, and somatization scales were considered in the current study due to their previously reported role in sleep and obesity (Algul et al., 2009).

Procedure

Clinical and physical assessments were conducted by experienced psychologists, psychiatrists and endocrinologists (all extensively trained in the use of the instruments). Subjective sleep quality and general health status were determined by using the questionnaires. Basic anthropometric information was obtained from the TANITA, and blood sampling took place prior to actigraphic recording after an overnight fast. As described in previous studies (Sauchelli et al., 2016), the Actiwatch was provided on the first day of assessment and collected after 7 days. All participants gave written informed consent to participate. The study was approved by the Institutional Research Ethics Committee of each institution and was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Analyses were carried out with Stata13.1 for Windows. Analysis of variance (ANOVA) adjusted according to participants' age was conducted to compare plasma orexin A, sleep and symptomatology (SCL-90R depression, anxiety and somatization scales) between diagnostic conditions. Orthogonal polynomial contrasts were included in the ANOVA procedures to assess the presence of linear and/or quadratic trends between means and Cohen's-*d* indicated the effect size of pairwise comparisons (moderate effect size was considered for $|d| > 0.50$ and large effect size for $|d| > 0.80$). Bonferroni-Finner's correction controlled the inflation in type-I error because of the multiple statistical comparisons. Partial correlations adjusted according to age were also

conducted to analyze the association between sleep time when measured with the PSQI (subjective assessment) and that indicated by the actigraph (objective assessment).

Structural Equation Modeling (SEM) in the OB and MOB subsamples was used to test the paths between BMI, orexin A concentrations, symptomatology levels and overall self-reported sleep quality. Path analysis procedures constitute in a straightforward extension of multiple regression modeling that can be used for both confirmatory and exploratory modeling, with the aim of estimating the magnitude and significance of "hypothesized" causal connections into a set of variables (von Oertzen, 2010). Goodness-of-fit was evaluated using the standard indices of fit, including chi-square (χ^2), Comparative Fit Index (CFI), Root Mean Square Error of Approximation (RMSEA), Standardized Root Mean Squared Residual (SRMR), and the Tucker-Lewis Index (TLI). Goodness-of-fit was established when (Bentler, 1990): χ^2 with a $p >$ .05, a CFI and TLI > .9, a RMSEA < .08 and a SMSR < .10. The global predictive capacity was measured through the coefficient of determination (CD).

Results

Comparison between weight groups

Table 1 shows the results of the ANOVA, adjusted according to participants' age, comparing plasma orexin-A concentrations, self-reported sleep (PSQI scores), actigraphy-based sleep time and psychopathology (SCL-90R depression/anxiety/somatization) across the three groups (lean controls, OB and MOB). Elevated plasma orexin-A concentrations were found to be present in the OB and MOB groups compared to the lean participants. Self-reported sleep quality and symptoms of anxiety, depression and somatization followed significant linear trends, being highest in the MOB group and lowest in the healthy controls. A quadratic trend was also present in self-reported sleep quality and sleep latency. When measured with the actigraph, only a quadratic trend was found in sleep time, whereby the OB participants slept longer than the MOB participants and controls, who did not differ in sleep time. Furthermore, sleep time measured via the actigraph did not correlate with that reported by the participants in the PSQI (HC: r = .306, p = .089; OB: r = .194, p = .342; MOB: r = .208, p = .198).

Path analysis

Figure 1 presents the SEM (adjusted according to participants' age) portraying the relationships between plasma orexin-A levels, overall self-reported sleep quality (PSQI-total), anxiety, depression and somatization symptoms (SCL-90R scales), and BMI in the OB and MOB participants. Table S1 displays complete indexes of the SEM model. Adequate goodness-of-fit was achieved: $\chi^2 = 0.38$ ($p = .944$), RMSEA = .01, CFI = .999, TLI = .999 and SRMR = .007. The global predictive capacity was high (CD = .577). The standardized coefficients of this model indicate that poorer sleep quality (a higher PSQI-total score) was associated with greater psychopathology (SCL-90R scales) and elevated plasma orexin-A levels. BMI was higher with impoverished sleep quality and increased symptoms of somatization. Orexin-A levels did not directly predict BMI. Sleep quality was a mediator role in the relationships between psychopathology and BMI, as well as in the link between plasma orexin-A concentrations and BMI.

Discussion

Given the reported relevance of poor sleep in obesity, and the role of orexin-A in the regulation of sleep and arousal, the present study aimed to evaluate whether an interaction between diminished sleep quality and plasma orexin-A concentrations could be influencing weight status. Both OB and MOB participants reported notably poorer sleep quality and less sleep compared to the lean participants. These findings concord with those of previous studies that have found that short sleep and sleep disturbances are related to an increased likelihood of obesity (Bailey et al., 2014; Bidulescu et al., 2010; Cappuccio et al., 2008). However, when sleep time was measured objectively with the actigraph, the OB group were found to sleep longer than the other two groups, whereas sleep time was similar between the MOB and control groups. These findings suggest that in our sample it is impoverished sleep quality (e.g. inefficient sleep and/or alterations during sleep) rather than the amount of sleep per se that is associated with obesity. In support, Meyer and colleagues (Meyer, Wall, Larson, Laska, & Neumark-Sztainer, 2012) found that short sleep correlated with BMI and greater odds of being obese only in the male participants but not in the female participants, while an association between difficulties in falling/maintaining sleep and BMI was only found in the female participants. The sample in the present consisted fully in adult women.

The link between poor sleep quality and obesity might be related to greater symptoms of depression and anxiety as seen in our OB and MOB groups. Evidence has shown an interaction

between obesity, psychological distress and problematic sleep (Algul et al., 2009). Furthermore, somatization symptoms are linked to several forms of pain that might also be having a detrimental effect on sleep. This could be particularly relevant in the reduced sleep time we observed in the MOB compared to OB group, whereby the pains might start to significantly interfere with restorative sleep. Studies in fibromyalgia, a chronic pain disorder of unknown etiology, show both morbid obesity and severe sleep disturbances that ameliorate after bariatric surgery (Masheb, White, & Grilo, 2016; Saber et al., 2008). Altered sleep is also implicated in disordered eating behavior, which contributes to weight gain. Binge eating (the consumption of large quantities of food within a short period of time) has been associated with sleep problems (Tzischinsky, Latzer, Epstein, & Tov, 2000) and obesity (Bulik & Reichborn-kjennerud, 2003). Obesity is also common in sleep-related eating disorders, consisting in recurrent episodes of eating at the transition from night-time sleep to arousal, which are often accompanied by anxiety and depression symptoms (Auger, 2006).

Our findings also suggest that sleep might act as a modulator in the role of plasma orexin A in BMI variation. Elevated plasma orexin A levels were identified in the OB and MOB participants compared to the lean controls. These findings are only partially consistent with the existing literature (Gupta et al., 2014; Heinonen et al., 2005). Studies have reported increases in prepro-orexin in the hypothalamus in situations of hypoglycemia or after fasting (Komaki et al., 2001; Sakurai et al., 1998), and intracerebroventricular injection of orexin in rats results in elevated food intake (Sakurai et al., 1998). Differently, the administration of SB-649868 or genetic ablation of orexin neurons inhibits such effects, resulting in increases in body weight despite hypophagia (Chemelli et al., 1999; Ishii et al., 2005). This contradictory influence has also been observed in patients with narcolepsy, who present a high prevalence of obesity despite hypophagia (Tsujino & Sakurai, 2013).

The exact mechanism that may be underlying the role of orexin-A in obesity is not fully understood. Orexin-A is generally considered as an appetite stimulator (Tsujino & Sakurai, 2009, 2013) that generates the experience of hunger to regulate eating behavior and food intake (Sakurai et al., 1998; Tsujino & Sakurai, 2013) by receiving metabolic cues from peripheral peptides (Sakurai, 2005; Toshinai et al., 2003). Orexin receptors have also been located in peripheral organs that are involved in feeding and metabolism such as adipose tissue, gastrointestinal tracts, pancreas and the adrenal gland (Kirchgessner & Liu, 1999; Ouedraogo, Näslund, & Kirchgessner, 2003). Yet, orexins also contribute to energy expenditure (Teske, Billington, & Kotz, 2010). They are implicated in the regulation of thermoregenesis-based

energy expenditure (Tupone, Madden, Cano, & Morrison, 2011), and the stimulation of skeletal glucose metabolism (Shiuchi et al., 2009). Evidence has demonstrated increased locomotor activity in rats placed in conditions of limited food availability that is accompanied by an upregulation of rat orexin receptor mRNA (Lu, Bagnol, Burke, Akil, & Watson, 2000).

The findings from the present study imply that orexin may be related to weight gain by impeding adequate sleep. In line with others (Akbulut et al., 2014; Komaki et al., 2001), we did not find a direct link between serum orexin-A and BMI. Rather, our results showed increased plasma orexin levels to be related to poorer sleep quality, which in turn was associated with greater BMI. Intracerebroventricular administration of orexin A results in a decrease of both rapid and non-rapid eye movement sleep and an increase in wakefulness (Hagan, Whitworth, & Moss, 1999). Orexin receptor antagonists have been found to facilitate restorative sleep (Winrow & Renger, 2014). In turn, sleep loss has been associated with a decrease in the appetite supressing hormone leptin, which generates the experience of satiety and halts food intake, accompanied by an increase in the appetite stimulating hormone ghrelin, which promotes continued consumption (Spiegel, Tasali, Leproult, Scherberg, & Van Cauter, 2011; Taheri, Lin, Austin, Young, & Mignot, 2004). These alterations are believed to contribute to metabolic imbalance and an intense appetite for high-carbohydrate food that results in increased BMI (Schmid, Hallschmid, Jauch-Chara, Born, & Schultes, 2008; Taheri et al., 2004). One might suggest that fluctuations in orexin functioning may in part be contributing to weight status via the modulation of sleep and the associated changes in the activity of hormones implicated in the regulation of energy balance. This suggests the presence of a feedback loop between hormones, sleep quality and energy balance.

It must be noted that the involvement of ghrelin and leptin activity was not evaluated in the current study. Furthermore, this study is cross-sectional in nature, and directionality cannot be determined without further analysis. Another limitation is that only women were included in the study and therefore findings cannot be extrapolated to men. Findings might also be partially influenced by the menstrual status of participants, which was not taken into account during data gathering. Animal studies have demonstrated that hormonal changes occur during the estrous cycle that are tightly synchronized with orexin function (Porkka-Heiskanen, Kalinchuk, Alanko, Huhtaniemi, & Stenberg, 2004) and sleep architecture (Schwierin, Borbély, & Tobler, 1998). In fact, a rise in plasma orexin A concentrations takes place when women enter menopause, which

has been associated with the parallel decline in estrogen (El-Sedeek, Korish, & Deef, 2010), and women in the early transition to menopause also show increased sleep difficulties such as insomnia (Bruyneel, 2015; Joffe, Massler, & Sharkey, 2010). The OB and MOB women in the present study were significantly older than the lean controls. Last, the classification of weight groups was based on the participants' BMI, which is the most universally used measure (WHO Consultation, 2000) but is limited as it is unable to distinguish between lean mass and body fat. The assessment of waist circumference and/or percentage body fat in addition to BMI may improve the accuracy of group categorization

Nonetheless, as far as known, this is the first study to examine the connections between sleep impairment and orexin-A in obese humans without a sleep disorder. Discrepancies from the lean population were found in OB and MOB in terms of plasma orexin-A concentrations and both self-reported and actigraphy-based sleep. An interaction between these variables also seems to influence fluctuations in BMI. It is therefore essential that they are taken into consideration when tackling the problem of obesity, from both pharmacological and psychological standpoints. Future studies might consider long-term assessment to explore changes throughout time and additional relevant hormonal compounds.

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Table 1.

Comparison of the main variables of the study between groups: ANOVA adjusted by age.

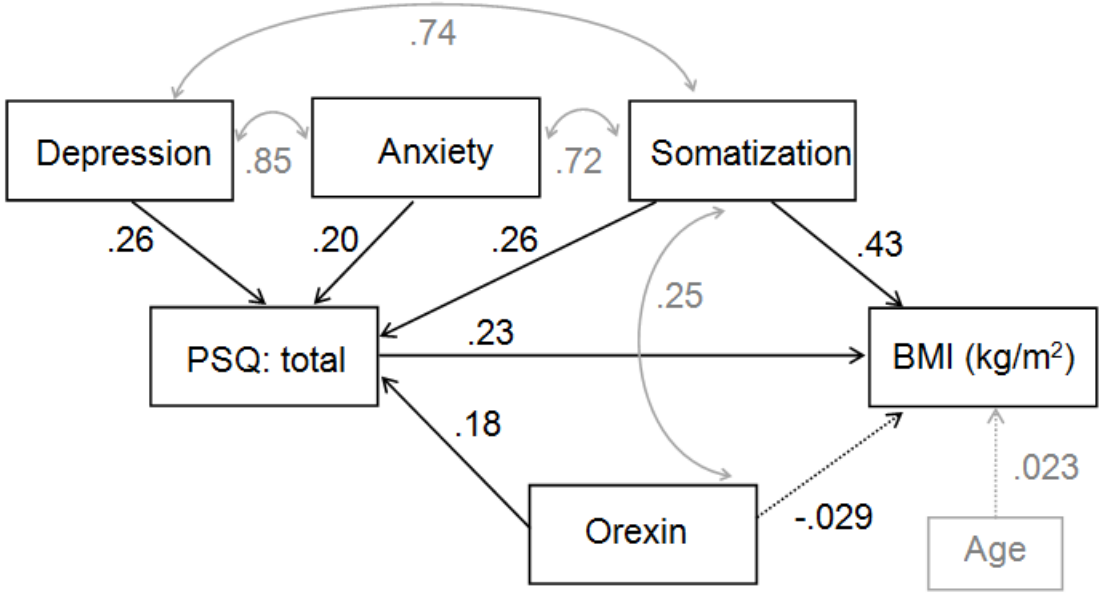
	Means and SD						Factor		Polynomial		Pairwise comparisons													
	HC		OB		MOB		Group		Trends (*p*-val)		HC versus OB					HC versus MOB					OB versus MOB				
	n=32		*n=26*		*n=40*		$F_{2;94}$	*p*	Linear	Quad.	MD	*p*	*95%CI(MD)*		*|d|*	MD	*p*	*95%CI(MD)*		*|d|*	MD	*p*	*95%CI(MD)*		*|d|*
Orexin-A	2.87	0.69	3.42	0.92	3.30	0.94	3.11	**.050***	**.042***	.116	-0.55	**.028***	-1.04	-0.06	**0.68**†	-0.44	**.042***	-0.86	-0.02	**0.53**†	0.11	.610	-0.33	0.55	0.12
PSQI: quality	0.57	0.71	1.53	0.79	1.66	0.73	19.37	**<.001***	**<.001***	**.023***	-0.96	**<.001***	-1.38	-0.54	**1.28**†	-1.09	**<.001***	-1.45	-0.73	**1.52**†	-0.13	.484	-0.51	0.24	0.18
PSQI: latency	0.70	0.73	1.66	0.92	1.59	0.96	10.32	**<.001***	**<.001***	**.017***	-0.97	**<.001***	-1.47	-0.47	**1.17**†	-0.89	**<.001***	-1.32	-0.46	**1.04**†	0.07	.744	-0.38	0.52	0.08
PSQI: duration	0.38	0.61	0.69	1.00	0.83	0.83	2.60	.079	**.025***	.655	-0.32	.178	-0.78	0.15	0.39	-0.46	**.025***	-0.85	-0.06	**0.63**†	-0.14	.509	-0.56	0.28	0.15
PSQI: alterations	1.04	0.25	1.77	0.61	2.05	0.60	32.62	**<.001***	**<.001***	.073	-0.73	**<.001***	-1.02	-0.44	**1.56**†	-1.01	**<.001***	-1.25	-0.76	**2.19**†	-0.28	**.036***	-0.54	-0.02	0.46
PSQI: medication	0.19	0.55	0.56	1.08	1.12	1.34	6.76	**.003***	**.001***	.707	-0.37	.228	-0.98	0.24	0.43	-0.94	**.001***	-1.46	-0.42	**0.91**†	-0.57	**.042***	-1.11	-0.02	0.46
PSQI: dysfunction	0.59	0.67	1.01	0.98	1.31	1.02	5.37	**.007***	**.001***	.796	-0.42	.108	-0.94	0.09	**0.50**†	-0.73	**.001***	-1.17	-0.29	**0.85**†	-0.31	.191	-0.77	0.16	0.31
PSQI: efficiency	0.10	0.30	0.72	0.99	0.79	0.91	6.84	**.003***	**.001***	.163	-0.62	**.008***	-1.07	-0.17	**0.85**†	-0.70	**.001***	-1.08	-0.31	**1.03**†	-0.08	.704	-0.48	0.33	0.08
PSQI: total	3.53	2.07	7.94	3.78	9.33	4.08	23.63	**<.001***	**<.001***	.076	-4.41	**<.001***	-6.38	-2.44	**1.45**†	-5.80	**<.001***	-7.49	-4.11	**1.79**†	-1.39	.122	-3.16	0.38	0.35
Actigraph-based sleep time	369.80	52.23	421.43	62.48	385.57	61.44	5.14	**.031***	.268	**.002**	-51.63	**.002***	-84.37	-18.89	**0.90**†	-15.77	.268	-43.86	12.33	0.28	35.86	**.017***	6.43	65.29	**0.58**†
SCL-90R: depression	0.67	0.52	1.36	0.90	1.70	0.78	15.95	**<.001***	**<.001***	.337	-0.69	**.002***	-1.11	-0.27	**0.94**†	-1.03	**<.001***	-1.39	-0.67	**1.55**†	-0.34	.078	-0.72	0.04	0.40
SCL-90R: anxiety	0.42	0.34	0.89	0.63	1.31	0.77	17.13	**<.001***	**<.001***	.871	-0.47	**.010***	-0.82	-0.12	**0.92**†	-0.89	**<.001***	-1.19	-0.58	**1.49**†	-0.42	**.010***	-0.74	-0.10	**0.60**†
SCL-90R: somatizat.	0.59	0.41	1.45	0.75	1.97	0.89	30.32	**<.001***	**<.001***	.329	-0.86	**<.001***	-1.27	-0.45	**1.42**†	-1.38	**<.001***	-1.73	-1.03	**1.97**†	-0.52	**.006***	-0.88	-0.15	**0.63**†

Note. SCL-90R: Symptom Check List questionnaire. HC: healthy controls. OB: obese. MOB: morbid obese. MD: mean difference. Depres: SCL-90R depression scale score. Anx: SCL-90R anxiety scale score. Somat.: SCL-90R somatization scale score.

*Bold: significant result (.05 level). †Bold: moderate to large effect size (|*d*|>0.50). Bonferroni's-Finner correction.

Higher scores in the PSQ sleep quality measures indicate poorer sleep

Figure 1


.74
Depression
.85
Anxiety
.72
Somatization
.26
.20
.26
.43
.25
PSQ: total
.23
BMI (kg/m²)
.18
.023
Orexin
-.029
Age