

Depression and Obesity among Untreated People, Diagnosed with Sleep Apnea Syndrome

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Foreword and Acknowledgement

Submitted in partial fulfillment of the requirements of the BSc Psychology degree, Reykjavík University, this thesis is presented in the style of an article for submission to a peer-reviewed journal.

The present study used data from a larger ongoing research supervised by Erla Björnsdóttir, which focused on mental health and insomnia among sleep apnea patients. The research took place at Landspítali – The National University Hospital of Iceland in 2012-2013. The National Bioethics Committe of Iceland has approved the research (10-048) and the person responsible for the accuracy of the research is Þórarinn Gíslason.

Abstract - English

Obstructive sleep apnea (OSA) is a common sleep disorder, affecting 2-4% of the adult population. Research on both community and clinical populations have indicated high rates of depression among OSA patients. Obesity is one of the greatest risk factors of OSA, affecting 70% of patients with OSA. Even though depression and obesity are prevalent, few studies have examined which factors contribute to depression and obesity among OSA patients. The aim of this study was to determine the degree to which lifestyle factors, along with participants' general state of health, independently affect the relationship between depression and obesity among OSA patients. The participants were 181 patients, newly diagnosed with sleep apnea syndrome. Depression was assessed with The Center for Epidemiological Studies-Depression Scale (CES-D) and obesity among participants was based on their body mass index (BMI). Results from multiple linear regression models revealed that gender and functional outcomes of sleep had the greatest influence on depressive symptoms while gender, age, severity of sleep apnea and participants' smoking habits had the greatest effect on BMI. These results indicate a need for health care workers to provide attention to multiple factors which may influence the development of depression and obesity among OSA patients.

Abstract - Icelandic

Kæfisvefn er algengur svefnsjúkdómur sem hrjáir 2-4% einstaklinga í öllum heiminum. Rannsóknir sem gerðar hafa verið á þátttakendum bæði í almennu sem og í klínísku þýði, hafa sýnt fram á hátt hlutfall þunglyndis meðal einstaklinga sem glíma við kæfisvefn. Offita er einn helsti áhættuþáttur kæfisvefns og er talið að um 70% einstaklinga með kæfisvefn glími við offitu. Þrátt fyrir að þunglyndi og offita séu algeng meðal kæfisvefnssjúklinga þá eru ekki margar rannsóknir sem hafa skoðað hvaða þættir það eru sem stuðla að þunglyndi og offitu meðal kæfisvefnssjúklinga. Markmið rannsóknarinnar var að kanna áhrif heilsu- og lífstílstengdra breyta á þunglyndi annars vegar og offitu hinsvegar. Þátttakendur voru 181 talsins, allir nýlega greindir með kæfisvefn. Þunglyndiskvarði til faraldsfræðirannsókna (CES-D) var notaður til að meta þunglyndi þátttakenda og offita þátttakenda var metin með líkamsþyngdarstuðlinum (BMI). Niðurstöður margvíðrar aðhvarfsgreiningar leiddu í ljós að kyn og virkni daglegs lífs með tilliti til syfju höfðu mest áhrif á þunglyndiseinkenni meðal þátttakenda en kyn, aldur, alvarleiki kæfisvefns og reykingar höfðu mest áhrif á BMI. Niðurstöðurnar gefa til kynna mikilvægi þess að heilbrigðisstarfsmenn veiti margvíslegum þáttum athygli sem haft geta áhrif á þróun þunglyndis og offitu meðal kæfisvefnssjúklinga.

Depression and obesity among untreated people, diagnosed with sleep apnea syndrome

The prevalence of sleep disordered breathing has increased substantially in the last two decades (Peppard et al., 2013). Obstructive sleep apnea (OSA) is the most ordinary form of sleep disordered breathing worldwide (Lam, Sharma, & Lam, 2010). Although the term OSA has been recognized in clinical circles for over 40 years now (Gastaut, Tassinari, & Duron, 1966), until recently awareness of the syndrome has been slow to develop outside the field of medicine (Young, Peppard, & Gottlieb, 2002).

OSA is characterized by repeated cessations of apneas and hypopneas during sleep (Young et al., 2002) which are due to obstruction of the upper airway, even during wakefulness, so an OSA patient's airway is smaller than usual (Pack, 2006). The apnea-hypopnea index (AHI) is most commonly used to measure the severity of OSA, by calculating the mean number of apneas and hypopneas per hour of sleep (Pack, 2006). When these take place more than five times a night, sleep apnea will be diagnosed. The severity of the symptom has been divided into three different stages: mild, moderate and severe sleep apnea. AHI $5 - \le 15$ is mild sleep apnea, $15 - \le 30$ is moderate sleep apnea and AHI ≥ 30 is considered severe sleep apnea (Pack, 2006).

OSA is a prevalent disorder, affecting 2-4% of the adult population (Epstein et al., 2009) and it is primary diagnosed in men, with approximately 4% of middle-aged men diagnosed in the population, compared to 2% of middle-aged women (Young et al., 1993). There are a numbers of other risk factors for the development of OSA. Age as well as family aggregation and genetic factors are thought to play a role in the development of OSA even though the underlying mechanism remains unclear (Young et al., 2002). Alchohol consumption, smoking and obesity are examples of risk factors that are prevalent but can be avoided with proper intervention (Young et al., 2002) and generally, the focus should be more on proper interventions because reducing these risk factors would benefit sufferers of OSA.

The effects of OSA can manifest in different ways. According to Asghari, Mohammadi, Kamrava, Tavakoli, and Farhadi (2012) OSA can cause sleep fragmentation as well as inducing noctural hypoxemia, which is a partial deficiency of oxygen in the blood of the person concerned. Later on it results in excessive daytime sleepiness, as well as poor performance on neruocognitive tasks, mood problems and dysfunction of the organ system (Asghari et al., 2012). The question of mood problems deserves to be examined more closely, as a high number of people has to struggle with not only the effects of above-mentioned symptoms of OSA but also with depression (Harris, Glozier, Ratnavadivel, & Grunstein, 2009; Schröder & O'Hara, 2005). A study by Sharafkhaneh, Giray, Richardson, Young, and Hirshkowitz (2005) indicated that 21.8% of middle-aged participants diagnosed with OSA also had been diagnosed with depressive disorder. Another study, conducted by McCall, Harding, and O'Donovan (2006), assessed depressive symptoms with the Beck Depression Inventory among OSA patients. The results showed that 28% of the women were categorized as having a moderate depression, compared with only 6% of the men. These findings are consistent with previous studies that have examined gender differences in depressive symptoms among OSA patients (Pillar & Lavie, 1998; Wahner-Roedler et al., 2007). The origin of depression in OSA is debated: is depression a primary consequence of OSA or is it secondary to the OSA symptoms (Andrews & Oei, 2004)? It has been recommended to view the mood disorder as a secondary to the medical disorder (Haba-Rubio, 2005).

Researchers do agree that obesity is the strongest risk factor for the development of OSA (Lam et al., 2010; Rossini, 2009), particularly central obesity (Young et al., 1993), and it is estimated that 70% of OSA patients are obese (Malhotra & White, 2002). Those numbers are even higher for the morbidly obese (Daltro et al., 2007). To demonstrate the need to prevent obesity among OSA patients, a study of 690 randomly selected subjects conducted by Peppard, Young, Palta, Dempesey, and Skatrud (2000) showed a six-fold increase in the risk

of developing sleep apnea, among subjects who showed a 10% weight gain. A loss of 10% weight, in the same study, predicted a 26% decrease in the AHI.

The growing epidemic of obesity is a major health problem (Mokdad et al., 2003). Obesity increases the chances of developing diabetes (Friedman, 2009), and since it has been represented as a major risk factor for hypertension (Chrostowska & Narkiewicz, 2008) and cardiovascular events (Van Gaal, Mertens, & De Block, 2006), a treatment for OSA therefore signifies a major benefit to public health. Mainly because it has been indicated that continous positive airway pressure (CPAP), which is the most effective treatment for OSA (Ejaz, Khawaja, Bhatia, & Hurwitz, 2011), has the potential to reverse the cardiovascular consequences of obesity when used on obese individuals (Arnardottir, Mackiewicz, Gislason, Teff, & Pack, 2009). In addition, these findings emphasize the need for diagnosing OSA and providing effective treatments, like CPAP, since studies have pointed out that a vast majority of the at-risk group of OSA sufferers remain undiagnosed (Young, Evans, Finn, & Palta, 1997; Kapur et al., 2002). Furthermore, one study by Foster et al. (2009) found that 86% of patients with type 2 diabetes were undiagnosed sufferers of OSA.

As mentioned above, depression and obesity are well-known among people who have to struggle with OSA. Since this is the case, it is appropriate to discuss whether there is an association between depression and obesity. Some studies indicate that there is no relationship between depression and being overweight (Ross, 1994), while others have shown that the risk of suicidal ideation (Carpenter, Hasin, Allison, & Faith, 2000) and depression (Roberts, Strawbridge, Deleger, & Kaplan, 2002) can be associated with obesity. One study conducted by Roberts, Deleger, Strawbridge, and Kaplan (2003) found that obesity increased the risk of future depression but depression did not increase the risk of obesity among participants in the future. In a study conducted by Aloia et al. (2005) where they examined the relationship between the severity of OSA and obesity on depressive symptoms among OSA patients, they

found that obesity by itself was relatated to depressive symptoms since obese patients seemed to score higher on the depressive scale than non-obese participants. When examining depressive symptoms and OSA, Pillar and Lavie (1998) suggested that the relationship between those two factors might be mediated by gender and the severity of OSA. In their results of 2,271 participants with sleep apnea syndrome they found that neither the existence nor the severity of OSA was associated with depression in their male population. However, the overall score among women with OSA was generally higher and as the severity increased the depressive symptoms also increased. In addition, it has been indicated that depressive symptoms in OSA patients can appear differently in men than in women, as well as the effects of OSA severity and obesity on depressive symptoms (Aloia et al., 2005).

While both depression and obesity are common among OSA patients some fare better than others, therefore it is important to identify factors, beyond OSA itself, that are associated with depression and obesity as it might assist health care workers, to identify factors that can reduce those undesirable symptoms or prevent that they occur. Lifestyle factors (*e. smoking, drinking, exercise*) are thought to play a role in increased risk of obesity (Holzapfel et al., 2010) as well as they are considered to be influential when it comes to the development of depression (Demura & Sato, 2003) and therefore it is important to examine these factors in relation to depression and obesity among OSA patients.

Given the prevalence of depression and obesity among OSA patients and the role of lifestyle factors associated with them in the literature of previous research, the main purpose of this study was to establish the degree to which lifestyle factors, along with participants' general state of health, independently contribute to the relationship between depression and obesity among OSA patients. The following research questions will be examined: a) Which lifestyle- and health related factors will affect depression and obesity among participants? b) How much impact will lifestyle factors and general health contribute to the relationship

between depression and obesity? c) Does gender mediate the difference between factors that affect depression and obesity?

Method

Participants

A total of 181 people were offered to participate in the study and no one declined to take part. Participants were all diagnosed with sleep apnea syndrome in the years 2010-2013, and on a waiting list for treatment at the Department of Respiratory Medicine and Sleep at Landspítali – The National University Hospital of Iceland. The gender ratio in the sample was 74.6 % (n=135) male and 25.4 % (n=46) female, which represents the patients population of OSA. The mean age was 53.70 years (SD = 10.52; lowest = 26 years, highest = 73 years). To be eligible for the study, the participants had to have been diagnosed with sleep apnea syndrome and to have had no treatment for the syndrome. All of the participants met these conditions. Participants received no payments or any other benefits for their participation.

Procedure

This study was approved by The National Bioethics Committee of Iceland and The Data Protection Authority was notified of the study. Newly diagnosed patients with sleep apnea syndrome were asked to participate in the study. Participants recieved a phone call from a member of the research team who explained the study procedure to them. They were then invited to participate in the study. After recieving an information letter to their home (see appendix A), an in-person meeting was scheduled for patients willing to participate at Landspítali, where all measures took place. Informed consent was obtained at the meeting (see appendix A), where participants were made aware of their right to determine their participation at any time without explanations. Also, participants were informed that their private information would be encoded and stored at Landspítali for the next 2-5 years, and deleted after that time unless the research team contacted the participants in the meantime.

After signing the consent form, participants answered a questionnaire about the sleep apnea syndrome and their state of health (see appendix B). After being advised not to hesitate to ask for help, if needed, the participant was left alone while answering the questionnaire to avoid any disturbance. Afterward, the participants height, weight and blood pressure were measured and a fasting blood test was performed. For each participant, the measurement lasted for one hour without any break but since participants had to attend the measurements on an empty stomach they were invited to get breakfast following the blood test.

Measures

A questionnaire including questions concerning participants' lifestyle and general state of health was administered. A part of the questions from this questionnaire was used in the present study (see appendix B). General state of health was assessed by asking participants about their medical history. The questions concerning their medical history were "have you ever been diagnosed with hypertension?", "have you ever been diagnosed with diabetes?" and "have you ever been diagnosed with asthma?". Questions concerning participants' lifestyle included questions on smoking ("have you smoked or used tobacco for at least one year?") and alcohol use ("do you drink alcohol?"). Other questions concerning lifestyle were "do you practice sports or any other regular physical activity (e.g., swimming, cycling)?" and "do you use sleep medications regularly?".

Depression was assessed with the Icelandic translation of the Center for Epidemiological Studies – Depression Scale (CES-D) (see appendix B), which was translated to Icelandic by Rafnson, Karlsson, Porvaldsson and Smári (as cited in Smári, Ólason, Arnarson, & Sigurðsson, 2008). CES-D is a 20 item scale, designed to measure depression in the general population (Radloff, 1977), where participants are asked to indicate their extent of behavior to each statement over the past week. Participants' responses to the statements are on a four-point Likert scale from 0 (rarely or none of the time) to 3 (most or all of the time).

Possible range of total score is from 0 to 60, where a higher score indicates more depressive symptoms. CES-D includes four components: depressed affect, positive affect, somatic/retarded activity, and interpersonal (Smári et al., 2008). Examples of the items on the list are "I was bothered by things that usually don't bother me", "I thought my life had been a failure", "I talked less than usual" and "I felt that people dislike me". The English version of CES-D has proven to be a reliable and valid measure of depression, with the internal consistency varying between .85 for the general population to .90 for a psychiatric population (Radloff, 1977). Studies on the psychometric properties of the Icelandic translation of CES-D were conducted in a study by Smári, Gylfadóttir, and Halldórsdóttir (2003) where the psychometric properties were found to be the same as in the English versions of the scale.

Assessment of obesity among participants was based on their body mass index (BMI), which is commonly used to classify overweight and obesity among adults (World Health Organization, 1998). BMI was calculated as the weight in kilograms divided by the square of the height measured by a scale. In the present study, the general criterion for obesity (BMI \geq 30) is not used, instead the results are interpreted as raw scores.

The Epworth Sleepiness Scale (ESS) (Johns, 1991) was used to determine the level of daytime sleepiness among participants (see appendix B). It is an eight-item questionnaire where participants are asked to rate their chances of dozing or falling asleep in eight different situations. It is a 4-point scale from 0 (would never doze) to 3 (high chance of dozing). Examples of situational statements on ESS are "Sitting and reading", "Sitting inactive in a public place (e.g. a theater or a meeting)", "Sitting and talking to someone". The total ESS score can range from 0 to 24, where a higher score indicates participants' higher level of daytime sleepiness. ESS has proven to be a reliable and valid measure of daytime sleepiness, with the internal consistency varying between .73 and .88 in a study of 144 patients and medical students (Johns, 1992).

The 12-Item Short-Form Health Survey (SF-12) (Ware, Kosinski, & Keller, 1996) was used to evaluate health-related quality of life among participants (see appendix B). SF-12 is a shorter form of the 36-item short-form health survey (SF-36) and it consists of 12 items which are based on a subset of 12 SF-36 items. SF-12 is summarized as the physical component summary and the mental component summary where a higher score indicates better health status. The statements on the SF-12 scale reflect general health in daily life and the participant is supposed to answer most of the statements with regard to his or her state of health during the past four weeks.

The Short Version of the Functional Outcomes of Sleep Questionnaire (FOSQ-10) (Chasens, Ratcliffe, & Weaver, 2009), was used to measure the impact of daytime sleepiness on daily behaviors among participants and sleep-related quality of life (see appendix B). It is a 4-point scale from 1 (extreme difficulty) to 4 (no difficulty). FOSQ-10 is a shortened version of FOSQ-30 and it has proven to be a reliable and valid measure of the functional outcomes of sleep, with the internal consistency .87 for a clinical population (Chasens et al., 2009). Examples of questions on FOSQ-10 are "Do you have difficulty concentrating on the things you do because you are sleepy or tired?" and "Do you have difficulty operating a motor vehicle for long distances (greater than 100 miles) because you become sleepy or tired?" The total score on FOSQ-10 can range from 0 to 40, where a higher score indicates participants' ability to overcome sleepiness while engaged in the activities of daily life.

Participants' severity of OSA was measured with an overnight sleep study done either at the hospital or at home. The measures of their apnea-hypopnea index, were not conducted in the present study since participants had all been diagnosed with OSA before starting their participation in the study. An overnight in laboratory polysomnography is a standard method to test for OSA. This method involves the recording of numerous variables during sleep, and the main purpose is to identify different types of apneas and hypopneas during sleep (Lam et

al., 2010). Since this process can be expensive and time-consuming (Lam et al., 2010) a newer technology allows the patients to undergo an unattended polysomnography at home (Pack, 2006).

Design and Data Analysis

As the questionnaire was administered once, the design of this study was cross-sectional. To test the main hypothesis, two predictor variables (general health and lifestyle factors) and two outcome variables (depression and BMI) were used.

SPSS version 20 was used for analyzing the data. Descriptive statistics were conducted to gather information on certain characteristics like the variance in age and other lifestyle and health related factors. Second, preliminary analysis was conducted to test if there were correlations between any of the predictor and outcome variables. Then a multiple linear regression was tested. The researcher ran two models for depression on the one hand and BMI coefficient on the other. These regression analyses were then run for each gender. Results were accepted as significant if the p-value was equal to or less than 0.05

Assumptions of multiple regression were tested for the models and two of them were broken. There were indications of heteroscedasticity for the depression model and the residuals were not normally distributed for both models. According to Field (2009) the errors are reasonably independent, since the Durbin-Watson statistic does fall within recommended limits of 1-3.

Results

Chronbach's alpha was tested to evaluate the reliability of scales used in the study. The results for Chronbach's alpha indicated good reliability for three of four measures used in the study: depression (α = .76), daytime sleepiness (α = .79) and functional outcomes of sleep (α = .83). The Chronbach's alpha for the health survey scale (SF-12) was not reliable (α = .00).

The descriptive statistics for scales used in present study are shown in Table 1.

Table 1

Descriptive statistics for scales used in the study.

	N	Mean	Std.Deviation	Range
Gender	181	1.25	.43	1-2
Age	181	53.70	10.52	26-73
Depression	169	12.87	9.79	0-52
BMI	180	34.23	6.53	20-67
General Health				
AHI	181	35.62	20.37	12-115
Hypertension	179	1.42	.55	1-3
Diabetes	180	1.91	.28	1-3
Asthma	176	1.86	.39	1-3
Day sleepiness	181	10.52	4.38	0-22
SF12 health	181	30.43	3.29	10-42
FOSQ-10	181	31.54	5.89	13-40
Lifestyle factors				
Smoking	181	1.37	.48	1-2
Drinking	178	1.25	.61	1-3
Exercise	175	1.69	.94	1-4
Sleep medication	178	1.81	.38	1-2

Note: AHI = The apnea-hypopnea index

SF-12 health = A 12-item short-form health survey

FOSQ = Functional outcomes of sleep questionnaire

To examine potential background covariates, the relationship between the predictor variables (lifestyle and general health) and the outcome variables (depression and BMI) was examined. As table 2 shows, significant correlations were found for nine variables in the study. Gender was positively related to both depression (r = .27, p < .01) and BMI (r = .19, p < .05) in the study. Age was negatively related to both depression (r = -.15, p < .05) and BMI (r = -.26, p < .01). There was a positive association between the severity of OSA (r = .18, p <

.05) and BMI. There was also a positive relationship between the predictor variable, smoking (r = .15, p < .05) and BMI. Daytime sleepiness (r = .18, p < .05) was positively related to depression as well as exercise (r = .19, p < .05) and drinking (r = .19, p < .05). Furthermore, sleep medication (r = -.27, p < .01) and functional outcomes of sleep (FOSQ) (r = -.54, p < .01) were negatively related to depression.

Table 2

Pearson bivariate correlations for the variables in the study.

	Depression	BMI
Gender	.27**	.19*
Age	15*	26**
AHI	14	.18*
Daytime sleepiness	.18*	.05
Sleeping pills	27**	02
FOSQ	54**	08
Bruxism	.09	02
Hypertension	.03	10
Diabetes	.13	10
Asthma	.02	01
SF12 health	15	04
Exercise	.19*	.06
Smoking	06	.15*
Drinking	.19*	.10
Depression	1	.121
BMI	.121	1

^{*}p < .05 (two-tailed test)

In table 3 the multivariate linear regression is presented. Significanty correlated variables were put in the linear regression model to check whether the predictive variables had any effect on depression. The interaction between the predictive variables, general health and lifestyle factors, was a significant predictor of depression. The model accounted for

^{**}p < .01 (two-tailed test)

34.7% of the variation of depression (F(7,158) = 11.485, p < .01). Table 3 demonstrates that functional outcomes of sleep had strong positive effects on depression ($\beta = -.452$, p < .01). Furthermore, gender had the second most effect on depression of all variables conducted in the model with a positive relationship ($\beta = .156$, p < .05). The other variables in the model were not significant (p = .102 - .547).

When controlled for gender the model accounted for 26.3% of the variation of depression (F(6,115) = 6.477, p < .01) among males compared with 41.3% for females (F(6,42) = 4.229, p < .05). The results indicate that functional outcomes of sleep had strong positive effects on depression, both for males ($\beta = -.412$, p < .01) and females ($\beta = -.576$, p < .01). Other variables tested in this model were not significant (p = .053 - .918) (see appendix C).

Table 3

Multiple linear regression analysis for depression, with general health and lifestyle factors as predictor variables.

	В	β	t	Sig.
(Constant)	40.982		5.370	.000
Gender	3.423	.156	2.260	.025
Age	105	113	-1.645	.102
Daytime sleepiness	117	051	658	.511
FOSQ	736	452	-5.565	.000
Exercise	.999	.098	1.428	.155
Drinking	.691	.041	.603	.547
Sleep medication	-2.751	110	-1.582	.116

a. Dependent variable: Depression

Note: FOSQ = Functional outcomes of sleep questionnaire

Gender, age, smoking and AHI explained a significant proportion of variance in BMI scores. The model accounted for 16.6% of the variation of BMI (F(4,179) = 8.736, p < .001). Table 4 demonstrates that age had strong negative effects on BMI ($\beta = -.262$, p < .01). Gender

had the second most effect on BMI of all variables conducted in the model with a positive relationship ($\beta = .244$, p $\le .01$). Furthermore, AHI also had an effect on BMI with a positive relationship ($\beta = .184$, p $\le .05$).

When controlled for gender the model accounted for 20.7% of the variation of BMI (F(3,133) = 11.301, p < .01) among males compared with 4.1% for females (F(3,45) = .594, p > .05). The results indicate that age had strong negative effects on BMI for males $(\beta = -.344, p < .01)$. AHI had the second most effect on BMI, with a positive relationship $(\beta = .266, p < .01)$. Other variables were not significant (p = .224 - .829) (see appendix C).

Table 4

Multiple linear regression analysis for BMI, with general health and lifestyle factors as predictor variables.

	В	β	t	Sig.
(Constant)	34.129		10.768	.000
Gender	3.643	.244	3.487	.001
Age	163	262	-3.768	.000
AHI	.059	.184	2.608	.010
Smoking	1.576	.117	1.658	.099

a. Dependent variable: BMI

Note: AHI = Apnea-Hypopnea index

Discussion

The current study was conducted to examine the relationship between lifestyle factors and general health on depression and BMI among untreated sleep apnea patients. The main aim of the present study was to determine the degree to which lifestyle factors, along with participants' general state of health, independently contributed to the relationship between depression and obesity among participants, as well as to examine the moderating effects of gender on these relationships. The main results indicated that functional outcomes of sleep and gender had the greatest influence on depressive symptoms among participants while age,

gender, severity of sleep apnea and participants' smoking habits had the greatest effect on BMI. According to these results, gender seems to be the primary force which influences both depression and BMI. This provides an answer to the research question about the possibility of gender differences in the present study. The results indicated that gender differences do occur, since the model demonstrated that lifestyle factors and general health have a much greater impact on women than men when it comes to depression. It can be related to findings from a study of Aloia et al. (2005) about different manifestation of depressive symptoms among gender, but it is hard to relate the findings to one explanation why this is the case. One possible suggestion why these factors have more impact on women, as Pillar and Lavie (1998) discussed in their study, might be due to the tendency of women to focus more on their depression and related factors, rather than men do. There were also gender differences when BMI was examined and the results indicated that the lifestyle factors and the health variables were only related to BMI in the case of men, but women.

The findings that functional outcomes of sleep do impact depressive symptoms among both genders are not surprising and relate to previous findings of Gooneratne et al. (2003), which state that functional impairment is related to daytime sleepiness among elderly subjects. The same results have been found in a study of nonelderly populations (Briones et al., 1996). These findings suggest that health care workers should not ignore implications of daytime sleepiness among patients since it can have multifactorial influence on patients' everyday lives. This is most when it comes to functional outcomes of sleep, like the individuals' ability to drive, meet friends and family or concentrate on daily things, to name a few. In addition to this, it is noteworthy that the level of daytime sleepiness, measured with The Epworth Sleepiness Scale, is not related to depression in the present study and that is inconsistent with previous findings which have indeed demonstrated an association between daytime sleepiness and depression (Bixler et al., 2005; Kjelsberg, Ruud, & Stavem, 2005). It

raises the question whether participants underreported their conditions of daytime sleepiness while overestimating the severity of their functional impairments. This is possible, as studies have shown that the older generation seems to be more satisfied with conditions that concerns quality of life compared with younger adults (Ancoli-Israel & Coy, 1994).

The results also revealed that severity of OSA was only related to BMI and that is consistent with previous findings from Peppard et al. (2000) where they found that a loss of weight predicted a decrease in the AHI. In the present study, these results were only found among men. It is noteworthy that severity of OSA was not linked to depression in the study and that is inconsistent with Aloia et al. (2004) findings but partly consistent with Pillar and Lavie's (1998) findings that the severity of OSA was not associated with depression among men but only among female participants. The causes for these findings are not obvious, but following speculations might shed some light on why the present study did not find relationship between AHI and depression. In the present study, the results were interpreted as a raw score instead of using the cut-off score 16 since the results did not give a significant evidence of depression among participants when tested in the study, even though the cut-off score of 16 is believed to be exact in about 75% of cases for further diagnosis of depression according to Pandya, Metz, and Patten (2005). It raises questions about if the frequency of depression is lower in Iceland, where the research took place, than elsewhere? According to Stefánsson, Líndal, Björnsson, and Guðmundsdóttir (1991) their findings demonstrate that the incidence of depression is similar in Iceland compared to other countries so that is probably not the explanation. Another indication could be related to how the severity of OSA was measured. In both studies, the severity of OSA was measured by using the respiratory disturbance index (RDI) but not AHI as the present study did.

The present study is however not without its limitations so the above findings should be interpreted with caution. Firstly, the researcher relied exclusively on self-reported rating scales so there is a chance that self-report bias influenced the results. Secondly, the cross-sectional nature of the present study inhibits us from drawing causal conclusions from the results. For example, we do not know whether functional outcomes of sleep in daily life lead to increased depression or whether depression resulted in impaired functional outcomes of sleep. Thirdly, the gender ratio was greatly skewed, which might influence the results, but since men are more likely to be diagnosed with OSA it is not surprising that there were fewer female participants.

Despite the above limitations, the present study provides indications that lifestyle- and health related factors play a role in increased risks of depression and obesity among untreated OSA patients. The findings indicate a need for health care workers to provide attention to multiple factors which may influence the development of depression and obesity. More research is needed in this field of area so future studies should focus more closely, and with bigger samples, on what factors contribute the most to depression and obesity among untreated OSA patients since untreated OSA concerns the whole of society. It can, for example, increase the risk of traffic accidents (Yamamoto et al., 2000) and lead do permanent work disability (Sivertsen et al., 2008). Future studies should consider to use standardized interviews to assess depression among participants since it has not been done before in Iceland, at least. It would also be interesting to assess obesity with not only the body mass index, but also with the waist circumference, which studies have indicated that foretell more about health risk than BMI does when used alone (Ardern, Katzmarzyk, Janssen, & Ross, 2003). It would also be interesting to examine how these factors contribute to depression and obesity after treatment of OSA.

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Appendix A





Rannsóknin "Líðan kæfisvefnssjúklinga fyrir og eftir meðferð – samspil offitu, bólguboðefna, erfða og meðferðarárangurs".

Ágæti viðtakandi,

Með þessu bréfi leitum við eftir þátttöku þinni í rannsókn sem kallast "Líðan kæfisvefnssjúklinga fyrir og eftir meðferð – samspil offitu, bólguboðefna, erfða og meðferðarárangurs". Við óskum eftir þátttöku fólks með nýgreindan kæfisvefn á meðalháu til háu stigi. Ekki eru sett sérstök útlokunar skilyrði nema að sjúklingur má ekki áður hafa gengist undir meðferð með svefnöndunartæki (e. CPAP).

Rannsakendur eru:

Ábyrgðarmaður rannsóknarinnar er Þórarinn Gíslason, yfirlæknir á Landspítala háskólasjúkrahúsi, Fossvogi, 108 Reykjavík, sími 543-1000 tölvufang thorarig@landspitali.is

Aðrir rannsakendur eru: Erla Björnsdóttir, sálfræðingur og doktorsnemi sími 860-8009, en rannsóknin er hluti af doktorsverkefni hennar. Einnig Bryndís Benediktsdóttir, læknir og Sigurður Júlíusson, háls-, nef- og eyrnalæknir.

Tilgangur og markmið rannsóknarinnar:

Tilgangur rannsóknarinnar er að kanna líðan kæfisvefnssjúklinga fyrir og eftir 4 mánaða meðferð með sérstöku tilliti til offitu, bólguboðefna og þess á hvaða stigi kæfisvefninn er. Rannsókninni er ætlað að afla nýrrar þekkingar sem mikil þörf er á. Kæfisvefn er meðal algengari langvinnra sjúkdóma og á Íslandi og hafa 5-6% miðaldra karla þegar greinst. Um það bil 2.500 Íslendingar nota að staðaldri svefnöndunartæki, nokkru fleiri karlar en konur. Offita og þunglyndi eru einnig algengir og þrálátir sjúkdómar og hefur tíðni þeirra aukist jafnt og þétt undanfarna áratugi. Offita er einn helsti áhættuþáttur kæfisvefns og tengsl þunglyndis við offitu eru vel þekkt. Það hefur hins vegar skort á rannsóknir sem athuga þátt kæfisvefns í þessum tengslum. Það er mikilvægt að vita hvort þunglyndi hafi áhrif á meðferð við kæfisvefni sem og að kanna hvaða áhrif bólguefni í blóði hafa á tengsl þessara raskana. Gera má ráð fyrir að draga megi af rannsókninni ályktanir sem gagnist í klínísku starfi við meðhöndlun kæfisvefnssjúklinga.

Þátttaka í rannsókninni felur í sér eftirfarandi:

Þátttaka í rannsókninni felur í sér tvær heimsóknir sem hvor um sig tekur u.þ.b tvær klukkustundir.

- Lagðir verða fyrir spurningalistar um svefn, svefnvenjur, lífstíl, lífsgæði, heilsu, lyfjanotkun og andlega líðan.
- Tekið verður staðlað greiningarviðtal (MINI) sem mælir meðal annars þunglyndi og kvíða.
- Blóðprufur verða teknar að morgni hjá öllum þátttakendum til að kanna þéttni bólguefna í blóði, blóðsykur og insúlin. Blóðprufu fylgja eymsl við stungu og stundum kemur fram mar á húð.
- Eftir 4ra mánaða kæfisvefnsmeðferð verður þátttakendum boðið í samskonar mat ásamt viðbótar spurningum um breytingar sem ætla má að geti tengst kæfisvefnsmeðferðinni.
- Í seinni heimsókininni verður lögð fram sérstök samþykkisyfirlýsing um erfðaefnissýni og sért þú samþykk(ur) því verða þá fryst sýni til erfðarannsókna.
- Í seinni heimsókninni verða teknar nýjar blóðprufur. Heimilir þú varðveislu blóðsýnis í Lífsýnasafni Landspítalans (LLR) verður hluti blóðsýna (50ml) sem tekin sem verða í síðari heimsókninni fryst til erfðarannsókna sem sótt verður um sérstaka heimild Vísindasiðanefndar og Persónuverndar til að framkvæma. Þú þarft að undirrita sérstaka heimild þína fyrir því að varðveita blóðsýni úr þér í Lífsýnasafni Landspítalans.

Með þetta í huga leitum við til þín um þátttöku. Meðfylgjandi er ítarlegt upplýsinga- og samþykkisblöð. Fljótlega munum við hafa samband við þig símleiðis og munum þá gjarnan svara öllum þeim spurningum sem þú kannt að hafa varðandi rannsóknina. Þér er auðvitað alls ekki á nokkurn hátt skylt að sinna málaleitan okkar. Þér er frjálst að hafna þátttöku eða hætta í rannsókninni á hvaða stigi sem er, án útskýringa og án afleiðinga á aðra meðferð.

Rannsóknin hefur verið samþykkt af Vísindasiðanefnd og samþykkt af Persónuvernd.

Með kærri kveðju,

Þórarinn Gíslason, yfirlæknir

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Líðan kæfisvefnssjúklinga fyrir og eftir meðferð - Samspil offitu, bólguboðefna, erfða og meðferðarárangurs -

Samþykkisyfirlýsing fyrir þátttakendur

Markmið þessarar rannsóknar eru margþætt:

- 1. Að kanna líðan (sérstaklega þunglyndi) kæfisvefnssjúklinga fyrir og eftir 4 mánaða meðferð með svefnöndunartæki með sérstöku tilliti til offitu, bólguboðefna og þess á hvaða stigi kæfisvefninn er.
- 2. Athuga hvort kæfisvefn, bólguboðefni (m.a. CRP, Leptín og IL-6) séu hugsanlega breytur sem skýri að hluta þekkt tengsl offitu og þunglyndis.
- 3. Að halda áfram gagnasöfnun hvað varðar meingerð, erfðir og meðferðarárangur kæfisvefnssjúklinga.

Samband kæfisvefns, dagsyfju og áhættu hjarta- og æðasjúkdóma er þekkt að hluta og eitt af viðfangsefnum þessarar rannsóknar, en tengslin við líðan, einkum þunglyndi eru þó megin markmið. Sérstaklega er kannað hvort líðan breytist við meðferð á kæfisvefni og hvort sú breyting sé háð magni bólguboðefna í blóði, líkamsbyggingu eða eðli kæfisvefnsins.

Ég sambykki að:

Að svara spurningalistum, gangast undir stutta líkamsskoðun, og að tekin verði blóðprufa (40 ml) til mælinga á bólguboðefnum. Í seinni heimsókn mun lagt fyrir sérstakt kynningarefni og samþykkisyfirlýsing vegna rannsókna á erfðaefni.

Að koma aftur í samskonar rannsóknir fjórum mánuðum eftir að CPAP meðferð hefst.

Að ábyrgðarmenn rannsóknar megi nálgast nauðsynlegar upplýsingar úr sjúkraskrám mínum eða gögnum heilbrigðisstofnana, sé slíkt nauðsynlegt framgangi rannsóknarinnar.

Samþykki að upplýsingar um mig verði varðveittar innan Landspítala og hafa megi samband við mig eftir 2-5 ár til eftirfylgni á rannsókn.

Ef ekki verður upplýsingum eytt strax við lok rannsóknar.

Samþykki að lífsýni mín verði varðveitt innan Lífsýnasafns Landspítala Rannsóknarsviðs (LLR) og eytt að rannsókn lokinni, samþykki ég ekki, með undirritun sérstakrar samþykkisyfirlýsingar, að þau verði varðveitt þar áfram til frekari nota í rannsóknir sem tengjast kæfisvefni.

Ég staðfesti hér með undirskrift minni að ég hef lesið upplýsingarnar um rannsóknina sem mér voru afhentar, hef fengið tækifæri til að spyrja spurninga um rannsóknina og fengið fullnægjandi svör og útskýringar á atriðum sem mér voru óljós. Ég hef af fúsum og frjálsum vilja ákveðið að taka þátt í rannsókninni. Mér er ljóst, að þó ég hafi skrifað undir þessa samstarfsyfirlýsingu, get ég stöðvað þátttöku mína hvenær sem er án útskýringa og án áhrifa á þá læknisþjónustu sem ég á rétt á í framtíðinni.

Mér er ljóst að rannsóknargögnin verða geymd dulkóðuð og að haft verður samband við mig að 2-5 árum liðnum á þeim forsendum sem íslensk lög og reglugerðir kveða á um þá. Mér hefur verið skýrt frá fyrirkomulagi trygginga fyrir þátttakendur í rannsókninni.

Dagsetning	
Nafn þátttakanda	
Undirritaður, starfsmaður rannsóknarinnar, sta eðli og tilgang rannsóknarinnar, í samræmi við	nðfestir hér með að hafa veitt upplýsingar um lög og reglur um vísindarannsóknir.
Nafn bess sem leggur sambykkisyfirlýsinguna	 fvrir

Appendix B

Questions and questionnaires used in the study

1.	Hefur þú greins	t með of háan	blóðþrýsting?
	□ Nei	□ Já	☐ Veit ekki
2.	Hefur þú greins	t með sykursý	ki?
	□ Nei	□ Já	□ Veit ekki
3.	Hefur þú greins	t með asthma'	?
	□ Nei	□ Já	□ Veit ekki
4.	Notar þú svefnly	yf reglulega?	
	□ Nei	□ Já	□ Veit ekki
5.	Hefur þú einhve	ertíma reykt e	ða notað tóbak í a.m.k. eitt ár?
	□ Nei	□ Já	□ Veit ekki
6.	Neytir þú áfengi	is?	
	□ Nei, ég hef alo	drei neytt áfeng	gis
	□ Nei, ég er hæt	t(ur) að neyta á	áfengis
	☐ Já, ég neyti áf	engis	
7.	Stundar þú íþró	ttir eða aðra ı	eglubundna hreyfingu (t.d. göngur, sund,
	hjólreiðar)?		
	□ Nei, ég kýs að	stunda ekki h	reyfingu
	□ Nei, ég get ek	ki stundað hrey	yfingu
	□ Já		
	□ Veit ekki		

$Center\ for\ Epidemiological\ Studies-Depression\ Scale\ (CES-D^{TM})$

Hversu oft leið þér á eftirfarandi hátt í síðastliðinni viku? Vinsamlega svaraðu hverri spurning með því að fylla í þann svarreit sem á best við þig.

	0	1	2	3	
	Sjaldan	Einstaka	Stundum eða	Mjög oft	
	eða aldrei	sinnumnokkr	um sinnum	eða alltaf	
Í síðustu viku :					
Fóru hlutir í taugarna á mér sem venjulega gera það ekki	ar 🗆				
Langaði mig ekki til að borða, ég var lystarlaus					
Leið mér þannig að ég gæti ekki losnað við dapurleikann þrátt fyrir hjálp fjölskyldu minnar og vina	g 🗆				
Fannst mér ég ekkert verri en annað fólk					
Átti ég í erfiðleikum með að hafa hugann v það sem ég var að ger					
Var ég dapur/döpur (Þunglynd(ur))					

Fannst mér allt erfitt sem ég gerði		
Var ég bjartsýn(n) á framtíðina		
Fannst mér líf mitt hafa misheppnast		
Var ég óttaslegin(n)		
Var svefn minn órólegur		
Var ég ánægð(ur)		
Talaði ég minna en venjulega		
Fann ég fyrir einmannaleika		
Var fólk óvingjarnlegt		
Naut ég lífsins		
Fékk ég grátköst		
Var ég sorgmædd(ur)		
Fannst mér að fólki líkaði illa við mig		
Kom ég mér ekki í "gang"		

Epworth Sleepiness Scale (ESS)

Hversu líklegt er að þú dottir eða sofnir við eftirfarandi aðstæður. Miðaðu við eðlilegt daglegt líf að undanförnu. Jafnvel þó þú hafir ekki gert eftirtalda hluti nýlega, reyndu að átta þig á því hvernig aðstæðurnar hefðu haft áhrif á þig. Notaðu eftirfarandi kvarða til þess að velja tölu sem á best við í hverju tilviki.

Aðstæður þar sem ég:

Líkur á að dotta/sofna:

Engar	Litlar	Talsverðar	Miklar
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
0	1	2	3
	0 0 0 0 0 0	0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1 0 1	0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2 0 1 2

The 12-Item Short-Form Health Survey (SF-12)

Þessi hluti könnunarinnar leitar svara við því hvernig þér finnst heilsufar þitt vera. Þessar upplýsingar leitast við að skýra hvernig þér líður og hvernig þér gengur að sinna daglegum athöfnum. Vinsamlega svaraðu hverri spurningu með því að fylla í þann hring sem á best við þig, jafnvel þó þú sért ekki alveg viss.

1. Þegar á heildina er litið,	hvernig myndi	r þú segja að l	neilsa þín væri?
☐ Frábær			
☐ Mjög góð			
□ Góð			
☐ Sæmileg			
□ Léleg			
Næstu spurningar fjalla um venjuleg störfum. Ef svo er, að hve miklu leyti		r núverandi heils	sufar þér þegar þú sinnir þessum
	Já, háir mér mikið	Já, háir mér nokkuð alls ek	Nei, háir mér kki
2. Hóflegt erfiði, svo sem			
að færa til húsgögn, ryksuga,			
leika keilu eða golf?			
3. Ganga upp nokkra stigapalla			
Á <u>síðustu 4 vikum</u> , hefur þú átt við ei heilsu þinnar?	ftirfarandi vandaı	mál í starfi eða d	aglegu lífi vegna líkamlegrar
4. Varð minna úr verki en þú hefði	r viljað?		
□ Já			
□ Nei			
5. Hindraði þig í að framkvæma ák	xveðin störf eða	athafnir?	
□ Já			
□ Nei			

☐ Góðan hluta tímans

Á síðustu 4 vikum, hefur þú átt við eftirfarandi vandamál í starfi eða daglegu lífi vegna tilfinningalegrar vanlíðunar þinnar (s.s. depurðar eða kvíða)? 6. Varð minna úr verki en þú hefðir viljað? □ Já □ Nei 7. Sinntir starfi þínu eða öðrum athöfnum af minni vandvirkni en vanalega? □ Já □ Nei 8. Á síðustu 4 vikum, hversu mikil áhrif höfðu verkir á dagleg störf þín (bæði innan heimilis og utan)? ☐ Engin ☐ Frekar lítil ☐ Í meðallagi ☐ Talsvert mikil ☐ Mjög mikil Næstu spurningar eru um almenna líðan bína síðastliðnar 4 vikur. Vinsamlega merkið við það svar sem kemst næst því að lýsa líðan þinni og hversu mikinn hluta tímans þér leið þannig Meirihluta Allan Góðan Minni-Lítinn Aldrei tímann tímans hluta hluta hluta tímans tímans tímans 9. Hefur þú verið róleg(ur) og yfirvegaður/yfirveguð? 10. Hefur þú verið full(ur) orku? 11. Hefur þú verið leið(ur) og dapur/döpur 12. Á síðastliðnum 4 vikum, hversu mikinn hluta tímans trufluðu líkamleg heilsa þín eða tilfinningaleg vandamál félagsleg samskipti þín (s.s. heimsóknir til vina, ættingja o.s.frv)? ☐ Allan tímann ☐ Meirihluta tímans

☐ Minnihluta tímans	
☐ Lítinn hluta tímans	
□ Aldrei	

Functional Outcomes of Sleep Questionnaire (FOSQ TM)

Sumir eiga erfitt með að gera hversdagslegar athafnir þegar þeir eru þreyttir eða syfjaðir. Tilgangur þessa spurningalista er að kanna hvort þú eigir almennt erfitt með að framkvæma tilteknar athafnir vegna þess að þú sért of þreyttur eða syfjaður. Þegar notast er við orðin "syfjaður" eða "þreyttur" í þessum spurningalista, er átt við þá tilfinningu að þú getir ekki haldið augunum opnum, að höfuðið er farið að drjúpa, að þig langi til að halla þér eða að þér finnist þú verða að leggja þig. Þessi orð eiga ekki við þá þreytu sem þú kannt að finna fyrir eftir líkamlega áreynslu eða líkamsrækt.

<u>Leiðbeiningar:</u> Vinsamlegast fylltu í einn svarreit fyrir hverja spurningu. Svaraðu eins nákvæmlega og þú getur. Fyllsta trúnaðar verður gætt við úrvinnslu gagnanna.

	Alls ekki	Já, svolítið erfitt	Já, frekar erfitt	Já, mjög erfitt
1. Áttu erfitt með að einbeita þér að hlutum sem þú ert að gera vegna þess að þú ert syfjuð/syfjaður?				
2. Áttu almennt erfitt með að muna hluti vegna þess að þú ert syfjuð/syfjaður?				
3. Áttu erfitt með að aka farartæki stuttar vegalengdir (minna en 150 km) vegna þess að þú verður syfjuð/syfjaður?				
4. Áttu erfitt með að aka farartæki langar vegalengdir (meira en 150 km) vegna þess að þú verður syfjuð/syfjaður?				
5. Áttu erfitt með heimsóknir til vina og vandamanna vegna þess að þú ert syfjuð/syfjaður?				
6. Hefur samband þitt við fjölskyldu, vini og				

	vinnufélaga orðið fyrir áhrifum þess að þú			
7.	ert syfjuð/syfjaður? Áttu erfitt með að			
	horfa á kvikmynd eða myndband vegna þess			
	að þú ert syfjuð/syfjaður?			
8.	Áttu erfitt með að vera			
	eins virk(ur) og þú vilt vera á kvöldin vegna þess að þú ert syfjuð/syfjaður?	1		
9.	eins virk(ur) og þú vilt vera á morgnana vegna			
10	þess að þú ert syfjuð/syfjaður? . Hefur löngun þín til			
	náins eða kynferðilegs sambands orðið fyrir áhrifum þess að þú ert syfjuð/syfjaður?			

Appendix C

Table 5.

Multiple linear regression analysis for depression among men.

	В	β	t	Sig.
(Constant)	33.822		3.861	.000
Exercise	1.600	.165	1.954	.053
Daytime sleepiness	072	035	356	.723
FOSQ	627	412	-4.095	.000
Sleep medication	-1.773	074	860	.392
Age	061	077	889	.376
Drinking	1.938	.131	1.544	.126

a. Dependent variable: Depression

Note: FOSQ = Functional outcomes of sleep questionnaire

Table 6.

Multiple linear regression analysis for depression among women.

	В	β	t	Sig.
(Constant)	67.568		34.577	.000
Exercise	148	015	103	.918
Daytime sleepiness	202	077	476	.637
FOSQ	-1.009	576	-3.540	.001
Sleep medication	-3.823	154	-1.071	.291
Age	154	135	971	.338
Drinking	-2.430	126	879	.385

a. Dependent variable: Depression

Note: FOSQ = Functional outcomes of sleep questionnaire

Table 7.

Multiple linear regression analysis for BMI among men.

	В	β	t	Sig.
(Constant)	40.928		12.335	.000
Age	209	344	-4.304	.000
АНІ	.082	.266	3.297	.001
Smoking	.431	.033	.394	.694

a. Dependent variable: BMI

Note: AHI = The apnea-hypopnea index

Table 8.

Multiple linear regression analysis for BMI among women.

	В	β	t	Sig.
(Constant)	35.539		6.202	.000
Age	041	066	418	.678
АНІ	012	034	217	.829
Smoking	2.644	.197	1.235	.224

a. Dependent variable: BMI

Note: AHI = The apnea-hypopnea index