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Associations and comorbid conditions

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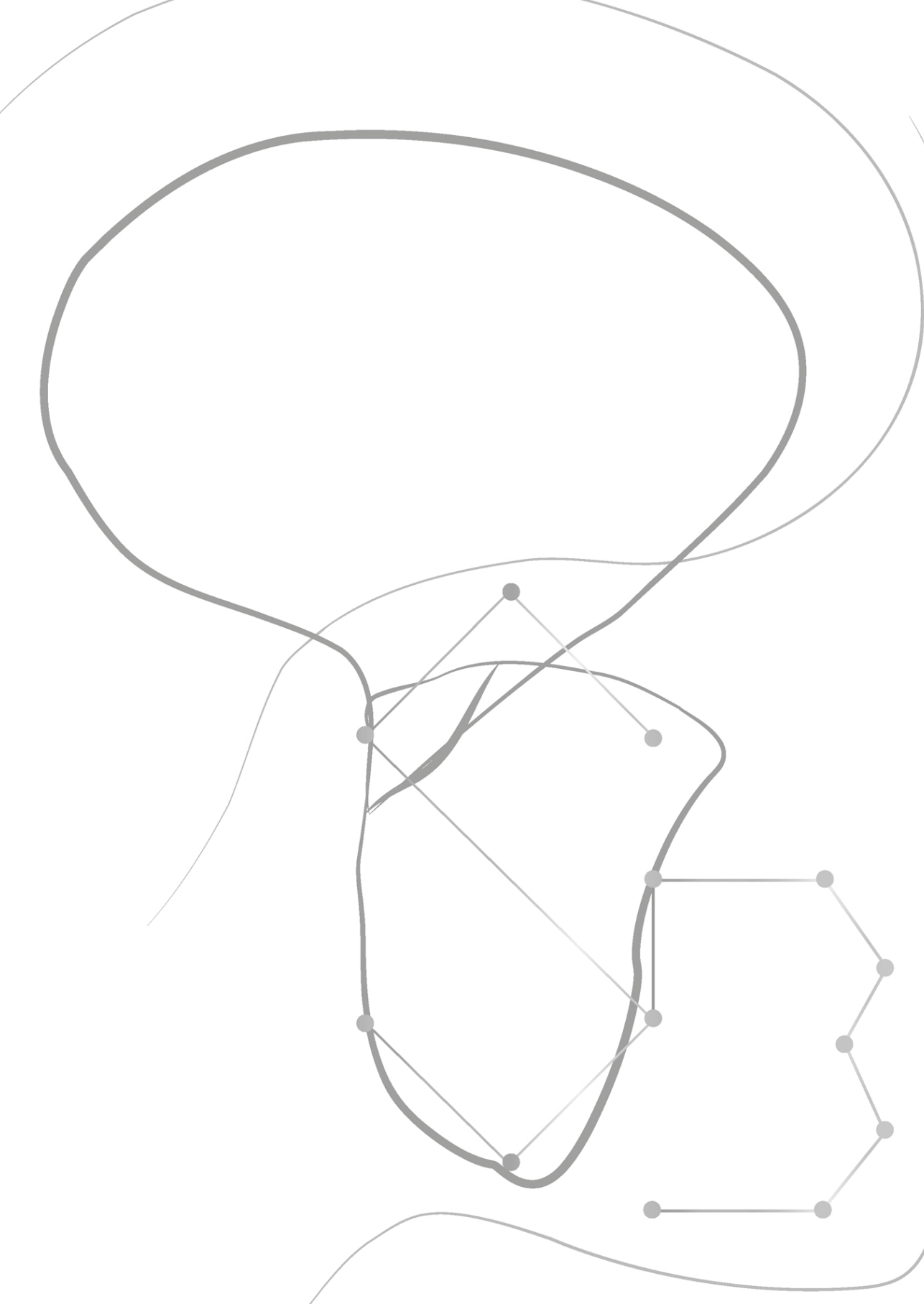
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CHAPTER 5

A NETWORK ANALYSIS OF SELF-REPORTED SLEEP BRUXISM IN THE NETHERLANDS SLEEP REGISTRY: ITS ASSOCIATIONS WITH INSOMNIA AND SEVERAL DEMOGRAPHIC, PSYCHOLOGICAL, AND LIFE-STYLE FACTORS

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A network analysis of self-reported sleep bruxism in the Netherlands sleep registry: its associations with insomnia and several demographic, psychological, and life-style factors.

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ABSTRACT

Objectives: To investigate the association between self-reported sleep bruxism and insomnia and their potential risk factors (e.g., depression and anxiety), and to construct a network model with all these factors.

Methods: We recruited 2251 participants from the Netherlands Sleep Registry. All participants completed questionnaires on self-reported sleep bruxism, insomnia, depression, anxiety, smoking frequency, and alcohol and caffeine consumption. The associations between self-reported sleep bruxism and other variables were analyzed by univariate analysis, multivariate logistic regression, and network analysis.

Results: Although univariate analysis showed that there was a positive association between sleep bruxism and insomnia ($P < 0.001$), this association disappeared in the multivariate logistic regression model ($P = 0.258$). However, multivariate logistic regression did show an association between self-reported sleep bruxism and anxiety (OR = 1.087, 95% CI 1.041-1.134). The network model showed that there was no direct link between self-reported sleep bruxism and insomnia. However, there was an indirect link between self-reported sleep bruxism and insomnia via anxiety.

Conclusions: Although self-reported sleep bruxism has no direct association with insomnia, anxiety is a bridging factor between these variables.

Keywords: Sleep bruxism; Insomnia; Anxiety; Network analysis

1. INTRODUCTION

Bruxism is an umbrella term covering several types of repetitive masticatory muscle activities during sleep (sleep bruxism; SB) or while awake (awake bruxism).¹ The condition is characterized by grinding or clenching of teeth or by bracing or thrusting lower jaw.¹ Recently, SB has been defined as "... a masticatory muscle activity during sleep that is characterized as rhythmic (phasic) or non-rhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals".² The prevalence of SB has been estimated at 12.8±3.1% in the general population, decreases with age, and does not differ between men and women.³ Possible, probable, and definite SB are assessed by self-report (questionnaires, oral history), clinical examination, and polysomnography, respectively.² Several negative consequences of SB have been suggested in the literature, such as advanced mechanical tooth wear, temporomandibular disorders (TMD), and headache,⁴⁻⁶ although there is conflicting evidence about their possible causal association with SB. Interestingly, it has also been proposed that SB may have a potentially protective effect on obstructive sleep apnea by preventing or terminating upper airway collapse.⁷ Hence, management of SB should always aim to find the desired balance between the condition's possible negative and positive consequences at the level of the individual patient. When management is indicated, the clinician must be aware of the paucity of evidence-based, safe, and effective strategies, in the absence of which SB should be managed non-invasively with behavioral strategies like sleep hygiene instructions or biofeedback, with orthopedic strategies like full-coverage hard acrylic resin intra-oral occlusal splints, or, when such strategies fail, with pharmacological strategies, provided that future research will identify effective and safe pharmacological substances to this purpose.⁸⁻¹⁰

SB is associated with many factors, such as biological, psychological, and life-style factors. For example, SB has been shown to occur after sleep micro-arousals, i.e., brief abrupt frequency shifts in the electroencephalogram (EEG), that may be accompanied by increases in heart rate and muscle tone.¹¹ Psychosocial factors are commonly reported in the etiology of SB as well, such as stress, anxiety, depression, and social factors like workplace dissatisfaction, although the evidence for these factors' role in the etiology of SB is still not definite.¹²⁻¹⁴ Also life-style factors, such as smoking, alcohol consumption, and drinking coffee, can be considered as risk factors of SB,¹⁴ while sleep-related disorders like obstructive sleep apnea (OSA), restless legs syndrome, REM sleep behavior disorder, and gastroesophageal reflux disease have been identified as comorbid conditions of SB.¹⁵ In addition, also insomnia has been suggested as a comorbidity of SB.^{5,16,17} Insomnia is characterized by several sleep complaints, i.e., difficulty initiating sleep, difficulty maintaining sleep, early morning awakening, and poor sleep quality, and

is related to daytime impairment.¹⁶ Known etiological factors of both SB and insomnia include biological factors like continued arousal during sleep, as well as psychological conditions like anxiety and depression.^{18,19} Other risk factors of insomnia are increasing age, being female, smoking, alcoholism, and caffeine dependence, while conditions like chronic pain and other sleep disorders (e.g., OSA, restless legs syndrome) have been identified as comorbidities of insomnia.¹⁶ Interestingly, some studies have reported an association between SB and insomnia symptoms, notably difficulty initiating sleep and difficulty maintaining sleep.²⁰⁻²²

Previous studies investigated associations between SB, insomnia, anxiety, and depression mainly univariately. Consequently, how these factors are associated with each other remains unclear. Therefore, this study aimed to investigate direct and indirect associations of self-reported SB with insomnia and other potential risk factors in a multivariate study design and subsequent network analysis. This novel approach will show all associations between all included factors and identify bridge factors or common factors between SB and insomnia. The associations of SB with insomnia and other potential risk factors may help clinicians consider which factors have to be treated to relieve SB, insomnia, and other conditions included in this study. Because SB and insomnia have several etiological factors in common, the hypothesis is that self-reported SB has positive direct associations with insomnia as well as with other potential risk factors, viz., psychological and life-style factors.

2. METHOD

2.1 Participants

Participants were good sleepers as well as people having sleep problems who participated in the Netherlands Sleep Registry (NSR; www.sleepregistry.org), an online questionnaire platform for sleep and related psychological research.²³ This registry aims to collect a wide range of characteristics in adults with good and poor sleep. Participants are queried in 17 domains that are relevant to insomnia. The multivariate data set has shown to be valuable to identify mechanisms and subtypes of insomnia.^{24,25} As an important notice, not all questionnaires are completed by every participant: participants can complete some questionnaires, but may skip others. Data collection in the context of the NSR was approved by the Medical Ethical Committee of the Academic Medical Center of the University of Amsterdam (29 September 2009, 09.17.1396) and the Central Committee on Research Involving Human Subjects (CCMO, 14 December 2011, CCMO11.1813/GK/jt), The Hague, the Netherlands.

In this study, we included the participants who completed the questionnaires that inquire about self-reported SB, age, sex, body mass index (BMI), insomnia, anxiety, depression, OSA risk, smoking, alcohol consumption, and drinking coffee, resulting in 2343 entries, completed between January 2011 and December 2017. 76 participants who had no clear moment of quitting smoking or quit smoking less than 1 year ago were excluded.²⁶ 16 participants filled the questionnaires twice, so we excluded the second entry of those participants. Finally, 2,251 participants, aged 18 to 87 years, were included for analyses. Participants were categorized into 2 groups based on self-reported SB: there were 1899 (84.4%) non-bruxers and 352 (15.6%) current sleep bruxers.

2.2 Questionnaires

The questionnaires included in this study provided information on SB, sex, age, body mass index (BMI), insomnia, anxiety, depression, OSA risk, and the frequency of tobacco smoking, alcohol consumption, and drinking coffee. BMI was first obtained from the Berlin questionnaire.²⁷ However, height or weight of 12 participants and both height and weight of 2 other participants were missing in this questionnaire, so we used 10 entries on height and 6 entries on weight from the demographic data to obtain a full set of BMI data.

The SB screening question was formulated as follows: 'Do you grind your teeth during sleep?'. The answer options were: current tooth grinding, former tooth grinding, and never have experienced tooth grinding during sleep. Former bruxers were not having SB at the time they answered this question. Therefore, the non-bruxers and former bruxers were combined in the non-bruxer group, while the current tooth grinders constituted the sleep bruxer group.

The Insomnia Severity Index (ISI) was used to evaluate the risk of insomnia. The ISI consists of 7 items, with response options on 5-point Likert scales (0-4; a higher score represents a worse condition). Total scores range from 0 to 28.²⁸ The cutoff for probable insomnia is a score of at least 10.^{25,29}

The Hospital Anxiety and Depression Scale (HADS) is a questionnaire for self-assessment of anxiety (HADS-A) and depression (HADS-D) levels.³⁰ There are 14 items, with responses on 4-point Likert scales (0-3; a higher score represents a worse condition). HADS-A and HADS-D are subscales of HADS, each containing 7 items. Each subscale has total scores ranging from 0 to 21. The cutoff score of presence of anxiety or depression is at least 8 for each subscale.³¹

The Berlin questionnaire (BQ) was used to evaluate the probability of having sleep apnea.²⁷ Ten questions cover three categories, viz., snoring, daytime sleepiness, and high blood pressure. Participants who scored positive on at least two categories were considered to have an increased probability of having sleep apnea, while participants who scored negative on all categories or positive on one category were considered to have a low probability.

Life-style factors considered were the frequency of smoking, alcohol consumption, and drinking coffee. Smoking questions addressed smoking status, i.e., non-smoker, former smoker, and current smoker; and smoking frequency. Smoking frequency was addressed with the question 'How frequently do you smoke tobacco?'. The answer options were: never, <1 time/month, 1-3 times/month, 1-2 times/week, 3-6 times/week, 1-3 times/day, and >3 times/day. We combined these answer options into 3 categories: never; sometimes (combining the answer options from ≤ 1 time/month up to and including 3-6 times/week); and frequent (combining the answer options 1-3 times/day and > 3 times/day). Participants who answered to be non-smokers skipped the question of smoking frequency, so only former and current smokers could answer this question. We included only former smokers who quit more than one year ago and coded smoking frequency as "never" for non-smokers and former smokers. Some current smokers smoke more than one type of tobacco. The highest frequency among those tobacco types was used.

To investigate the frequency of alcohol consumption, we used the question 'How frequently do you drink alcohol?'. The answer options were: never, ≤ 1 time/month, 2-4 times/month, 2-3 times/week, and ≥ 4 times/week. As for smoking frequency, we combined the answer options into 3 categories. The final answer options were: never, sometimes (combining the answer options ≤ 1 time/month and 2-4 times/month), and frequent (combining the answer options 2-3 times/week and ≥ 4 times/week).

To investigate the frequency of drinking coffee, we used the question 'How frequently do you drink coffee?'. The answer options were: no or <1 time/month, 1-3 times/month, 1 time/week, 2-4 times/week, 5-6 times/week, 1 time/day, 2-3 times/day, 4-5 times/day, and ≥ 6 times/day. Again, to enable a uniform analysis of the frequencies of smoking, alcohol consumption, and drinking coffee, we combined the answer options into 3 categories. The final answer options were: never or rarely (never or <1 time/month), sometimes (combining the answer options from 1-3 times/month up to and including 5-6 times/week), and frequent (combining the answer options from 1 time/day up to and including ≥ 6 times/day).

2.3 Statistical analysis

In order to assess the associations between self-reported SB, insomnia, and other potential risk factors, we took three steps, viz., univariate analysis, multivariate analysis, and network analysis. For the first two steps, self-reported SB was used as the dependent variable.

First, univariate analyses were performed to assess the associations between self-reported SB and each of the independent variables separately. We performed normality tests to check the normal distribution of the continuous variables using Kolmogorov-Smirnov test. Then, we performed chi-square test to analyze the association between self-reported SB and the categorical independent variables (sex, OSA risk, smoking frequency, alcohol consumption, and drinking coffee). Because all continuous variables were non-normally distributed, we used Mann-Whitney U test to assess the differences in age, BMI, ISI, and HADS scores between sleep bruxers and non-bruxers.

Second, to investigate the association of self-reported SB with all independent variables, we conducted a multivariate binary logistic regression, where we predicted self-reported SB by sex, age, BMI, insomnia, anxiety, depression, OSA risk, smoking frequency, alcohol consumption, and drinking coffee. Non-bruxer was used as the reference category. Statistical significance was determined at $P < 0.05$ in both the univariate and multivariate analyses.

Third, to evaluate how all variables relate to each other in a multivariate system, we estimated a Mixed Graphical Model (MGM)³². In the MGM, using the R-package *'bootnet'* (version 1.4.3),³³ we included self-reported SB ("current bruxer", "non-bruxer"), sex ("male", "female"), OSA risk ("low risk", "high risk"), smoking ("never", "sometimes", "frequent"), alcohol consumption ("never", "sometimes", "frequent"), and drinking coffee ("never or rarely", "sometimes", "frequent") as categorical variables; and age, BMI, insomnia, anxiety and depression scores as continuous variables. Contrary to the multivariate binary logistic regression performed in the second step, the network model does not require to specify a single outcome variable, but rather includes all variables as 'outcome' and 'predictor'. When estimating the association between any two variables, the model takes all the other variables included in the network into account. As such, the estimated relationships represent the unique association between two variables, while controlling for all other variables in the network (i.e., the conditional dependence relationships). This allows us to estimate and visualize how all variables relate to one another, and to investigate both direct and indirect associations. All variables are included as *nodes*. The unique association between two variables are included as *edges*. A regularization technique called 'least absolute shrinkage and selection operator'

(LASSO) was used to reduce the inclusion of spurious or false positive edges. A tuning parameter λ (lambda) controls the level of regularization that is applied: higher values lead to more regularization and thus sparser networks, whereas with lower values less regularization is applied and more edges will be estimated. The tuning parameter cannot be set directly, but is selected by optimizing the Extended Bayesian Information Criterion (EBIC). When optimizing the EBIC, a hyperparameter γ (gamma) needs to be selected. This parameter is typically set between 0 and 0.5, where 0 is more lenient such that more edges are included, and thereby errs on the side of discovery, whereas 0.5 is more stringent and errs on the side of caution.³⁴ In this analysis, the hyperparameter γ was set to 0.5 to maximize specificity and avoid chance of including false positive edges in the network.

From the estimated network model, we can identify potential bridge factors. Originally, bridge symptoms were defined as symptoms that overlap between two disorders (e.g., concentration problems is a symptom of both depression and anxiety, and can be seen as a symptom that 'bridges' the two disorders).^{35,36} In the current study, we defined potential bridge factors as factors that may bridge the link between SB and insomnia.

In the estimated network, the visualization with '*qgraph*' (version 1.6.5)³⁷ shows how each variable is associated with the other variables. In the visualization, all categorical variables are shown as squares, whereas all continuous variables are shown as circles. Edges between each node show positive or negative correlations between those nodes. Blue edges represent positive correlations, while red edges represent negative correlations. Finally, we have conducted stability checks to evaluate the robustness of the estimated network. We used the bootstrapping method to investigate the network's accuracy.³³ Bootstrapping would repeatedly estimate a model from simulated data and show in a plot of 95% of bootstrapped confidence intervals (CIs). If the bootstrapped CI of that edge does not cover zero, this edge is strong enough to present in the network. The nonparametric bootstrap with 1000 samples was used to have more consistency than using fewer samples. (See the bootstrapped confidence intervals of the network model in the appendix, **Figure A1**)

The univariate and multivariate analyses were performed in IBM SPSS Statistics 23 software (IBM Corp, Armonk, NY, USA). The network analysis was performed in R (version 4.0.2, Vienna University of Economics and Business, Vienna, Austria).

2.4 Sample size estimation

For the multivariate binary logistic regression analysis, based on the rule of thumb, if events per variable (EPV) is larger than 10,³⁸ it indicates that the logistic regression

analysis included sufficient sample size. In this study, the event of interest is “sleep bruxer”. Since the number of potential predictors is 13, the minimum required number of events should therefore be 130. In the study, we had 352 events, i.e., sleep bruxers, which was larger than 100. Therefore, the logistic regression analysis is sufficiently powerful.

Currently, there is no any power analysis available for the network analysis.

3. RESULTS

Our study sample included 352 current self-reported sleep bruxers and 1899 non-bruxers. 1699 (75.5%) of the participants were female, and 552 (24.5%) of the participants were male. Mean age of the sleep bruxers was 49.4±13.5 years, and mean age of the non-bruxers was 51.5±14.2 years. 1072 participants (47.6%) had ISI scores of at least 10 and were thus identified as probable insomnia patients.

3.1 Univariate analysis

Table 1 shows the distribution of the independent variables in the sleep bruxer and non-bruxer groups. SB was significantly associated with age, insomnia, anxiety, depression, OSA risk, smoking, alcohol consumption, and drinking coffee (all $P < 0.05$).

Table 1. Description of independent variables in non-bruxers and sleep bruxers.

		Non-bruxer (N=1899)	Sleep bruxer (N=352)	Total (N=2251)	P
ISI (0-28)	Median (IQR)	9 (12)	11 (12)		<0.001 ^b
Sex	Male	479 (86.8%)	73 (13.2%)	552 (24.5%)	0.072 ^a
	Female	1420 (83.6%)	279 (16.4%)	1699 (75.5%)	
Age	Median (IQR)	53.9 (20.2)	51.4 (20.3)		0.006 ^b
BMI	Median (IQR)	23.9 (4.8)	24.0 (6.1)		0.952 ^b
HADS-A (0-21)	Median (IQR)	5 (5)	6 (6)		<0.001 ^b
HADS-D (0-21)	Median (IQR)	2 (4)	4 (6)		<0.001 ^b
OSA	Low risk	1660 (87.4%)	284 (80.7%)	1944 (86.4%)	0.001 ^a
	High risk	239 (12.6%)	68 (19.3%)	307 (13.6%)	
Smoking	Never	1667 (87.8%)	294 (83.5%)	1961 (87.1%)	0.002 ^a
	Sometimes	44 (2.3%)	3 (0.9%)	47 (2.1%)	
	Frequent	188 (9.9%)	55 (15.6%)	243 (10.8%)	

Table 1. Continued

		Non-bruxer (N=1899)	Sleep bruxer (N=352)	Total (N=2251)	P
Alcohol consumption	Never	259 (13.6%)	70 (19.9%)	329 (14.6%)	0.007^a
	Sometimes	666 (35.1%)	121 (34.4%)	787 (35.0%)	
	Frequent	974 (51.3%)	161 (45.7%)	1135 (50.4%)	
Drinking coffee	Never or rarely	283 (14.9%)	69 (19.6%)	352 (15.6%)	0.003^a
	Sometimes	162 (8.5%)	43 (12.2%)	205 (9.1%)	
	Frequent	1454 (76.6%)	240 (68.2%)	1694 (75.3%)	

IQR = Interquartile range; ISI = Insomnia Severity Index; HADS-A = HADS-Anxiety; HADS-D = HADS-Depression; BMI = Body mass index; OSA = Obstructive sleep apnea.

^a Chi-Square test ^b Mann-Whitney U test, Bold = significant at 0.05

3.2 Multivariate analysis

The outcomes of the multivariate binary logistic regression analysis, as shown in **Table 2**, indicate that there was no significant association between self-reported SB and insomnia when adjusted for the other variables ($P = 0.258$). In this multivariate model, only anxiety and frequent smoking were found to be significantly associated with self-reported SB. People with more severe anxiety had higher odds of being a sleep bruxer than a non-bruxer ($OR = 1.087$; $P < 0.001$). When compared with never smoking, patients who smoke frequently had significantly higher odds of being a sleep bruxer than a non-bruxer ($OR = 1.605$; $P = 0.006$).

3.3 Network model

The results of the network analysis are visualized in **Figure 1**. When we focus specifically on the links with self-reported SB, we see that also the network model estimates no direct link between self-reported SB and insomnia. However, as the network model also visualizes indirect relations, it is noteworthy that both self-reported SB and insomnia are related to anxiety. As such, anxiety may be seen as a “bridge factor” linking self-reported SB and insomnia. Similar to the multivariate analysis, the link between self-reported SB and anxiety was positive, indicating that SB patients tend to report more anxiety. Contrary to the multivariate analysis, in this network model, self-reported SB only links to anxiety, not smoking frequency. This indicates that when controlling for all the other variables in the network, the link found between self-reported SB and smoking in the multivariate analysis is no longer present.

Table 2. Binary logistic regression model of factors related to sleep bruxism. Reference = non-bruxers (N= 2251).

		Sleep bruxer (N=352) vs non-bruxer (N=1899) ^a			
		B (SE)	OR	95% CI	P
ISI		0.011 (0.010)	1.011	0.992-1.031	0.258
Sex	Female	reference	.	.	.
	Male	-0.125 (0.150)	0.882	0.657-1.184	0.404
Age		-0.007 (0.005)	0.993	0.984-1.002	0.150
BMI		0.012 (0.015)	1.012	0.983-1.041	0.416
HADS-A		0.083 (0.022)	1.087	1.041-1.134	<0.001
HADS-D		-0.014 (0.020)	0.986	0.948-1.026	0.485
OSA	Low risk	reference	.	.	.
	High risk	0.270 (0.176)	1.310	0.928-1.848	0.125
Smoking	Never	reference	.	.	0.006
	Sometimes	-0.923 (0.607)	0.397	0.121-1.306	0.129
	Frequent	0.473 (0.173)	1.605	1.143-2.255	0.006
Alcohol consumption	Never	reference	.	.	0.189
	Sometimes	-0.311 (0.174)	0.732	0.520-1.031	0.074
	Frequent	-0.255 (0.171)	0.775	0.554-1.084	0.136
Drinking coffee	Never or rarely	reference	.	.	0.052
	Sometimes	0.188 (0.225)	1.207	0.777-1.874	0.403
	Frequent	-0.246 (0.168)	0.782	0.563-1.086	0.142

β = regression coefficient; SE = standard error; OR = odds ratio; CI = confidence interval; ISI = Insomnia Severity Index; HADS-A = HADS-Anxiety; HADS-D = HADS-Depression; BMI = Body mass index; OSA = Obstructive sleep apnea; Bold = significant at 0.05.

^a Reference category.

When we specifically focus on insomnia and anxiety, insomnia has positive links to age, anxiety, depression, and OSA risk. Anxiety and age are negatively associated in the network model, i.e., younger participants have higher HADS-A scores, and vice versa. Also, women tend to have higher anxiety scores than men.

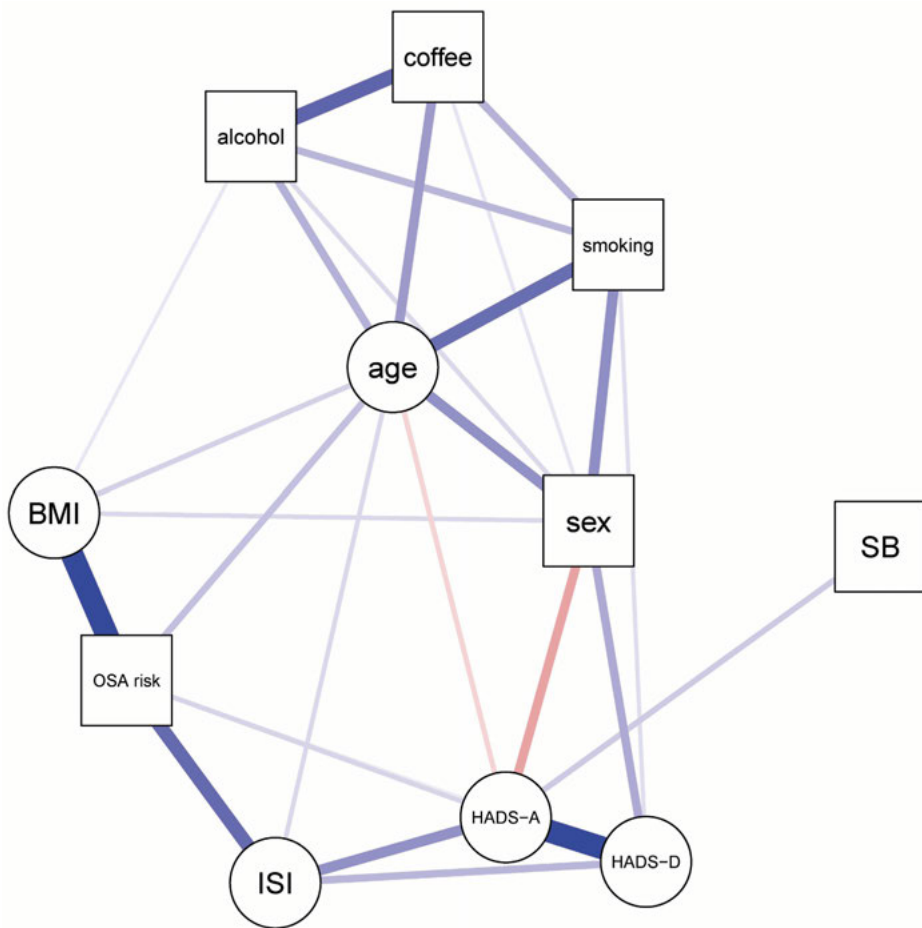


Figure 1 Network model of self-reported SB, insomnia, demographic, psychological, and lifestyle factors (n= 2251). The squares represent categorical variables; the circles, continuous variables. The blue lines represent positive associations; the red lines, negative associations. Thicker and darker colored lines refer to stronger associations. SB, self-reported sleep bruxism; BMI, Body Mass Index; sex, male sex; ISI, Insomnia Severity Index; HADS-A, HADS-Anxiety; HADS-D, HADS-Depression; smoking, smoking frequency; alcohol, alcohol consumption; caffeine, drinking coffee.

4. DISCUSSION

The present study aimed to investigate how self-reported SB and insomnia are related when controlling for age, sex, psychological factors, and life-style factors. Although we found that insomnia predicted self-reported SB in the univariate setting, this effect disappeared when age, psychological, and life-style factors were taken into account. Of these factors, only anxiety and frequent smoking predicted self-reported SB. Interestingly, after including all factors in a network model, we found that self-reported SB was only related to anxiety. Crucially, such network models allow us to investigate both direct and indirect effects. Our model showed that self-reported SB and insomnia were both strongly related to anxiety. In this way, anxiety could act as a “bridge” between self-reported SB and insomnia, suggesting that the link between the two may be through their common links to anxiety. This bridge factor might be a treatment target, because as such it may eliminate comorbidity between two disorders.³⁶

4.1 SB, insomnia, and psychological factors

Our demonstration that insomnia and self-reported SB are only indirectly associated puts previously reported findings in perspective. A study in Japanese adolescents found that SB was associated with insomnia symptoms, which are difficulty initiating sleep, difficulty maintaining sleep, and early morning awakening.³⁹ In addition, a Finnish twin cohort study also found an association between possible SB and insomnia.⁴⁰ Further, SB was correlated with reduced self-perceived sleep quality.⁴¹ An association between SB and insomnia was also found in a study by Maluly et al., which investigated SB in the general population.¹⁷ Unfortunately, Maluly et al. did not include psychological factors in their analysis. This is, however, crucial, because SB has been found to be correlated with stress, depression, anxiety, and other psychological factors.^{12,42} Van Selms et al. found that SB was associated with short sleep duration rather than with insomnia.⁴³ Our present study suggests that also this reported association of SB with short sleep duration may be indirect.

The positive association between self-reported SB and anxiety in this study was in line with previous findings in possible (i.e., self-reported) SB patients in the general population¹³ as well as in probable (i.e., clinically assessed) SB healthy adults in Brazil.⁴⁴ In the present study, anxiety serves as a bridge factor of self-reported SB not only to insomnia but also to depression, OSA risk, age, and sex (**Figure 1**). In contrast to the cross-sectional study by Neu et al.,⁴¹ there was no difference in anxiety between definite (i.e., PSG-confirmed) SB patients and controls. At the same time, depression did not have direct association with self-reported SB, so it might be hypothesized that mechanisms underlying SB overlap more with mechanisms involved in anxiety than in depression.

Our finding of no direct association between self-reported SB and depression is in line with a PSG study that found no difference in depressive symptom severity between SB and non-SB patients.⁴⁵ As Camparis et al. reported more severe depressive symptoms in SB patients with orofacial pain than in SB patients without orofacial pain,⁴⁶ pain may be responsible for the higher depressive symptom severity in SB patients.

Which underlying factors may be responsible for the direct association between SB and anxiety and the mediation of anxiety in the indirect association of SB with insomnia? One factor to consider is cortisol, the stress hormone produced by the adrenal cortex and regulated by the hypothalamic-pituitary (HPA) axis. A high level of cortisol was found to be associated with SB and anxiety.^{47,48} Also insomnia patients can have elevated cortisol and anxiety,⁴⁹ and dysregulation of the HPA axis is associated with disturbed sleep and anxiety.^{50,51} A study on anxiety and its effects on sleep architecture has also shown that poor sleep continuity is associated with decreasing executive functions, and that deficits in executive function cause an inability to cope with anxiety symptoms.⁵⁰ The arousal system in the brain is also associated with SB, insomnia, and anxiety.^{51,52} So, SB and insomnia may share a common underlying mechanism with anxiety. Consequently, reducing anxiety may alleviate both SB and insomnia. Assessment and management of psychological status during treatment of SB and insomnia are therefore recommended for all healthcare professionals who are involved in the care for these patients.

4.2 Life-style factors

Frequent smoking increased the risk of having self-reported SB, in line with previous findings.^{14,53} In the Finnish twin cohort study, heavy smokers that smoked at least 10 cigarettes per day were associated with frequent self-reported SB.⁵⁴ In contrast, a study in definite SB did not reveal any association between SB and smoking.⁵⁵ The present study did not include the amount of tobacco smoking, so it is suggested to investigate both amount and frequency of smoking in future studies. Contrary to previous studies, which reported that drinking alcohol and coffee increased the risk of having SB,^{14,40,53} there was no association between self-reported SB on the one hand and alcohol consumption and drinking coffee on the other hand in the present study. In the literature, alcohol consumption and its consequences, such as heavy drinking and hangover, were found to be positively related to SB.^{14,40} These associations of SB with alcohol and coffee might depend on the quantity of alcohol or coffee intake. Although the network model did not show direct association between insomnia and life-style factors, heavy alcohol consumption⁵⁶ and smoking⁵⁷ were associated with insomnia symptoms, and drinking coffee could alter sleep quality.⁵⁸ It would be advisable for patients to reduce their alcohol and caffeine intake. However, the amount of alcohol and coffee drinking should also be investigated further.

4.3 Strengths and limitations

There are several strong points of this study. First, the large sample provided sufficient statistical power and a high probability of reliable results. Second, we used network analysis to analyze our data. Unlike univariate and multivariate analyses that need to set predictors and outcomes, this approach could investigate all associations between all included variables and present how they are associated. While the logistic regression analysis assesses associations between a single dependent variable and several independent variables (predictors), it does not take the inter-relationships among the predictors into account. With the network analysis, all variables in the model act as both dependent variable and independent variable. As such, the network analysis includes all the relationships among the predictors into the model.³⁴ Thus, the network analysis allows to discover not only direct effects but also indirect effects. This 'predictive mediation' could show that two variables A and B are not directly connected (i.e., A-B), but that they are indirectly connected via variable C (i.e., A-C-B).³⁴ This adds an extra dimension to the conventional regression analyses. The network analysis elucidated direct and indirect associations, which previous studies have not been able to discern, such as the association between BMI and OSA risk,⁵⁹ the association between OSA risk and insomnia,⁶⁰ and the associations among insomnia, depression, and anxiety.¹⁹ Third, validated questionnaires, viz., ISI, HADS, and BQ, were used in this study, so the assessment of insomnia, anxiety, depression, and OSA risk can be considered valid.

This study has several limitations as well. First, within the Netherlands Sleep Registry cohort, almost half of the participants have an ISI score of 10 or more, suggestive of insomnia. In the general population, the prevalence of insomnia is only about 7-23%.⁶¹ Hence, cases with probable insomnia were overrepresented in our study as compared to the general population. Interestingly, even in this population with a high prevalence of insomnia, the association between self-reported SB and insomnia was only indirect, while the overrepresentation to near 50% optimized the statistical power to detect associations. Thus, a direct association between SB and insomnia in the general population seems unlikely. Second, on the NSR online platform, participants are free to quit answering questionnaires and continue later. Consequently, some questionnaires might not be answered at the same time. For example, participants might have completed the HADS-A and HADS-D at another point in time than when they completed the questionnaires on SB and/or insomnia. Thus, associations between self-reported SB and other variables that are only momentary might have been missed. Third, SB was obtained by self-report. Self-report is frequently used in epidemiologic and clinical research because of its simplicity and cost-effectiveness. However, as compared to self-reported sleep grinding, reports from a bed partner have a higher validity.⁶² In addition, self-report has a low accuracy when comparing with electromyography or

polysomnography (PSG).^{63,64} The gold standard assessment of SB, viz, PSG with an audio-video record, should give an accurate, definite diagnosis,^{2,65} but this technique is time-consuming and expensive, so it is not feasible to use in a large sample. Nevertheless, caution is called for when interpreting the present findings, which are fully based on self-report. Fourth, the SB screening question did not include other bruxism-related jaw-muscle activities like clenching teeth, bracing, or thrusting. Hence, self-reported SB might not have included all sleep bruxers.

5. CONCLUSION

Within the limitations of the present study, we conclude that there is a weak but positive indirect association between self-reported SB and insomnia, with anxiety acting as a bridging factor. Consequently, when treating SB and insomnia, management of anxiety should not be overlooked. The associations of self-reported SB, insomnia, and anxiety in this study may help physicians and dentists to consider that SB and insomnia have a multifactorial etiology, especially with psychological factors playing a role. To assess and manage these conditions, interprofessional collaboration is mandatory.

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APPENDIX |

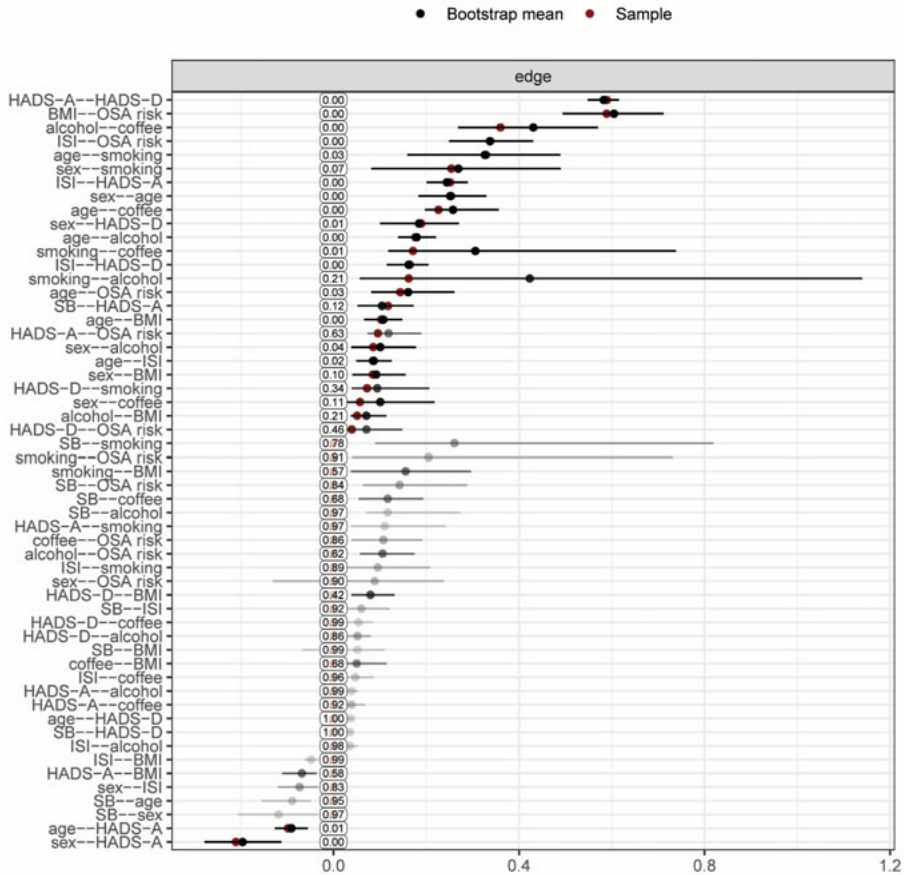


Figure A1. Bootstrapped confidence intervals of network model Only the black CIs were the edges in the network model. Edges with pale greyish CIs were the edges omitted from the network. The strongest edge was at the top of the plot and followed by the weaker edges. The left side of y-axis refers to negative edges, and the right side of the y-axis refers to positive edges. The overlapping bootstrapped CIs showed that those edges were not significantly different from the other edges.