UNIVERSIDADE FEDERAL DE SANTA CATARINA
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

Helena Polmann

Associação entre bruxismo do sono e ronco

Florianópolis
2024

Helena Polmann

Associação entre bruxismo do sono e ronco

Tese submetida ao Programa de Pós-Graduação em Odontologia da Universidade Federal de Santa Catarina para a obtenção do título de Doutora em Odontologia.

Orientadora: Prof.ª Dr.ª Graziela De Luca Canto

Florianópolis
2024

Ficha catalográfica gerada por meio de sistema automatizado gerenciado pela BU/UFSC.
Dados inseridos pelo próprio autor.

Polmann, Helena
Associação entre bruxismo do sono e ronco / Helena Polmann ; orientadora, Graziela De Luca Canto, 2024.
104 p.

Tese (doutorado) - Universidade Federal de Santa Catarina, Centro de Ciências da Saúde, Programa de Pós Graduação em Odontologia, Florianópolis, 2024.

Inclui referências.

1. Odontologia. 2. Bruxismo do sono. 3. Ronco. I. Canto, Graziela De Luca. II. Universidade Federal de Santa Catarina. Programa de Pós-Graduação em Odontologia. III. Título.

Helena Polmann

Associação entre bruxismo do sono e ronco

O presente trabalho em nível de Doutorado foi avaliado e aprovado por banca examinadora composta pelos seguintes membros:

Prof. Dr. Gabriel Natan de Souza Pires
Universidade Federal de São Paulo, São Paulo, Brasil

Prof.ª Dr.ª Bianca Marques Santiago
Universidade Federal da Paraíba, Paraíba, Brasil

Prof.ª Dr. ª Michele Bolan
Universidade Federal de Santa Catarina, Santa Catarina, Brasil

Certificamos que esta é a **versão original e final** do trabalho de conclusão que foi julgado adequado para obtenção do título de Doutora em Odontologia

ICP-Edu
Documento assinado digitalmente
Mariane Cardoso Carvalho
Data: 03/06/2024 09:01:28-0300
CPF: ***.647.159-**
Verifique as assinaturas em https://v.ufsc.br

Prof. Dr.ª Mariane Cardoso Carvalho

Coordenadora do Programa

ICP-Edu
Documento assinado digitalmente
Graziela de Luca Canto
Data: 03/06/2024 08:03:38-0300
CPF: ***.310.659-**
Verifique as assinaturas em https://v.ufsc.br

Prof. Dr.ª Graziela De Luca Canto

Orientadora

Florianópolis, 2024

AGRADECIMENTOS

Gostaria de expressar minha profunda gratidão a Deus, cuja orientação e graça foram fundamentais em cada etapa desta jornada acadêmica. Obrigada por tudo.

À Universidade Federal de Santa Catarina e ao Programa de Pós-Graduação em Odontologia, expresso minha profunda gratidão pela oportunidade de uma educação pública e de qualidade durante a graduação e pós-graduação. Assim como todos professores e funcionários que tive a oportunidade de conviver nesse período. Espero poder devolver à comunidade tudo que foi me ensinado nesse período.

À minha orientadora, Graziela de Luca Canto, devo uma imensa dívida de gratidão. Sou profundamente grato por sua orientação dedicada e inspiradora. Também agradeço toda a equipe COBE, em especial Carla Massignan, Cristine Miron Stefani e Karyn Lehmkuhl. Vocês todas são exemplos de dedicação ao trabalho e à pesquisa acadêmica.

Às minhas queridas colegas cobetes Jéssica Conti Réus, Patrícia Pauletto, Júlia Meller, Renata Paz e Lia Honnef, expresso minha mais profunda gratidão. Obrigada pela companhia, parceria e amizade que levarei por toda a vida.

Ao Dr. Israel Maia por abrir as portas do Hospital Baía Sul para realização dessa pesquisa. Obrigada por acreditar na nossa pesquisa. À equipe do Hospital Baia Sul que nos recebeu para a realização dessa pesquisa, em especial à Eliny dos Santos Machado Ferreira e Salete Iop (in memorian).

À equipe EPISONO, por aceitarem minha proposta para a realização dessa pesquisa. Meus sinceros agradecimentos para os pesquisadores Milton Maluly, Gabriel Natan de Souza Pires, Monica Levy Andersen e Sérgio Tufik. Senti-me extremamente privilegiada por poder fazer parte dessa equipe.

A Joyce Duarte obrigada por ter iniciado esse grande projeto. Minha profunda admiração por tudo que você é e construiu.

Ao meu noivo, Alexandre, meu companheiro e incentivador, expresso minha sincera admiração. Sua presença ao meu lado trouxe alegria e equilíbrio à minha jornada acadêmica, e estou profundamente grata por sua constante apoio e incentivo.

À minha mãe, Fabiana, obrigada por sempre acreditar em mim. Não teria chegado ao final dessa caminhada sem apoio. Te amo.

Ao meu pai, Robson, obrigada por tudo. Obrigada por sempre ser um exemplo de ética, trabalho duro e perseverança. Te amo.

A toda minha família, agradeço o apoio, a compreensão das inúmeras faltas em encontros familiares. Amo muito todos vocês.

A todos aqueles que, de alguma forma, contribuíram para este trabalho, meu mais sincero obrigado. Suas influências e apoio foram inestimáveis e profundamente apreciados.

RESUMO

O bruxismo do sono é uma atividade muscular mastigatória rítmica. O ronco é definido como vibrações audíveis das vias aéreas superiores produzidas no momento da respiração. Embora a associação entre essas condições tenha sido estudada na literatura, ainda existem muitas lacunas. O objetivo dessa tese foi avaliar a associação entre bruxismo do sono e ronco em adultos. Dois estudos foram realizados: 1) um estudo descritivo; 2) um estudo observacional com dados provenientes de uma amostra populacional. O primeiro estudo incluiu indivíduos encaminhados para polissonografia, com suspeita de distúrbios do sono, no Hospital Baia Sul, Florianópolis. Os dados foram coletados utilizando questionários, avaliação clínica e resultados da polissonografia. A análise estatística foi executada pelo software Jamovi. A associação entre bruxismo do sono ronco não foi significativa ($p>0,05$). Regressões logísticas não-ajustadas e ajustadas foram realizadas em relação aos períodos de sono (REM, NREM e tempo total de sono). A variável dependente foi o bruxismo do sono. Durante o sono REM, a regressão logística ajustada mostrou que o ronco ~~e~~ está associado aos episódios de bruxismo do sono. Idade, sexo e classificação do índice de massa corporal não foram associados com bruxismo do sono. Em relação aos outros períodos do sono, a regressão logística não foi considerada significativa. Outras variáveis relacionadas à arquitetura do sono, assim como qualidade do sono e sonolência não foram associados ao bruxismo do sono. O segundo estudo utilizou dados da terceira edição do estudo EPISONO, um estudo de base populacional realizado em São Paulo em 2007. A amostra incluiu 502 indivíduos adultos sem apneia obstrutiva do sono. Os dados foram coletados usando questionários, avaliação clínica e os resultados da polissonografia. A análise estatística foi realizada pelo programa Jamovi. A associação entre bruxismo do sono e ronco não foi significativa ($p>0,05$). Regressões logísticas não-ajustadas e ajustadas foram realizadas em relação à severidade do bruxismo do sono. A variável dependente foi o bruxismo do sono. A regressão logística ajustada indicou uma associação entre sintomas de ansiedade e bruxismo do sono leve. Uma regressão logística ajustada também foi utilizada para avaliar as variáveis do sono, demonstrando que a duração do sono REM apresentou associação com bruxismo do sono. No primeiro estudo, o ronco foi associado a episódios de bruxismo do sono durante o período REM. Não houve associação do bruxismo do sono com sexo, idade, índice de massa corporal, variáveis relacionadas à arquitetura do sono, qualidade do sono ou sonolência. Em conclusão ao segundo estudo, os sintomas de ansiedade e a duração do período REM podem estar associadas ao bruxismo do sono. No entanto, o bruxismo do sono e ronco, consumo de cigarro e álcool não foram associados. Além disso, não houve associação entre bruxismo do sono e variáveis relacionadas à arquitetura do sono. Como conclusão da tese, é possível evidenciar a complexidade do bruxismo do sono, apresentando associação com ronco em uma amostra descritiva; e associação com sintomas de ansiedade e porcentagem do sono REM em um estudo observacional com dados de uma amostra populacional.

Palavras-chave: Bruxismo do sono; Ronco; Polissonografia; Associação; Estudo observacional.

ABSTRACT

Sleep bruxism is a rhythmic jaw muscle activity, while snoring is defined as audible vibrations of the upper airways produced during breathing. Although the association between these conditions has been studied in the literature, there are still gaps. The aim of this thesis was to evaluate the association between sleep bruxism and snoring in adult individuals. Two studies were conducted: 1) a descriptive study; 2) an observational study with data from a population-based sample. The first study included individuals referred for polysomnography (PSG) at Baia Sul Hospital in Florianópolis. Data were collected using questionnaires, clinical evaluation, and polysomnography results. Statistical analysis was performed using the Jamovi software. The association between sleep bruxism and snoring was not significant ($p>0.05$). Unadjusted and adjusted logistic regressions were performed regarding sleep periods (REM, NREM, and total sleep time). The dependent variable was sleep bruxism. During REM sleep, adjusted logistic regression showed that snoring is associated with episodes of sleep bruxism. Age, sex, and body mass index classification were not associated with sleep bruxism. Regarding other sleep periods, logistic regression was not considered significant. Other variables related to sleep architecture, as well as sleep quality and drowsiness, were not associated with sleep bruxism. The second study used data from the third edition of the EPISONO study, a population-based study conducted in São Paulo in 2007. The sample included 502 adult individuals without obstructive sleep apnea. Data were collected using questionnaires, clinical evaluation, and polysomnography results. Statistical analysis was performed using the Jamovi program. The association between sleep bruxism and snoring was not significant ($p>0.05$). Unadjusted and adjusted logistic regressions were performed regarding the severity of sleep bruxism. The dependent variable was sleep bruxism. Adjusted logistic regression indicated an association between anxiety symptoms and mild sleep bruxism. Adjusted logistic regression was also used to assess sleep variables, demonstrating that the duration of REM sleep was associated with sleep bruxism. In the first study, snoring was associated with episodes of sleep bruxism during the REM period. There was no association between sleep bruxism and sex, age, body mass index, sleep architecture-related variables, sleep quality, or drowsiness. In conclusion to the second study, anxiety symptoms and REM sleep duration may be associated with sleep bruxism. However, sleep bruxism and snoring, smoking, and alcohol consumption were not associated. Additionally, there was no association between sleep bruxism and variables related to sleep architecture. As a conclusion of the thesis, it is possible to highlight the complexity of sleep bruxism, presenting an association with snoring in a descriptive sample, and an association with anxiety symptoms and percentage of REM sleep in an observational study with data from a population sample.

Keywords: Sleep bruxism. Snore. Polysomnography. Observational study.

LISTA DE QUADROS

LISTA DE ABREVIAÇÕES E SIGLAS

PORTUGUÊS

AAMS	Academia Americana Medicina do Sono
AOS	Apneia Obstrutiva do Sono
BS	Bruxismo do Sono
EEG	Eletroencefalograma
EMG	Eletromiografia
PSG	Polissonografia
RS	Revisão Sistemática
TTS	Tempo Total de Sono

INGLÊS

AIC	Akaike information criterion
BMI	Body mass index
CI	Confidence Interval
EPISONO	The Sao Paulo Epidemiologic Sleep Study
ICSD	International Classification of Sleep Disorders
NREM	Non Rapid Eyes Moviment
PSG	Polysomnography
REM	Rapid Eyes Moviment
RPSGT	Registered Polysomnographic Technologist
SB	Sleep Bruxism
SR	Systematic Review
STAB	Standardized Tool for the Assessment of Bruxism
TST	Total Sleep Time
VIF	Variance Inflation Factor

LISTA DE SÍMBOLOS

®	Marca Registrada
=	Igual
<	Menor
>	Maior
≥	Maior ou Igual
α	alfa
β	beta

SUMÁRIO

1 APRESENTAÇÃO

Essa tese é composta por duas pesquisas. A primeira faz parte do Macroprojeto de pesquisa intitulado “Associação entre bruxismo do sono e apneia obstrutiva do sono” conduzido em Florianópolis no ano de 2019. A segunda é parte integrante do Macroprojeto de Pesquisa intitulado EPISONO (*The Sao Paulo Epidemiologic Sleep Study*), realizado na cidade de São Paulo no ano de 2007. Ambos os trabalhos foram redigidos em forma de artigo na língua inglesa.

2 INTRODUÇÃO

O bruxismo do sono (BS) é uma atividade da musculatura mastigatória que ocorre durante o período de sono, não sendo considerada uma desordem do movimento ou um distúrbio do sono. Dependendo do padrão da atividade, ela pode ser caracterizada como rítmica (fásica) ou não-rítmica (tônica). Quando essa atividade acontece durante momentos de vigília, é denominada bruxismo em vigília (Lobbezoo *et al.*, 2018).

Uma revisão sistemática (RS) realizada em 2013 encontrou uma estimativa de prevalência para BS de 12,8% (±3,1%), quando o BS foi avaliado por meio de exame clínico e/ou questionários. O BS avaliado por polissonografia (PSG) apresentou uma prevalência de 7,4% compreendendo 75 pacientes em uma amostra total de 1019 indivíduos (Maluly *et al.*, 2013).

O BS pode manifestar-se de forma isolada ou associar-se a outras comorbidades, tais como refluxo gastresofágico, insônia, dor de cabeça, dor orofacial e transtorno do movimento periódico dos membros (Mayer *et al.*, 2016; Martynowicz *et al.*, 2018). Atualmente, há uma crescente investigação acerca da associação entre BS, ronco e apneia obstrutiva do sono (AOS) (Michalek-Zrabkowska, Monika *et al.*, 2020; Smardz *et al.*, 2021). No que se refere à relação entre BS e AOS, muito já foi estudado na literatura; contudo, não há um consenso estabelecido sobre essa associação (De Luca Canto *et al.*, 2014; Jokubauskas;Baltrušaitytė, 2017; Da Costa Lopes *et al.*, 2020). Uma recente revisão de escopo mapeou a literatura existente sobre BS e AOS, incluindo amostras compostas de adultos e crianças (Pauletto *et al.*, 2022). Os autores concluíram que, até o momento, ainda não é possível confirmar a relação entre BS e AOS em adultos. Em crianças, a associação parece ser possível, mas não há evidências suficientes para apoiá-la.

Em busca de possíveis outros fatores associados aos episódios de BS, pesquisadores iniciaram a avaliação do ronco em associação à presença de BS. Embora o ronco seja um sinal associado comumente à AOS, o estudo do ronco em pacientes sem apneia está crescendo (Zucconi *et al.*, 1993; Zicari *et al.*, 2014). Em uma amostra de 3,136 adultos brasileiros, com uma média de 44 anos e predominantemente do sexo feminino, a prevalência de ronco habitual foi de aproximadamente 50% (95% IC: 48,1 a 52,8%) (Noal *et al.*, 2008). Uma recente RS (Huang *et al.*, 2023) avaliou a associação entre ronco e desordens do sono. Dentre os estudos incluídos, quatro estudos (Abe *et al.*, 2012; Kato *et al.*, 2012; Palinkas, Marcelo *et al.*, 2019; Emodi-Perlman *et al.*, 2022)

associaram ronco com BS. Um estudo com 90 brasileiros não apneicos avaliados via PSG sugeriu que pacientes com BS tendem a ter a presença de ronco durante o sono (Palinkas, Marcelo *et al.*, 2019). Outro estudo com mulheres israelenses fez avaliação de BS por questionários e encontrou que as pacientes roncadoras apresentavam mais sintomas de BS, como dor nos músculos mastigatórios ao acordar, em comparação com pacientes não-roncadores (Emodi-Perlman *et al.*, 2022). Pacientes japoneses com e sem BS foram avaliados com o dispositivo portátil *BiteStrip*, e não apresentaram diferença entre os grupos em relação ao ronco (Abe *et al.*, 2012). Outro estudo também avaliou a população japonesa, mais especificamente moradores de uma área rural. Os participantes apresentaram 2,58 mais chances de apresentar BS possível quando roncavam do que quando não apresentavam essa condição (Kato *et al.*, 2012). Dentro da evidência encontrada, a revisão sistemática não pode concluir a presença ou não de associação entre BS e ronco, sugerindo a realização de novos estudos sobre a temática.

Existem poucos estudos sobre a temática na literatura e apenas um realizado com pacientes brasileiros. Sendo assim, este estudo propõe a execução de uma nova análise avaliando variáveis complementares ao último estudo brasileiro, como sexo, idade e avaliação da estrutura do sono relacionadas ao BS e ronco. Além disso, duas populações distintas serão avaliadas: pacientes com suspeita de distúrbios do sono e pacientes não apneicos.

3 REVISÃO DE LITERATURA

3.1 SONO

O sono tem sido um tópico de curiosidade e estudo ao longo do tempo. O sono é um estado neurofisiológico e apresenta componentes comportamentais específicos, caracterizado por uma suspensão reversível da resposta sensorial e motora a estímulos externos (Buysse, 2014; Tavares *et al.*, 2022). Apesar dos consideráveis avanços científicos nos estudos sobre o tema, ainda não há consenso quanto à definição exata do sono e sua função (Tavares *et al.*, 2022). É considerado um processo ativo, ligado funcionalmente à vigília (Kleitman, 1987). O sono é um dos processos fisiológicos indispensáveis para regulação e manutenção do equilíbrio orgânico dos seres vivos.

A arquitetura do sono humano é dividida em dois principais estágios: NREM e REM (Eban-Rothschild *et al.*, 2017). O sono NREM subdivide-se em três estágios: N1, N2 e N3 (Franken; Dijk, 2009). Cada um desses estágios é caracterizado por uma progressiva diminuição na frequência das ondas cerebrais registradas no eletroencefalograma (EEG) (Tavares *et al.*, 2022). O ciclo de sono inicia-se no estágio N1 e corresponde de 2-5% do tempo total de sono (TTS). É o período de transição entre a vigília e o sono, caracterizado por sonolência superficial. O estágio N2 do sono NREM compreende cerca de 45-55 % do TTS. Nesta fase, o sono é tranquilo, mas o indivíduo pode ser facilmente despertado. O estágio N3 é caracterizado pela presença de ondas cerebrais de baixa frequência, chamadas de sono de sondas lentas ou sono delta (AAMS, 2014). Em seguida, ocorre o início do sono REM. Essa fase normal do sono que corresponde a 20% e 25% do TTS, com uma duração média de 90 a 110 minutos. Em uma noite normal, ocorrem de 4 a 6 ciclos, com o sono NREM ocorrendo na primeira metade do sono, e o sono REM na segunda metade. O sono é um estado contínuo e progressivo, em que os estágios se alternam de forma gradual (Tavares *et al.*, 2022).

Alterações no início, duração ou condutas anormais relacionadas ao sono são caracterizadas como distúrbios do sono pela terceira Classificação Internacional de Distúrbios do Sono, do inglês "*International Classification of Sleep Disorders*" (ICSD-3) (AAMS, 2014).

3.2 BRUXISMO DO SONO

3.2.1 Definição

Atualmente, em indivíduos saudáveis, o BS não deve ser considerado um distúrbio, mas um comportamento que pode ser um fator de risco (e/ou protetor) para certas consequências clínicas, como por exemplo a presença de refluxo (Lobbezoo *et al.*, 2018). Quando o indivíduo não apresenta nenhuma consequência clínica é considerado um "normo-bruxismo"; porém, quando há associação com sinais e sintomas prejudiciais o bruxismo é chamado de "pato-bruxismo" (Svensson;Lavigne, 2020).

3.2.2 Etiologia

O BS possui etiologia multifatorial que ainda não está totalmente definida na literatura. Atualmente, entende-se que a etiologia do bruxismo está relacionada a fatores centrais, e não periféricos (Lobbezoo;Naeije, 2001). Justificativas para a ocorrência do BS podem estar relacionadas aos mecanismos relacionados aos microdespertares, alterações do sistema autônomo simpático, alteração da atividade cardíaca, predisposição genética, fatores psicossociais e fatores exógenos (café, tabaco, medicamentos psicotrópicos) (Melo *et al.*, 2019; Polmann *et al.*, 2019; Wieckiewicz *et al.*, 2020; Michalek-Zrabkowska *et al.*, 2021; Polmann *et al.*, 2021)

A ativação do sistema autônomo simpático resulta em um aumento da taxa cardíaca, aumento da pressão arterial, taxa de respiração, assim como a ocorrência de micro despertares relacionados ao BS (Carra *et al.*, 2015). Além disso, uma ativação cortical pode ser observada durante a EEG em episódios de BS (Kato *et al.*, 2001). Devido aos micros despertares, o BS pode provocar interrupções e aumentar a instabilidade do sono (AAMS, 2014). Os despertares podem ser frequentemente observados durante o sono, principalmente no estágio N2 (da Mota Gomes *et al.*, 2010; López *et al.*, 2015). Quando ocorrem, levam a mudanças transitórias entre um estágio de sono mais profundo para um mais leve. Quando os despertares são avaliados por meio de uma EMG, é possível constatar o aumento da tonicidade muscular (Bonnet *et al.*, 1992). Em um estudo epidemiológico com 1019 indivíduos, 52,4% dos episódios de BS foram relacionados a despertares (Maluly *et al.*, 2013).

As alterações fisiológicas do sono podem resultar em um aumento da atividade muscular mastigatória rítmica. Essa atividade está relacionada a funções fisiológicas, tais como aumentos do pH relacionados ao refluxo gastroesofágico e a movimentos de deglutição (Lavigne *et al.*, 2001). Embora isto possa ocorrer em pacientes sem BS, é mais evidente nos pacientes com BS, sendo utilizada como medida para avaliação do mesmo (Lavigne *et al.*, 2007).

3.2.3 Sinais e sintomas

As principais manifestações clínicas do BS, com base em autorrelatos e exame clínico, incluem desgaste dentário, apertamento mandibular, e fadiga ou dor muscular na região mandibular (AAMS, 2014; Stuginski-Barbosa *et al.*, 2017). Além de consequências deletérias como quebra de dentes e/ou restaurações, dor de cabeça, dor orofacial e problemas temporomandibulares (Reus *et al.*, 2021). Entretanto, a presença desses sinais e sintomas não necessariamente indica a presença ativa da condição, visto que o comportamento do bruxismo pode alterar-se com o tempo (Lobbezoo *et al.*, 2013).

3.2.4 Avaliação e classificação

Os métodos de detecção do bruxismo são discutidos há mais de 30 anos na literatura (Lavigne *et al.*, 2021). Em 2013, o BS foi categorizado como “possível” quando avaliado por meio de autorrelato; “provável” quando há avaliação clínica, e “definitivo” quando o diagnóstico é feito com eletromiografia (EMG).

A EMG permite a identificação e classificação do BS. A avaliação do exame é realizado seguindo manuais estabelecidos e consolidados na literatura pela Associação Americana de Medicina do Sono (AAMS, 2014; Berry *et al.*, 2017). Para isso, é utilizada a avaliação da atividade muscular mastigatória rítmica. Um episódio de BS pode ser identificado quando há elevações fásicas ou tônicas relacionadas aos músculos da mastigação. Essas elevações podem ser chamadas de surtos e devem apresentar pelo menos o dobro de uma atividade basal da EMG. Para um novo episódio ser identificado, é necessário um intervalo de pelo menos 3 segundos entre os surtos. Seguindo esses critérios, os eventos do BS são classificados em:

- Evento fásico: ocorrem pelo menos três surtos breves na EMG (0,25 a 2,0 segundos cada). Essas contrações musculares rítmicas são características do ranger de dentes;
- Evento tônico: episódio com surto mantido por mais de 2 segundos. O apertamento é caracterizado por esse tipo contração;
- Misto: combinação dos dois padrões.

O último consenso de 2018, autodenominado um "trabalho em construção" sugere a divisão da formas de avaliação entre métodos 1) Instrumentais: EMG e 2) Não-instrumentais: autorrelato e avaliação clínica (Lobbezoo *et al.*, 2013). Ainda assim, a relevância clínica e optimização desses métodos para pesquisa ainda não está totalmente estabelecida (Lavigne *et al.*, 2021). Uma RS avaliou diferentes métodos de detecção do BS (questionários, avaliação clínica e dispositivos portáveis). A meta-análise concluiu que questionários e avaliação clínica podem ser utilizados como métodos de rastreamento para a condição, mas não conseguem identificar bem os indivíduos sem a condição. A melhor acurácia diagnóstica foi identificada dos dispositivos portáveis, especialmente a EMG de quatro canais (Casett *et al.*, 2017).

Visto que o bruxismo é uma condição multifatorial, sua classificação com métodos dicotômicos de avaliação ainda gera controvérsias na literatura (Manfredini *et al.*, 2019). É necessário a avaliação de todos os fatores de risco e hábitos relacionados à condição. Recentemente, experts no assunto publicaram uma sugestão de método de avaliação para o bruxismo. Esse instrumento denominado STAB (*Standardized Tool for the Assessment of Bruxism)* tem como objetivo avaliar o status e as consequências da condição no indivíduo (eixo A) e seus fatores de risco e etiológicos (eixo B). Possui 14 domínios em 66 itens, associando autorrelato do paciente, avaliação clínica pelo avaliador e uso de instrumentos tecnológicos, como EMG (Manfredini *et al.*, 2023b).

3.3 RONCO

As desordens respiratórias do sono englobam um espectro de condições, iniciando com o ronco primário até condições mais severas como AOS (AAMS, 2014). O ronco é considerado um fenômeno acústico (Koutsourelakis *et al.*, 2012). De acordo com o ICSD-3), o ronco primário é definido como "vibrações audíveis das vias aéreas superiores durante a respiração durante o sono, sem a presença de episódios de apneia ou hipoventilação" (AAMS, 2014). Essas vibrações audíveis podem ocorrer na

inspiração ou expiração e têm intensidade suficiente para causar desconforto ao parceiro/a de cama ou pessoas próximas. O ronco ocorre de forma contínua, principalmente quando o indivíduo dorme em posição supina (AAMS, 2014).

Inúmeros termos são utilizados para denominar o ronco na literatura, como “ronco primário”, “ronco habitual”, “ronco simples”, “ronco benigno”, “ronco não apneico”, “ronco contínuo”, “ronco rítmico”, “ronco não perigoso”. O ronco primário ocorre quando o ronco é detectado sem alguma comorbidade sistêmica associada no paciente, (Counter;Wilson, 2004) também podendo ser chamado de ronco não-apneico (Deary *et al.*, 2014). O ronco primário e o ronco simples são considerados equivalentes. O ronco habitual adiciona um elemento de frequência à definição. Considera-se como habitual, quando o paciente ronca pelo menos três vezes por semana (O'Brien *et al.*, 2013).

O som produzido pelo ronco é proveniente da vibração das vias aéreas superiores. Devido ao estreitamento do espaço orofaríngeo ou nasofaríngeo, o ar passa de forma turbulenta pela parede posterior da faringe, úvula, palato mole e base de língua (AAMS, 2014).

Os fatores de risco para essa condição incluem congestão nasal, inflamação ou obstrução das vias áreas superiores, ingestão de álcool, aumento do índice de massa corporal, medicamentos depressivos do sistema nervoso central, retrognatismo (Lavigne *et al.*, 1999) e/ou pacientes do sexo masculino (Deary *et al.*, 2014). O paciente com ronco pode se queixar de boca seca e apresentar irritação nos tecidos da mucosa oral (Lavigne *et al.*, 1999). O ronco é considerado um sinal clínico relevante para o diagnóstico da AOS, sendo o questionamento da sua presença parte de questionários validados para sua detecção (Chung *et al.*, 2016; Chiu *et al.*, 2017).

O ronco pode ser classificado de forma subjetiva, por meio de questionários ou objetiva, utilizando microfones e transdutores de pressão nasal, por exemplo. O critério diagnóstico segundo ICSD-3 (AAMS, 2014) abrange os seguintes itens:

a) Relato de terceiro da presença do ronco
b) Não há evidência de insônia ou sonolência excessiva resultante do ronco.
c) Queixa de boca seca ao acordar.
d) A PSG demonstra todos os seguintes itens:
    1) Sons inspiratórios ou expiratórios que ocorrem frequentemente em episódios prolongados durante o tempo total de sono;

2) Sem despertares abruptos associados, dessaturação de oxigênio arterial ou perturbações cardíacas;
3) Padrão normal de sono;
4) Padrão respiratório normal durante o sono.

e) Os sintomas não atendem aos critérios diagnósticos de outros distúrbios do sono (ou seja, síndrome de apneia central do sono, AOS, síndrome de hipoventilação alveolar central ou laringoespasmo relacionado ao sono).

A presença mínima dos critérios A e B é necessária para o diagnóstico de ronco primário.

Recentemente, um novo modelo de classificação do ronco utilizando a polissonografia foi proposto. A porcentagem de ronco foi determinada calculando a duração acumulada dos eventos de ronco dividida pelo TTS. Um episódio de ronco foi definido como três ou mais eventos consecutivos de ronco ocorrendo com intervalos iguais ou inferiores a 10 segundos. O índice de ronco foi definido como o número de episódios de ronco por hora de sono (Kim *et al.*, 2022). Entretanto, esse modelo ainda não foi adotado como padrão para método classificatório.

Quanto ao critério de severidade, o ronco é classificado em leve, moderado e grave. O ronco leve não ocorre todas as noites e ocorre somente em posição supina. O ronco moderado ocorre todas as noites, pode ocasionalmente incomodar os outros e normalmente cessa pela mudança na posição do corpo. Por fim, é categorizado como ronco grave quando ocorre todas as noites, incomoda os outros e não é alterado pela mudança na posição corporal. O ronco pode ainda ser classificado em relação à duração em agudo, subagudo ou crônico. Quando presente por menos de três meses é considerado agudo; por mais de três meses, mas menos de um ano como subagudo; e sendo crônico quando está presente por um ano ou mais (AAMS, 2014).

3.4 BRUXISMO E RONCO

Considera-se a hipótese de que a atividade muscular mastigatória rítmica associada ao BS possa ocorrer com o propósito de lubrificar as estruturas da orofaringe durante o sono, período no qual as taxas de salivação são mais baixas (Carra *et al.*, 2015). Além disso, pacientes que apresentam ronco também podem apresentar xerostomia, caracterizada pela sensação de boca seca (AAMS, 2014).

Um estudo conduzido com participantes chineses investigou a validade diagnóstica do questionário STOP BANG ao incorporar a pergunta adicional "Você sente sua boca seca ao acordar pela manhã?". O objetivo da pesquisa foi avaliar se essa adição poderia aprimorar a especificidade do questionário para pacientes diagnosticados com AOS. A amostra do estudo incluiu um total de 207 indivíduos submetidos tanto ao questionário quanto ao exame de polissonografia. Os resultados revelaram que os pacientes identificados como roncadores apresentaram 2,67 vezes mais probabilidade de apresentar ressecamento da mucosa em comparação com pacientes não roncadores (Zhang *et al.*, 2021).

Um estudo recente, utilizando amostra de conveniência, identificou 968 participantes com bruxismo possível (Huang *et al.*, 2022). A avaliação de bruxistas foi feita com *Oral Behaviours Checklist* enquanto o ronco primário foi identificado com o questionário de oito perguntas STOP BANG. Os participantes foram divididos em "baixo risco de apneia" quando tiveram apenas duas respostas "sim" e "alto risco de apneia", quando tiveram respostas afirmativas para três ou mais questões. Após essa divisão, os pacientes classificados como "baixo risco de apneia" que apresentavam entre as duas respostas afirmativas a referente ao ronco "*Do you snore?"* considerados roncadores primários. Desse modo, setenta e um indivíduos (7,3%) do total da amostra foram classificados dessa maneira. Ao realizar a regressão logística múltipla e pela regressão em rede não foi encontrada influência do BS ou outros fatores associados.

Outro estudo, do tipo transversal descritivo, avaliou um grupo de 137 pacientes não apneicos na Polônia. Todos os indivíduos apresentavam BS e ronco com idade média de 34,03±10,04. Foi avaliado a influência que a idade e gênero exerceram sobre o BS e ronco através do exame PSG (Smardz *et al.*, 2021). Ambas as condições foram consideras mais intensas em homens. Em pacientes mais velhos o ronco foi mais frequente no estágio N2 e apresentaram uma quantidade menor de episódios de BS. Um estudo observacional avaliou pacientes não apneicos com BS e ronco e a relação com a posição durante o sono por meio da PSG. Os autores encontraram uma correlação entre BS fásico e ronco na posição supina e não supina, concluindo que a posição durante o sono afeta a intensidade de ambas as variáveis (Michalek-Zrabkowska, Monika *et al.*, 2020). Diante da complexa interação entre BS e ronco, evidenciada por estudos recentes, é necessário realizar uma nova investigação que aprofunde a compreensão dessa relação.

4 OBJETIVOS

4.1 OBJETIVO GERAL

Verificar se há associação entre bruxismo do sono e ronco em adultos brasileiros. A hipótese nula (H0) é que não há associação entre bruxismo do sono e ronco. A hipótese alternativa (H1) é que existe associação entre as duas variáveis.

4.2 OBJETIVOS ESPECÍFICOS

4.2.1 Estudo Baia Sul

a) Avaliar a possível associação entre bruxismo do sono e ronco em indivíduos com suspeita de distúrbios do sono;
b) Avaliar a associação entre bruxismo do sono com sexo, idade e índice de massa corporal;
c) Avaliar a associação do bruxismo do sono com características da arquitetura do sono e variáveis relacionadas ao sono, como qualidade do sono e sonolência.

4.2.2 Estudo EPISONO

a) Avaliar a possível associação entre bruxismo do sono e ronco em indivíduos não apneicos;
b) Avaliar a associação do bruxismo do sono com sexo, idade, índice de massa corporal, álcool, tabagismo e ansiedade;
c) Investigar a associação entre bruxismo do sono e características da arquitetura do sono e variáveis relacionadas ao sono.

5 ARTIGO 1[1]

Association between sleep bruxism and snoring in adults through polysomnographic: a descriptive study

Authors

Helena Polmann, DDS, MSc[1,2], Patrícia Pauletto, DDS, PhD[1,3], Jéssica Conti Réus DDS, MSc[1], Joyce Duarte de Sá, DDS, PhD[4] Israel Maia, MD, MSc[4], Graziela De Luca Canto, DDS, PhD[1,2.]

Affiliations

[1] Brazilian Centre for Evidence-Based Research (COBE), Federal University of Santa Catarina, Florianópolis, Brazil.

[2] Department of Dentistry, Federal University of Santa Catarina, Florianópolis, Brazil

[3]Faculty of Dentistry, Universidad de las Americas (UDLA), Quito, Ecuador.

[4]Curitiba University Center-Unicurtiba, Curitiba, Paraná, Brazil.

[5]Baía Sul Research Institute, Florianópolis, Santa Catarina, Brazil.

Correspondence Author

Helena Polmann, Department of Dentistry, Federal University of Santa Catarina, University Campus, Mailbox 476-Trindade, Florianópolis, Santa Catarina, Brazil.
Email: hpolmann@hotmail.com

Conflict of Interest

The authors declare that have no conflict of interest.

Funding

The authors declare no funding to develop this research.

[1] Artigo formatado para submissão ao periódico *SLEEP*

Abstract

This study was performed to assess the association between sleep bruxism and snoring in adults and the possible association of variables within both conditions, such as age, sex, and body mass index. Additionally, sleep structure characteristics, quality of sleep and sleepiness were compared between groups with and without sleep bruxism. Individuals with suspected sleep disorders (n=61), referred for a single-night video polysomnography, were selected for this observational study. Questionnaires and clinical examinations were conducted prior to the polysomnographic exam. Polysomnographic scoring was performed according to the American Academy of Sleep Medicine criteria. Statistical analyses were executed with the Jamovi software. The logistic regressions were performed regarding sleep periods (REM, NREM and total sleep time). Rhythmic masticatory muscle activity index during these sleep periods was the dependent variable. Only variables with p-value <0.05 were included in the adjusted logistic regression. No association was found between sleep bruxism and snoring (p>0.31); and the effect size was considered small V=0.171. Logistic regression showed that the snore index can influence the rhythmic masticatory muscle activity index within the REM period of sleep, with an odds ratio of 1.018 (95% CI: 1.005 to 1.03; p=0.05). The same logistic regression showed that the desaturation index presented an odds ratio of 5.01 (95% CI: 0.96 to 26.13; p=0.056), but the effect size was considered medium (>3.5). Age, sex, and body mass index classification were not associated with sleep bruxism. Regarding the sleep structure and other sleep variables, no statistical difference was found within groups with and without sleep bruxism. Therefore, within the limitations of this study, snoring appears to be associated with sleep bruxism episodes during the REM period. No association was found between sleep bruxism and sex, age, body mass index. Concerning sleep architecture characteristics, only episodes of desaturation may be associated with sleep bruxism during the REM sleep. Quality of sleep or sleepiness were not associated with sleep bruxism.

Keywords: Sleep bruxism; snoring; polysomnography

Introduction

According to the international consensus, sleep bruxism (SB) is defined as muscle activity during sleep, expressed as rhythmic (phasic) or weak (tonic), rather than sleep disturbance as a movement disorder [1]. In 2013, a categorization system was proposed based on the detection approach, and it was updated in 2018 [1,2]. Since then, SB can be defined as "possible" when assessed through self-report, "probable" when there is clinical evaluation, and "definitive" when the detection is executed through electromyography (EMG) and/or polysomnography (PSG) [2].

The relationship between SB and sleep-disordered breathing (SDB) has been studied several times through the years [3]. SDB encompasses a spectrum of conditions, ranging from primary snoring to more severe conditions such as obstructive sleep apnea (OSA) [4]. Most studies with different designs have investigate the association between SB and OSA. However, despite all these efforts, the current literature cannot confirm or refute the casual effect of both conditions [5,6].

Nevertheless, the investigation of snoring associated with SB has been increased over the years. Snoring is considered an acoustic phenomenon [7]. The sound produced by snoring comes from the vibration of the upper airways. Due to the narrowing of the oropharyngeal or nasopharyngeal space, air passes turbulently through the posterior wall of the pharynx, uvula, soft palate, and base of the tongue [4]. These audible vibrations can occur during inhalation or exhalation and are intense enough to cause discomfort to the bed partner or people nearby. Most articles assess snoring as a subjective factor by means of questionnaires, self-report, or third-party accounts [4,8].

A recent systematic review evaluated the association between snoring and sleep disorders, such as SB [9]. Thirty-six studies were included, and 4 evaluated snoring and SB. The included studies (n=4) evaluated snoring by means of questionnaire, and three presented a positive association between both conditions [10,11]. Within the available evidence in the systematic review, no association was indicated.

The literature is still scarce regarding studies that detected both conditions using PSG [12-15]. Therefore, the aim of this study is to evaluate the possible association between SB and snoring in adults through polysomnography. Moreover, assess the association between SB and sex, age, and sleep variables, regarding sleep architecture, quality of sleep and sleepiness.

Methods

Study Design

This observational descriptive study was reported following STROBE (Strengthening the Reporting of Observational Studies in Epidemiology [16,17]. The checklist can be found in Appendix A.

The study was conducted following the Helsinki Declaration of 1964 and the research project was submitted for approval by the Human Research Ethics Committee under number: 2.620.213 and CAAE: 84783518600000121 of the Federal University of Santa Catarina. The Free Informed Consent Form can be accessed in Appendix B.

Setting

The study was carried out with individuals referred to a night-time PSG upon prior medical request at a private hospital located in Florianópolis, Brazil.

The PSG exam was performed on alternate days on the same room, due to the presence of only one PSG specialist technician overseeing the procedure. While the initial plan aimed for data collection to extend from January to December, it was performed from January to October 2019, covering a nine-month follow-up period. It happened because at the end of October the technician resigned for personal reasons and a replacement was not recruited. And, unfortunately, in March 2020, the COVID-19 pandemic emerged, and the sleep laboratory was closed, limiting the study's sample size. Given the non-probabilistic nature of the sample, a sample size calculation was not conducted [18,19].

Eligibility Criteria

1) Inclusion Criteria: adult patients (≥18 years) scheduled for PSG without neurological or movement impairment. 2) Exclusion Criteria: patients with incomplete physical or PSG exams.

Data sources/ measurement

Data collection occurred in three stages on the same night: (1) questionnaires, (2) clinical exams, and (3) PSG. One of the three researchers (H.P., J.C.R. and P.P.) individually conducted the self-filled questionnaires and physical exams in the hospital bedroom where the patients were allocated.

Questionnaire

Information was collected prior to the PSG exam regarding basic demographic variables such as age, and sex. In addition to specific questionnaires for the Epworth Sleepiness Scale (ESS) [20] and PSQI-BR (the Brazilian version of the Pittsburgh Sleep Questionnaire Index) [21]. The questionnaires were self-filled out on electronic tablet, using the electronic form. Each participant was assigned a number to fill out the form, and self-adhesive labels with the corresponding number were attached to the medical records and PSG exam, ensuring blinding of the results and confidentiality of identity.

Clinical Exam

The same calibrated digital scale (Digital Glass G-Tech, ACCUMED, China) was employed to assess the patient's weight in kilograms, while a tape measure was utilized for height in meters from all patients. During measurement, the patient assumed a standing position with arms extended alongside the body, spine straight, eyes focused on a fixed point, and the head positioned at a 90º angle from the floor. Furthermore, the patient's heels and knees were in contact, and the buttocks rested against the wall. The researcher responsible for data collection conducted weight and height measurements on the day of the PSG exam. Body mass index (BMI) was computed by dividing the weight by the square of the height using a formula implemented in Microsoft® Excel 16.29.1 (Microsoft Office 2019, Microsoft, Redmond, United States). The BMI was subsequently calculated, and patients were categorized following the World Health Organization cutoff points: BMI>18.5 to 24.9kg/m² (normal weight); BMI≥25 up to 29.9kg/m² (overweight); and BMI>30.0kg/m² (obesity) [22].

Polysomnography

Single sleep tests were performed overnight in the same dark and silent hospital room, using conventional type I PSG testing equipment (Alice V©; Respironics, Andover, MA, USA), following the recommendations proposed by the American Academy of Sleep Medicine [4]. Duarte *et al.*, 2022[23] previously provided a description of PSG type I equipment characteristics and the placement of electrodes on participants' bodies. The following sleep variables were used total sleep time, sleep onset, REM onset, wakefulness after sleep onset and oxygen saturation (SpO_2). The assessment of the saturation level of arterial oxygen levels was carried out using pulse oximetry. An episode of arterial desaturation was considered when oxygen levels were below 97%, as

determined by technical configurations of PSG. All tests were monitored by the same specialist in polysomnography (E.S.M.F).

To calibrate the PSG instruments and adequately recognize the signals, the subjects were instructed, prior to the beginning of the recordings, to perform voluntary snoring movements under the instruction of the same specialist PSG technician. Leg movements, opening, closing, and moving the eyes, clenching, laterality, protrusion, rhythmic jaw contractions, as well as swallowing and coughing movements were performed to record basal amplitudes.

Sleep Bruxism

The assessment of SB events was estimated using the rhythmic masticatory muscle activity (RMMA) found in the EMG. Events of RMMA separated by three-second intervals were considered SB episodes if they followed one of the following patterns: 1) tonic (at least one masseteric EMG firing longer than 2 seconds); 2) phasic (three or more masseteric EMG shots lasting between 0.25 and 2 seconds); or 3) mixed (both types of shooting). Patients were considered without SB when they had less than 2 episodes per hour of sleep, classified as mild/moderate SB when they had between 2 and 4 episodes/hour of sleep and as severe SB when they had more than 4 episodes of SB/hour of sleep [24].

Obstructive Sleep Apnea

Events related to OSA were classified according to American Academy of Sleep Medicine definitions,[4] using the apnea-hypopnea index (AHI). Individuals were considered with OSA when AHI ≥5. An obstructive sleep apnea event was determined when there was an interruption in airflow ≥ 90% for a minimum of 10 seconds. Detailed information regarding detection of obstructive sleep apnea has been previously published [23].

Snore

The assessment of the presence or absence of snoring was also carried out using acoustic sensors (microphones) properly installed in the cervical region [4]. An event of snoring was considered when any volume above 56 hertz recorded during sleep. A new snoring event was considered when a sound happened in an interval longer than 3 seconds. A patient was considered to have the condition when they had more than one snoring event per night.

The Alice V© program generated reports with the main information from the PSG exam. The analyses were conducted by a single evaluator (J.D.), who remained blind to the clinical data collection phase.

Statistical methods

The Jamovi statistical software (Version 1.6) was used to analyze the data. The normal distribution of quantitative variables was verified using the Shapiro-Wilk test. Quantitative variables with a normal distribution were presented using mean and standard deviation (SD), variables without a normal distribution were expressed using the median and interquartile range (IQR). To compare two groups with quantitative variables, the t test was used when the distribution of both variables was considered normal. For comparisons without normal distribution, the Mann-Whitney test was applied.

To explore the association between SB and snoring, qualitative variables underwent Pearson's qui-square test was used. When expected values were below five the exact fisher teste was executed. The effect size of the variables according to each test was evaluated [25,26]. Proportion data were presented in percentage form and with a confidence interval (CI). The significance level adopted was 5%. A binominal logistic regression was performed. Three different analyses were carried out, covering: 1) total sleep time (TST); 2) NREM sleep; 3) REM sleep. The RMMA index during these sleep periods was the dependent variable. The included variables in these analyses were: snore index (total of snore events during the period of sleep), SpO_2, age, sex, BMI, and obstructive sleep apnea. Sleep apnea was independently included in the unadjusted analyses since participants were referred to the PSG exam for suspected breathing or sleep problems. The overall evaluation of the model was performed with the F-test, only models with a p-value <0.05 were considered significant. The unadjusted analyses accepted variables with p-value <0.02. The adjusted model included variables with p-value <0.05 [27]. The variance inflation factor (VIF) was calculated to detect multicollinearity, values below five were considered to ensure the absence of multicollinearity between predictors.

The test power ($1 - \beta$ err) was calculated through post hoc test in G*Power software (version 3.1.9.7) using the proportion of patients with sleep bruxers and no sleep bruxers groups. One tail and value of α error as 0.05 were considered.

SB was considered the dependent variable and categorized as absent or present. The independent variable was snoring, classified as present or absence. For logistic regression, SB was represented as RMMA activity and snoring as number of episodes. Adjustment variables were grouped regarding demographics: age, sex, height, weight; questionnaire variables: Epworth Sleepiness Scale and Pittsburgh Sleep Quality. Moreover, variables related to sleep setting were also used. In this study, OSA was considered a potential confounding factor. All analyses and variables studied, as well as the form of categorization, are available in Appendix D.

Results

Participants and descriptive data

Ninety-five individuals agreed to participate in the study; however, 34 individuals were excluded due to problems in the SB analyses in the PSG or for not completing the full-night examination. Ultimately, sixty-one individuals were included in the final analysis with a median age of 46.8 ±14.2, being 47.4% females (95% CI: 35.5% to 59.8%). The flowchart of the included participants can be seen at Figure 1. Table 1 summarizes the main general characteristics of the participants.

Outcome data

Within the 61 participants, 75.4% (95% CI: 63.32% to 84.49%) were detected as definite SB. Regarding the severity of SB, approximately 39% (95% CI: 28.06% to 51.88%) were classified as mild/moderate and 36% (95% CI: 25.18% to 48.61%) as severe SB. Snoring was detected by PSG in 91.8% of individuals (95% CI: 82.2% to 96.45%).

Main results

The chi-square test did not show statistically significant values between definite SB and snoring ($p>0.05$). The effect size assessment was considered small using Cramér's V evaluation ($V=0.171$), demonstrating a small association between the two variables. SB was not associated with age, sex, BMI classification, quality of sleep or sleepiness ($p>0,05$). Regarding sleep characteristics, only RMMA activity present statistical difference within groups. Table 2 provides a comprehensive overview of the medians of sleep variables.

Other analyses

Conducting a linear regression was not feasible due to non-compliance with the analysis's assumptions, notably the lack of normality in the variables. Therefore, it was decided to conduct an analysis of the influence of variables on the occurrence of bruxism through logistic regression. From the three different analyses carried out regarding TST, NREM and REM periods, only the unadjusted model related to the analysis of REM sleep presented statistically significant results (AIC 78,8; R^2 0,389; p=0,017; VIF<5). As detailed in Table 3, it is observed that the snoring index exhibited a modest association with RMMA during REM period, with a small effect size shown through OR (<1.5). The desaturation index presented an OR of 5.01 (95% CI: 0.96 to 26.13; p=0.056, however the effect size was considered medium (>3.5). Regarding the post hoc test, a low value was found (<0.8).

Discussion

The main aim of this study was to evaluate the association between SB and snoring in individuals from a sleep laboratory. The presence of snoring may have a slight association with the rate of SB episodes during REM sleep. These results should be analyzed with caution, given the low effect size of this assessment. Previously studies have also found a positive association within these variables using PSG [28,29], however none have evaluated both conditions through sleep periods. When evaluating the TST and the NREM periods, none of the variables showed a significant association with RMMA index. However, the number of RMMA and snore episodes were higher at NREM than REM period. A previously study have found that SB episodes are more frequent during the NREM period [30]. When detected at REM period, the SB activity might be a subclinical manifestation of REM sleep behavior disorder - a parasomnia characterized by the enactment of vivid dreams during sleep [31].

A noteworthy aspect of this study is the utilization of the type I PSG examination for SB and snoring. This subtype is the most comprehensive, requiring the setup of electrodes in certain areas of the patient's body in a sleep laboratory or hospital setting, making it capable of detecting various sleep disorders [32]. There are only few studies that use PSG to evaluate the relationship between SB and snoring. Despite PSG being regarded as the reference test for detecting SB [33], its widespread adoption is limited. This limitation is primarily attributed to its high cost and the acceptable diagnostic

accuracy offered by alternative and more accessible diagnostic methods for patients [34]. Moreover, the ability to evaluate sleep architecture is a characteristic feature of this exam, allowing for a detailed period evaluation.

During REM period, it was detected that desaturation index present a medium effect size with the RMMA activity. A previously study analyzed young individuals found that transient hypoxia might be associated with RMMA episodes [35]. Hypoxia is a consequence of desaturation events. The analysis of hypoxia indices is carried out through subjective means, such as saturation assessment by oximetry [36]. A regular rate of desaturation when the individual is awake or sleeping is 96% to 97% [37].

Sex, age, and BMI did not present a statistical significance difference between the groups with and without SB A study that analyzed a data based population also did not find differences regarding these variables when comparing groups with and without definite SB [38]. Alternatively, a study performed by Smardz *et al.*, 2021 [13] evaluated the influence of sex and age on SB and snoring. With a sample of 127 participants evaluated via PSG, the results indicated male sex as a possible predisposing factor for the coexistence of SB and snoring.

This article aimed to evaluate if OSA was a potential confounding factor regarding the association between SB. However, this condition did not influence the presence of SB. The possible association between SB and OSA has been exhaustively searched over the years, and yet no conclusive findings have been reached [5]. In addition of environmental factors, both conditions appear to have a complex genetic genesis [39]. Recently articles have evaluated genetic parameters associated with etiopathogenesis of both conditions. Serotonin and dopamine pathways might be linked to these health issues; however further studies are necessary [40]. Despite this, the genetic analysis of this study's population has been previously published and did not show an association with the presence of SB and OSA [23].

The limitation regarding a single-night PSG exam should be taken for precaution, since maybe patients with low RMMA frequency might not be detected with the exam [41]. The results of this study were obtained from a sample from a private hospital and cannot be extrapolated to all adults. All researchers were trained and blinded to assessments other than their own, the inclusion criteria were broad, the external validity of the study is limited. The results can be extrapolated to an adult population over 40 years of age, overweight, and suspected of having respiratory disorders.

Conclusion

No association within sleep bruxism and snoring was found. However, during REM period, RMMA activity and snoring index were associated. No significant association was found between sleep bruxism and sex, age, or body mass index. Regarding, sleep architecture characteristics, only episodes of desaturation may be associated with sleep bruxism during the same REM sleep. Quality of sleep or sleepiness were not associated with sleep bruxism.

References

1. Lobbezoo F, et al. International consensus on the assessment of bruxism: Report of a work in progress. *J Oral Rehabil.* 2018;45(11);837-844.

2. Lobbezoo F, et al. Bruxism defined and graded: an international consensus. *J Oral Rehabil.* 2013;40(1);2-4.

3. De Luca Canto G, et al. Sleep bruxism and sleep-disordered breathing: a systematic review. *J Oral Facial Pain Headache.* 2014;28(4);299-305.

4. AAMS. *The International Classification of Sleep Disorders: (ICSD-3).* American Academy of Sleep Medicine; 2014.

5. Pauletto P, et al. Sleep bruxism and obstructive sleep apnea: association, causality or spurious finding? A scoping review. *Sleep.* 2022;45(7);1-17.

6. Jokubauskas L, Baltrušaitytė A. Relationship between obstructive sleep apnoea syndrome and sleep bruxism: a systematic review. *J Oral Rehabil.* 2017;44(2);144-153.

7. Koutsourelakis I, et al. Clinical and polysomnographic determinants of snoring. *J Sleep Res.* 2012;21(6);693-699.

8. Chung F, et al. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. *Chest.* 2016;149(3);631-638.

9. Huang Z, et al. Associations between snoring and dental sleep conditions: A systematic review. *J Oral Rehabil.* 2023;50(5);416-428.

10. Emodi-Perlman A, et al. Symptoms of Nocturnal Masticatory Muscle Activity among Women of Different Age Groups and Their Association to Obstructive Sleep Apnea-A Cross Sectional Study. *J Clin Med.* 2022;11(5);1-9.

11. Kato T, et al. Age is associated with self-reported sleep bruxism, independently of tooth loss. *Sleep Breath.* 2012;16(4);1159-1165.

12. Michalek-Zrabkowska M, et al. The Relationship between Simple Snoring and Sleep Bruxism: A Polysomnographic Study. *Int J Environ Res Public Health.* 2020;17(23);1-19.

13. Smardz J, et al. Influence of age and gender on sleep bruxism and snoring in non-apneic snoring patients: A polysomnographic study. *J Sleep Res.* 2021;30(3);e13178.

14. Hosoya H, et al. Relationship between sleep bruxism and sleep respiratory events in patients with obstructive sleep apnea syndrome. *Sleep Breath.* 2014;18(4):837-844.

15. Palinkas M, et al. Analysis of the sleep period and the amount of habitual snoring in individuals with sleep bruxism. *Med Oral Patol Oral Cir Bucal.* 2019;24(6);e782.

16. Vandenbroucke JP, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Annals of Internal Medicine.* 2007;147(8);W-163-W-194.

17. Von Elm E, *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *The Lancet.* 2007;370(9596);1453-1457.

18. Guo S, Hussey DL. Nonprobability sampling in social work research: Dilemmas, consequences, and strategies. *Journal of Social Service Research.* 2004;30(3);1-18.

19. Althubaiti A. Sample size determination: A practical guide for health researchers. *J Gen Fam Med.* 2023;24(2);72-78.

20. Bertolazi AN, et al. Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. *J Bras Pneumol.* 2009;35(9):877-883.

21. Bertolazi AN, et al. Validation of the Brazilian Portuguese version of the Pittsburgh sleep quality index. *Sleep Med.* 2011;12(1);70-75.

22. Seidell JC, Flegal KM. Assessing obesity: classification and epidemiology. *Br Med Bull.* 1997;53(2);238-252.

23. Duarte J, et al. Is there an association of genetic polymorphisms of the catechol-O-methyltransferase gene (rs165656 and rs174675) and the 5-hydroxytryptamine receptor 2A gene (rs4941573 and rs6313) with sleep bruxism in individuals with obstructive sleep apnea? *Arch Oral Biol.* 2022;133:105315.

24. Rompré P, et al. Identification of a sleep bruxism subgroup with a higher risk of pain. *J Dent Res.* 2007;86(9);837-842.

25. Normando D, Honório HM. *Bioestatística quase sem fórmulas*. 2023.

26. Sullivan GM, Feinn R. Using effect size—or why the P value is not enough. *J Grad Med Educ.* 2012;4(3);279-282.

27. Ranganathan P, et al. Common pitfalls in statistical analysis: logistic regression. *Perspect Clin Res.* 2017;8(3);148.

28. Michalek-Zrabkowska M, et al. The relationship between simple snoring and sleep bruxism: A polysomnographic study. *I Int J Environ Res Public Health.* 2020;17(23);8960.

29. Palinkas M, et al. Analysis of the sleep period and the amount of habitual snoring in individuals with sleep bruxism. *Med Oral Patol Oral Cir Bucal.* 2019;24(6);e782-e786.

30. Lavigne G, et al. Neurobiological mechanisms involved in sleep bruxism. *Crit Rev Oral Biol Med* . 2003;14(1);30-46.

31. Yap AU, Chua AP. Sleep bruxism: Current knowledge and contemporary management. *J Conserv Dent.* 2016;19(5);383.

32. de Abreu HF. *Prática em Medicina do Sono.* Thieme Revinter; 2020.

33. Casett E, et al. Validity of different tools to assess sleep bruxism: a meta-analysis. *J Oral Rehabil.* 2017;44(9);722-734.

34. Manfredini D, et al. Standardized Tool for the Assessment of Bruxism (STAB). *J Oral Rehabil.* 2023 ;51(1):29-58.

35. Dumais I, et al. Could transient hypoxia be associated with rhythmic masticatory muscle activity in sleep bruxism in the absence of sleep-disordered breathing? A preliminary report. *J Oral Rehabil.* 2015;42(11);810-818.

36. Neff TA. Routine oximetry: a fifth vital sign? *Chest.* 1988;94(2);227.

37. Pellegrino GM, et al. Effects of air stacking on dyspnea and lung function in neuromuscular diseases. *Arch Phys Med Rehabil.* 2021;102(8);1562-1567.

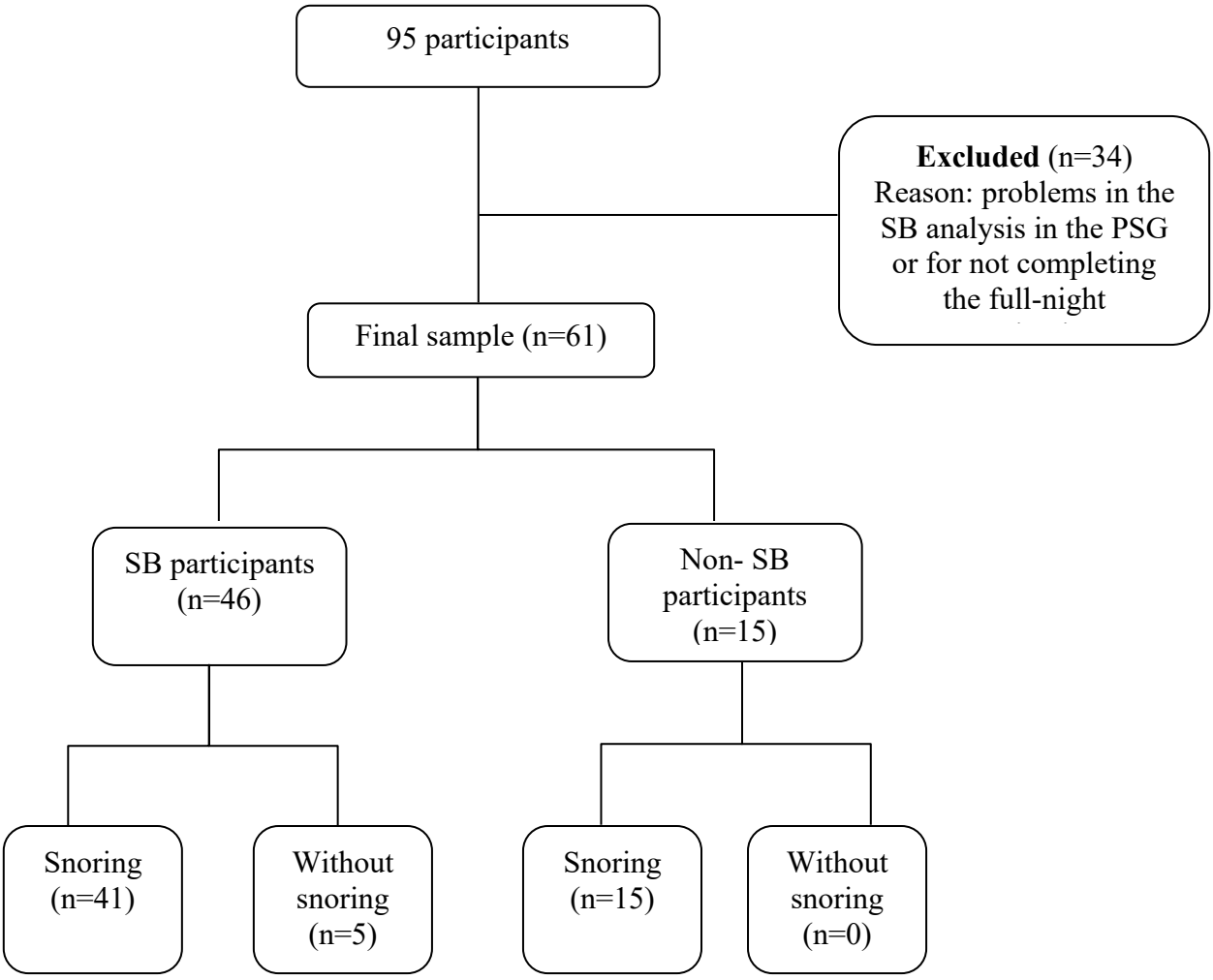
38. Maluly M, et al. Sleep bruxism and its associations with insomnia and OSA in the general population of Sao Paulo. *Sleep Medicine.* 2020;(75);141-148.

39. Palmer LJ, Redline S. Genomic approaches to understanding obstructive sleep apnea. *Respir Physiol Neurobiol.* 2003;135(2-3);187-205.

40. Wieckiewicz M, et al. Genetic basis of sleep bruxism and sleep apnea—response to a medical puzzle. *Sci Rep.* 2020;10(1);1-14.

41. Hasegawa Y, et al. Is there a first night effect on sleep bruxism? A sleep laboratory study. *J Clin Sleep Med.* 2013;9(11);1139-1145.

Figure 1. Flowchart of study participants.



Legend:

SB: sleep bruxism

PSG: polysomnography

Table 1. Characteristics of Participants.

		Sleep Bruxism n=46		No Sleep Bruxism n=15					
		N	**% (CI 95%)**	**N**	**% (CI 95%)**	**Total N**	**Measure of effect- OR (CI 95%)**	**p-value**	**V-Cramer**
Sex	**Female**	20	68.97 (50.77 - 82.73)	9	31.03 (17.27 - 48.23)	29			
	Male	26	81.25 (64.69 - 91.11)	6	18.75 (8.89 - 35.31)	32	0.51 (0.15 - 1.67)	0.416	-0.14
BMI	**Normal***	14	87.5 (63.98 - 9.65)	2	1.25 (0.35 - 36.02)	16			
	Overweight	10	66.67 (41.72 - 84.83)	5	33.33 (15.17 - 58.28)	15	3.5 (0.56 - 21.81)	0.169	+0.25
	Obese	22	73.33 (55.55 - 85.81)	8	26.67 (14.19 - 44.45)	30	2.54 (0.47 - 13.77)	0.235 †	0.16
Age (yrs)	**<40**	15	75 (53.13 - 88.81)	5	25 (11.19 - 46.87)	20			
	>40	31	75.61 (60.66 - 86.18)	10	24.39 (13.82 - 39.34)	41	0.96 (0.28 - 3.33)	0.596 †	-0.01
Sleep Quality	**Good Sleep Quality***	11	84.62 (57.77 - 95.68)	2	15.38 (4.32 - 42.23)	13			
	Poor Sleep Quality	28	73.68 (57.99 - 85.03)	10	26.32 (14.97 - 42.01)	38	1.96 (0.36 - 10.44)	0.347 †	0.11
	Presence of sleep disorder	7	70 (39.68 - 89.22)	3	30 (10.78 - 60.32)	10	2.35 (0.31 - 17.85)	0.366 †	0.18

ESS	**Normal Sleep***	27	79.41 (63.2 - 89.65)	7	20.59 (10.35 - 36.8)	34			
	Average sleepiness	3	75 (30.06 - 95.44)	1	25 (4.56 - 69.94)	4	1.28 (0.11 - 14.33)	0.628 †	0.03
	Abnormal sleepiness	16	69.57 (49.14 - 84.4)	7	30.43 (15.6 - 50.86)	23	1.68 (0.49 - 5.69)	0.596	0.11

Odds Ratio=OR; Body Mass Index=BMI; Epworth Sleepiness Scale=ESS.

*references.

† fisher test was used when the expected cell number was below five.

Table 2. Median of sleep variables.

	Sleep Bruxism n=46		No Sleep Bruxism n=15		
	Median/(Mean)	**IQR/(SD)**	**Median/(Mean)**	**IQR/(SD)**	**p-value**
TST (min)	382	352-411	353	328-425	0.947
Sleep Onset (min)	13.8	7.13-28.5	20.5	8.25-40.8	0.609
REM Onset (min)	177	123-284	166	135-247	0.938
WASO (min)	36	17.3-64.4	49	19-68.5	0.731
REM (min)	(50)	(30.4)	(47.8)	(25.4)	0.803†
NREM (min)	341.5	278-361	320	306-364	0.860
SpO_2 TST (n)	38	8-117	52	33-93	0.524
SpO_2 NREM (n)	25.5	7-105	33	20-76	0.639
SpO_2 REM (n)	5	0.25-16.8	11	3-34.5	0.097
RMMA TST (episodes)	23.5	17-50	7	7-10	**<0.001**
RMMA NREM (episodes)	21	21-47	6	6-8	**<0.001**
RMMA REM (episodes)	1.5	1.5-4	1	1-1	**0.036**
Snoring TST (n)	196	67-466	103	24-579	0.953
Snoring NREM (n)	185	60.8-309	52	14-478	0.706
Snoring REM (n)	9.5	0-69.5	1	0-54.5	0.674

Total sleep time= TST; Wakefulness after sleep onset = WASO; Oxygen desaturation =$SpO_{2.;}$ † t-student

Table 3. Logistic regression sleep bruxism and snoring

Variables	Unadjusted Model Odds Ratio (CI 95%) AIC 78.8; R^2 0.389 p=0.017		Adjusted Model Odds Ratio (CI 95%) AIC 73.1 R^2 0.206 p=0.002	
	RMMA REM/h	**p-value**	**RMMA REM/h**	**p-value**
Snoring REM/h	1.017 (1.00-1.03)	**0.016**	**1.018 (1.005-1.03)**	**0.006**
SpO_2/h	15.656 (1.70-144.10)	**0.015**	5.010 (0.9606-26.131)	0.056
Age [a]	1.149 (0.29-4.53)	0.843		
Sex [b]	1.260 (0.35-4.53)	0.724		
BMI	0.239 (0.04-1.34)	0.103		
OSA[c]	0.895 (0.77-1.04)	0.139		

[a] Reference: <40 years old

[b] Reference: female

[c] Reference: absence of OSA

Appendix A - STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	22
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	22
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	23
Objectives	3	State specific objectives, including any prespecified hypotheses	23
Methods			
Study design	4	Present key elements of study design early in the paper	24
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	24
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	24
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	24,25
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*24,25,26,27*
Bias	9	Describe any efforts to address potential sources of bias	27
Study size	10	Explain how the study size was arrived at	24
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Appendix C
Statistical methods	12	(*a*) Describe all statistical methods, including those	27

		used to control for confounding	
		(*b*) Describe any methods used to examine subgroups and interactions	27
		(*c*) Explain how missing data were addressed	27
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	28
		(b) Give reasons for non-participation at each stage	28
		(c) Consider use of a flow diagram	35
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	28,37,38
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	37,38
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	28,29
		(*b*) Report category boundaries when continuous variables were categorized	Appendix C
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	-
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-

Discussion			
Key results	18	Summarise key results with reference to study objectives	29
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	30
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	29,30
Generalisability	21	Discuss the generalisability (external validity) of the study results	30
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	21

Appendix B – Free Informed Consent Form

UNIVERSIDADE FEDERAL DE SANTA CATARINA
CENTRO DE CIÊNCIAS DA SAÚDE
PROGRAMA DE PÓS-GRADUAÇÃO EM ODONTOLOGIA

TERMO DE CONSENTIMENTO LIVRE E ESCLARECIDO

Eu, Joyce Duarte, doutoranda do Programa de Pós-Graduação em Odontologia, do Centro Ciências da Saúde da Universidade Federal de Santa Catarina (UFSC), sob orientação da Prof.ª Dr.ª Graziela De Luca Canto, convido você a participar da pesquisa intitulada "Associação entre bruxismo do sono e síndrome da apneia e hipopneia obstrutiva do sono em adultos".

O objetivo deste documento é dar a você informações suficientes sobre a pesquisa a qual você está sendo convidado a participar.

OBJETIVO DO ESTUDO

Este estudo tem por objetivo avaliar se existe associação entre o bruxismo do sono, caracterizado por rangimento ou apertamento dos dentes durante o sono e a síndrome da apneia e hipopneia obstrutiva, um problema respiratório onde há bloqueio total ou parcial da respiração durante o sono, através de dados obtidos por exame físico, questionários e exames de polissonografia.

PROCEDIMENTOS

- Em um primeiro momento, serão aplicados questionários específicos para identificar sinais e sintomas de bruxismo do sono e síndrome da apneia e hipopneia obstrutiva do sono.
- Será realizado um exame físico da sua boca e músculos da mastigação e posteriormente uma raspagem da mucosa oral, para avaliar as possíveis causas genéticas do Bruxismo do Sono. O exame físico e raspagem da mucosa oral terão a duração entre 5 e 10 minutos. O exame físico é como qualquer exame odontológico de rotina, e não terá nenhuma consequência. Se não se sentir à

vontade para a realização do exame, este será interrompido imediatamente. Os usos das células da mucosa bucal serão unicamente para essa pesquisa e saliento que logo após essa análise, elas serão descartadas de forma apropriada.

- Serão coletados também dados demográficos básicos como sexo, idade, estado civil e ocupação. Poderão também ser requisitadas outras informações, tais como peso, altura ou informações relevantes para o tema de pesquisa.
- Se constatadas necessidades de tratamento odontológico durante a avaliação clínica, você será orientado a buscar tratamento nas clínicas odontológicas da Universidade Federal de Santa Catarina.
- Toda a pesquisa envolve riscos, por isto se você não se sentir confortável para realizá-la, poderá desistir a qualquer momento. Nesta pesquisa os riscos são: desconforto ao realizar o exame clínico bucal, cansaço e aborrecimento em responder os questionários, quebra de sigilo, ainda que involuntário e não intencional. Para minimizar o risco de quebra de sigilo, seus dados terão um número para identificação, e não o seu nome. No entanto, como benefício direto, você terá uma avaliação clínica e levantamento de necessidades odontológicas, assim como os devidos encaminhamentos para o serviço. Como benefício indireto, você poderá contribuir para a elucidação e compreensão da fisiopatologia do bruxismo do sono e da apneia e hipopneia obstrutiva do sono.
- Os procedimentos da pesquisa (exame físico e aplicação de questionários), bem como os materiais utilizados, serão custeados pela Instituição proponente da pesquisa (UFSC).

PARTICIPAÇÃO VOLUNTÁRIA

Sua participação nesse estudo não é obrigatória e não haverá custos nem pagamentos pela mesma. Uma vez que você decidiu participar do estudo, você pode retirar seu consentimento de participação a qualquer momento, sem prejuízos de qualquer natureza. Não haverá reembolso, uma vez que com a participação na pesquisa você não terá custo.

JUSTIFICATIVA DO ESTUDO

O estudo servirá para a compreensão dos fatores associados ao bruxismo do sono, ou seja, se problemas respiratórios do sono causam, ou não, o ranger/apertar de dentes durante o sono.

PERMISSÃO PARA REVISÃO DE REGISTROS, CONFIDENCIALIDADE E ACESSO AOS REGISTROS

Será solicitada permissão para acesso aos registros dos exames de polissonografia realizados pelo hospital. Sua identidade não será revelada e os dados serão analisados e mantidos em sigilo. Os dados obtidos por meio dos questionários, exames físico e exames de polissonografia serão utilizados em publicações futuras e você terá acesso a eles a qualquer momento da pesquisa.

CONTATO COM OS PESQUISADORES

Se você tiver alguma dúvida em relação ao estudo, você deverá entrar em contato com a pesquisadora do estudo Joyce Duarte, pelo telefone (48) 3721-4952 ou via e-mail: joyceduarteortodtm@gmail.com ou da pesquisadora responsável, Graziela De Luca Canto, professora do Departamento de Odontologia, Centro de Ciências da Saúde – UFSC (Campus Trindade), telefone (48) 3721-4952 e e-mail delucacanto@gmail.com. Esta pesquisa atende a Resolução do CNS 466/2012 e conta com a aprovação do CEPSH/UFSC (Rua Desembargador Vitor Lima, nº 222, Trindade, Florianópolis, Prédio Reitoria II, 4º andar, sala 401). Caso você apresente alguma dúvida em relação a questões éticas, o contato com o Comitê de Ética dessa Instituição pode ser realizado por meio do telefone (48) 3721-9206 ou e-mail: cep@reitoria.ufsc.br.

DECLARAÇÃO DO PESQUISADOR

A pesquisadora responsável por esta pesquisa, Prof.ª Dr.ª Graziela De Luca Canto, se compromete a seguir a Resolução CNS n. 466/12 em todos os seus itens, entre os quais destacam-se: ressarcimento ou indenização de custos gerados em função da pesquisa, desde que estes sejam comprovados. O suporte, custeio, ressarcimento ou

indenização serão de responsabilidade dos pesquisadores deste projeto, seguindo o que rege a resolução CNS n. 466/12.

DECLARAÇÃO DE CONSENTIMENTO DO PACIENTE

Eu_____, CPF_____, RG_____, residente à _____, estou ciente que me é garantido o livre acesso a todas as informações e esclarecimentos adicionais sobre o estudo durante e depois da minha participação. Declaro ter sido informado e estar devidamente esclarecido sobre os objetivos deste estudo. Recebi garantias de total sigilo e de obter novos esclarecimentos sempre que desejar, assim como afirmo também ter recebido uma via do presente Termo de Consentimento Livre e Esclarecido. Assim, concordo em participar voluntariamente deste estudo e sei que posso retirar meu consentimento a qualquer momento, sem qualquer prejuízo.

Florianópolis ___ /___ / _____

_____

Assinatura do participante

_____

Assinatura da pesquisadora: Joyce Duarte

_____

Assinatura da pesquisadora responsável: Graziela De Luca Canto

Appendix C - Descriptive Statistics.

Name	Type	Variable treatment
Definite Sleep Bruxism	Categorical (Absent=0 and Present=1)	Dependent Variable
RMMA index	1. Continuous 2. Categorical (Absent=0; Mild/Moderate=1; Severe=2)	Dependent Variable
Snoring	Categorical (Absent=0 and Present=1)	Independent Variable
Snoring index	Continuous	Independent Variable
Age (years)	Categorical (Less than 40 years=0 and Greater than 40 years=1)	Adjustment Variable
Sex	Categorical (Female; Male)	Adjustment Variable
BMI	Categorical (Normal Weight= BMI>18.5 to 24.9 kg/m²; Overweight= BMI ≥25 to 29.9 kg/m²; Obesity= BMI >30.0 kg/m²)	Adjustment Variable
ESE	Categorical (Normal Sleep=0; Moderate Sleepiness=1; Abnormal Sleepiness=2) 1 - 6: Normal sleep 7 - 8: Moderate sleepiness 9 – 24: Abnormal sleepiness (possibly pathological)	Adjustment Variable
Sleep Quality	Categorical (Good; Poor; Presence of Sleep Disorder) Scores from 0-4 indicate good sleep quality, 5-10 indicate poor quality, and above 10 indicate a sleep disorder	Adjustment Variable
Obstructive Sleep Apnea	Categorical (Absent=0 and Present=1)	Adjustment Variable
SpO_2 Index/hour	Continuous	Adjustment Variable
TST	Continuous in minutes (min)	Adjustment Variable
Sleep Onset	Continuous in minutes (min)	Adjustment Variable
REM Onset	Continuous in minutes (min)	Adjustment Variable
WASO	Continuous in minutes (min)	Adjustment Variable
NREM	Continuous in minutes (min)	Adjustment Variable
REM	Continuous in minutes (min)	Adjustment Variable

Attachment A - Consubstantiated Opinion

UNIVERSIDADE FEDERAL DE SANTA CATARINA - UFSC

PARECER CONSUBSTANCIADO DO CEP

DADOS DO PROJETO DE PESQUISA

Título da Pesquisa: ASSOCIAÇÃO ENTRE BRUXISMO DO SONO E APNEIA OBSTRUTIVA DO SONO EM ADULTOS

Pesquisador: Graziela De Luca Canto

Área Temática: Genética Humana:
(Trata-se de pesquisa envolvendo Genética Humana que não necessita de análise ética por parte da CONEP;);

Versão: 2

CAAE: 84783518.6.0000.0121

Instituição Proponente: CENTRO DE CIÊNCIAS DA SAÚDE

Patrocinador Principal: Financiamento Próprio

DADOS DO PARECER

Número do Parecer: 2.620.213

Apresentação do Projeto:

Trata o presente projeto, intitulado "Associação entre bruxismo do sono e apneia obstrutiva do sono em adultos" de uma pesquisa submetida pelo Profa. Graziela De Luca Canto, que assina a folha de rosto como pesquisador responsável juntamente com a Profa. Elena Riet Correa Rivero, coordenadora do PPG Odontologia/CCS/UFSC. O projeto é um estudo do tipo transversal analítico com o objetivo de investigar a associação entre bruxismo do sono e síndrome da apneia obstrutiva do sono em adultos e, secundariamente, as associações destas com a qualidade de vida e características do sono. Os participantes da pesquisa serão pacientes encaminhados para o Hospital Baía Sul para realização de exames de polissonografia (PSG). Os participantes (n=110) serão convidados a participar do estudo em uma situação prévia ao exame de PSG pois já terão seu encaminhamento para a realização do exame por motivo de suspeita de apneia ou outros problemas relacionados ao sono. Os dados dos participantes serão coletados por meio de anamnese, exame físico da boca e músculos da mastigação, coleta de células epiteliais da mucosa oral e aplicação de diversos questionários específicos.

Objetivo da Pesquisa:

Objetivo geral

Investigar a associação entre bruxismo do sono e apneia obstrutiva do sono em adultos.

Endereço: Universidade Federal de Santa Catarina, Prédio Reitoria II, R: Desembargador Vitor Lima, nº 222, sala 401
Bairro: Trindade **CEP:** 88.040-400
UF: SC **Município:** FLORIANOPOLIS
Telefone: (48)3721-6094 **E-mail:** cep.propesq@contato.ufsc.br

Objetivos específicos

- Avaliar se existe associação entre a presença de BS e de apneia obstrutiva do sono e qualidade de vida.
- Avaliar a acurácia de questionários e exame físico comparados ao padrão de referência PSG no diagnóstico de BS e SAHOS.
- Verificar a associação entre uso de medicamentos antidepressivos e ocorrência de bruxismo do sono.
- Verificar a associação entre presença de tórus mandibular e presença de bruxismo do sono.
- Realizar uma análise quantitativa da presença de atividade rítmica da musculatura mastigatória e apneias por hora;
- Realizar uma avaliação quantitativa e qualitativa da distribuição dos episódios de bruxismo nas diferentes fases do sono;
- Verificar a presença de outras características do sono associadas aos episódios de bruxismo do sono, exemplos: movimentos de membros, despertares, posições, presença de ronco.
- Analisar os polimorfismos genéticos relacionados ao bruxismo do sono.

Avaliação dos Riscos e Benefícios:

De acordo com o que foi citado no TCLE apresentado:

Riscos: Toda a pesquisa envolve riscos, por isto se você não se sentir confortável para realizá-la, poderá desistir a qualquer momento. Nesta pesquisa os riscos são: desconforto ao realizar o exame clínico bucal, cansaço e aborrecimento em responder os questionários, quebra de sigilo, ainda que involuntário e não intencional. Para minimizar o risco de quebra de sigilo, seus dados terão um número para identificação, e não o seu nome.

Benefícios: Como benefício direto, você terá uma avaliação clínica e levantamento de necessidades odontológicas, assim como os devidos encaminhamentos para o serviço. Como benefício indireto, você poderá contribuir para a elucidação e compreensão da fisiopatologia do bruxismo do sono e da apneia e hipopneia obstrutiva do sono.

Comentários e Considerações sobre a Pesquisa:

Pode contribuir para o conhecimento generalizável sobre o tema.

UNIVERSIDADE FEDERAL DE SANTA CATARINA - UFSC

Considerações sobre os Termos de apresentação obrigatória:

Adequados.

Recomendações:

Sem recomendações.

Conclusões ou Pendências e Lista de Inadequações:

Considerando que todas as pendências indicadas foram devidamente atendidas, não há nenhuma inadequação no presente processo.

Considerações Finais a critério do CEP:

Este parecer foi elaborado baseado nos documentos abaixo relacionados:

Tipo Documento	Arquivo	Postagem	Autor	Situação
Informações Básicas do Projeto	PB_INFORMAÇÕES_BÁSICAS_DO_PROJETO_1081179.pdf	13/04/2018 10:41:53		Aceito
Outros	RESPOSTA_AS_PENDENCIAS.docx	13/04/2018 10:41:20	Joyce Duarte	Aceito
Declaração de Manuseio Material Biológico / Biorepositório / Biobanco	Declaracao_UFPR.pdf	12/04/2018 20:40:28	Joyce Duarte	Aceito
Outros	Instrumentos_da_Pesquisa.docx	12/04/2018 20:38:49	Joyce Duarte	Aceito
Projeto Detalhado / Brochura Investigador	Plataforma_Brasil_Projeto_Bruxismo.docx	12/04/2018 20:38:03	Joyce Duarte	Aceito
Declaração de Instituição e Infraestrutura	Declaracao_Baia_Sul.pdf	12/04/2018 20:35:55	Joyce Duarte	Aceito
TCLE / Termos de Assentimento / Justificativa de Ausência	TCLE_projeto.docx	12/04/2018 20:31:14	Joyce Duarte	Aceito
Folha de Rosto	FolhadeRosto.pdf	08/03/2018 10:30:08	Joyce Duarte	Aceito

Situação do Parecer:

Aprovado

Necessita Apreciação da CONEP:

Não

FLORIANOPOLIS, 25 de Abril de 2018

Assinado por:
Luiz Eduardo Toledo
(Coordenador)

Endereço: Universidade Federal de Santa Catarina, Prédio Reitoria II, R: Desembargador Vitor Lima, nº 222, sala 401
Bairro: Trindade **CEP:** 88.040-400
UF: SC **Município:** FLORIANOPOLIS
Telefone: (48)3721-6094 **E-mail:** cep.propesq@contato.ufsc.br

6 ARTIGO 2[2]

Association between sleep bruxism and snoring in non-apneic adults: a transversal polysomnographic study

Authors

Helena Polmann, DDS, MSc[1,2], Patrícia Pauletto, DDS, PhD[1,3] Jéssica Conti Réus, DDS, MSc[2], Gabriel Natan Pires, PhD[4,5], Milton Maluly, DDS, PhD[4,5], Monica Levy Andersen, PhD[4], Sergio Tufik, MD, PhD[4], Graziela De Luca Canto, DDS, PhD[1,2]

Affiliations

[1]Brazilian Centre for Evidence-Based Research (COBE). Federal University of Santa Catarina. Florianópolis. Brazil.

[2] Department of Dentistry. Federal University of Santa Catarina. Florianópolis. Brazil

[3] Faculty of Dentistry. Universidad de las Americas (UDLA). Quito. Ecuador.

[4]Departmento de Psicobiologia. Universidade Federal de São Paulo (UNIFESP). São Paulo. Brazil.

[5]Sleep Institute. São Paulo. Brazil

Correspondence Author

Helena Polmann. Department of Dentistry. Federal University of Santa Catarina. University Campus. Mailbox 476-Trindade. Florianópolis. Santa Catarina. Brazil.

Email: hpolmann@hotmail.com

Conflict of Interest

The authors declare that have no conflict of interest.

Funding

The authors declare no funding to develop this research.

[2] Artigo formatado para submissão ao periódico *SLEEP*

Abstract

This study aimed to evaluate the association between sleep bruxism and snoring in non-apneic adults from an epidemiologic study. Additionally, the objective was to assess the association of sleep bruxism with sex, age, body mass index, alcohol, smoking, and anxiety in patients with sleep bruxism and without the condition. This study also investigated the association between sleep bruxism and characteristics of sleep architecture. Data from the third edition of the EPISONO study was used. Out of 1042 initially considered, 502 individuals without obstructive sleep apnea met the eligibility criteria and comprised the final sample, with a median age of 34 years old. Polysomnography scoring was performed according to the American Academy of Sleep Medicine criteria, and used to assess sleep bruxism, snoring and obstructive sleep apnea. Statistical analyzes were performed with the Jamovi software. The association and effect size between sleep bruxism and snoring, consumption of coffee, alcohol was not significant ($p>0.05$). Logistic regression analyzes were performed regarding variables such as: snoring, age, sex and body mass index and anxiety. The adjusted model indicated an association of mild sleep bruxism and mild anxiety symptoms. Only variables with p-value <0.05 were included in the adjusted logistic regression Regarding sleep variables, the REM duration presented association the presence of sleep bruxism. In conclusion, there was no evidence of an association between sleep bruxism and snoring in a non-apneic population. Likewise, the association with age, sex, body mass index, consumption of coffee and alcohol. However, it seems that anxiety symptoms and the duration of the REM period may be associated with the occurrence of sleep bruxism in this non-apneic sample.

Keywords: Sleep bruxism; snoring; polysomnography

Introduction

The phenomenon known as bruxism, may manifest both during wakefulness and sleep, with a specific designation, sleep bruxism (SB), assigned to occurrences during sleep. This activity, whether rhythmic or non-rhythmic, is typically viewed as a behavioral aspect rather than a disorder in healthy individuals [1]. To further classify and understand it, different detection methods can be employed, leading to the categorization of SB into possible, probable, and definite. A possible SB is found when assessed through self-report, "probable" when a clinical evaluation is performed with or without self-report, and "definitive" when the detection is executed through an instrumental method, such as electromyography (EMG) and polysomnography (PSG) [2].

Sleep bruxism can present as an isolated phenomenon or be associated with other comorbidities, including: gastroesophageal reflux, insomnia, headache, orofacial pain, periodic limb movement disorder [3,4], as well psychological conditions [5,6]. The multifaceted dynamics of sleep disorders prompt a deeper exploration into the intricate interplay among SB, snoring, and their potential association with obstructive sleep apnea (OSA). Notably, contemporary research is expanding to explore the association among these three variables [7,8].

Concerning the relationship between SB and OSA, extensive literature has addressed this topic; however, there is no established consensus on this association [9-11]. A recent scoping review conducted by Pauletto *et al.*, 2022 [12] aimed to map the existing literature between SB and OSA, encompassing studies involving both adults and children. The authors concluded that it is not yet possible to confirm the relationship between SB and OSA in adults. In the case of children, the association appears possible; nevertheless, the available evidence is currently insufficient to firmly support such a connection.

Nonetheless, the examination of the association between snoring and SB has experienced a surge in attention over the years. Snoring, regarded as an acoustic phenomenon, involves sound generated by the vibration of the upper airways [13]. The audible vibrations stem from turbulent airflow through the posterior wall of the pharynx, uvula, soft palate, and base of the tongue, caused by the constriction of the oropharyngeal or nasopharyngeal space [14]. Most of the articles evaluate snoring subjectively, employing methods such as questionnaires, self-reports, or third-party

accounts [15]. PSG can be used as an objective assessment of snoring. However, studies that assess SB and snoring using a non-apneic sample are scarce. A study with 90 non-apneic Brazilians evaluated via PSG suggested that patients with SB tend to snore during sleep [16]. A polysomnography study evaluated non-apneic patients with SB and snoring and the relationship with sleep position (supine and non-supine). The authors found a correlation between SB classified as phasic and snoring in the supine and non-supine positions and concluded that the position during sleep affects the intensity of both variables [7].

Although several population-based studies evaluating sleep based on PSG are available [17] there is currently no research examining the association between the individuals with SB and snoring in a population-based sample that excludes apnea. Therefore, the aim of this study was to investigate the association between SB and snoring in non-apneic patients. Moreover, we aimed to evaluate the association between SB and sex, age and body mass index (BMI). The association with SB and consumption of alcohol, smoking, and anxiety was also investigated. The possible association regarding sleep architecture characteristics were also studied.

Methods

Study Design

This is an analytical cross-sectional study reported following STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) [18,19]. The complete checklist can be found at Appendix A.

This is study was based on the database of EPISONO, a cross-sectional population-based sleep study performed in 2007, from July to December. The studied aimed comprising a representative sample of the city of São Paulo, Brazil. Details regarding the rationale, sample definition, data collection, polysomnography and further methodological information are available elsewhere [20]. The EPISONO study was approved by the Ethics Committee of Federal University of São Paulo (UNIFESP) (CAAE: 01570712.4.0000.5505) and was registered with ClinicalTrials.gov (Identifier NCT00596713). The Ethics Committee can be found at Appendix B.

Setting and Participants

Inclusion criteria consisted in individuals between 20 and 80 years old. Exclusion criteria included the following categories of individuals: 1) Pregnant or breastfeeding women; 2) Individuals with physical or mental disabilities; 3) Night shift workers; 4) Individuals with apnea-hypopnea index (AHI) higher than 5 events per hour in PSG.

Data sources/ measurement

Participants underwent a full-night in-lab (type-I) PSG laboratory test (EMBLA-S7000. Embla Systems Inc. Broomfield. CO. USA), in which sleep is monitored for one night, following the recommendations proposed by the AASM [21]. All PSGs performed, and sleep progress were scored visually according to standardized criteria for sleep investigation, sleep-related events, and leg movements were scored according to criteria established by the American Academy of Sleep Medicine Manual for Scoring Sleep and Associated Events [21]. Four percent of all PSGs were rescored randomly by a Registered Polysomnographic Technologist by the Board of Registered Polysomnographic Technologist to ensure that PSG scoring had been performed correctly.

To calibrate the instruments and accurately detect the signals, participants were instructed, before the recordings began, to perform voluntary movements such as snoring, leg movements, opening and closing their eyes, squeezing, moving their jaws laterally and forward, and rhythmic contractions of the jaw, as well as swallowing and coughing movements, in order to record baseline amplitudes.

Sleep Bruxism

The condition was detected in the PSG through the evaluation of rhythmic masticatory muscle activity (RMMA). The sensors were attached non-invasively using adhesive tape. Calibration was performed so that these sensors were positioned in the part with the largest volume of the masseter and temporal muscles [22]. Established criteria was followed for assessment: a) Each RMMA episode must present EMG activity with an amplitude of at least twice the baseline amplitude; b) The rapid RMMA

episode represents an EMG activity with at least three episodes lasting 0.25 to 2 seconds; c) The tonic RMMA episode presents an increase in EMG lasting at least two seconds; d) An interval of at least three seconds of baseline activity must occur before a new episode of RMMA occurs [14].

The application of the above criteria was carried out in two phases: 1) The PSG specialist technician visually evaluated all PSGs, separating those that had the potential to present at least two RMMA episodes/h; 2) The PSG included in the previous phase were evaluated by a trained dental surgeon (M.M.). PSGs exams that were not selected in the previous phase received "#NULL" values and were not considered for the assessment of SB.

After applying the above criteria, the individuals were placed in two different groups: 1) Without SB (<2 RMMA episodes/h); 2) With SB (≥2 RMMA episodes/h). Moreover, for descriptive analysis, individuals with the presence of SB were also classified with low-frequency SB (from 2 to 3.9 episodes/h), and high-frequency SB (4 or more episodes/h) [23].

Snoring

Snoring was assessed using microphones. An episode of snoring was considered when at least three were detected within an interval of 10 seconds. After that, it was classified in a qualitative process as present or absent by the PSG technician during the PSG exam.

Obstructive Sleep Apnea

The breathing events were assessed according to the American Academy of Sleep Medicine criteria [21]. Participants were diagnosed with OSA if they exhibited an AHI between 5.0 and 14.9, in addition to at least one of the following complaints: interruption of breathing during sleep, loud snoring, fatigue and/or daytime drowsiness. Individuals with AHI >15 were diagnosed with OSA regardless of additional complaints [24].

Questionnaires

The consume of alcohol and smoking was assessed with the Portuguese version of the ASSIST questionnaire [25]. Smoking and alcohol consumption in the past 3 months was derived from a question with five answer options: no, 1–2 times/3 months, monthly, weekly, and daily or almost daily. Participants were grouped as non-consumers when answered: no and consumers if any of the following options was selected: 1–2 times/3 months, monthly, weekly, and daily or almost daily.

Anxiety symptoms were evaluated with the Portuguese-validated Beck Anxiety Inventory – BAI [26]. The questionnaire evaluated 21 anxiety symptoms providing a classification of anxiety severity: minimal, mild, moderate, and severe. Both were assessed before the PSG exam by group of 10 psychologists.

Physical Assessments

General physical assessments were performed prior to PSG. Two trained physical education teachers performed weight (kg), height (m) measurements and BMI calculation. Detailed information has been provided previously [20].

Statistical methods

Statistical analyzes were performed using the Jamovi statistical software (Version 1.6). For all statistical analyzes, the significance level was set at $\alpha=0.05$. Normal distribution of quantitative variables was verified using the Shapiro-Wilk test. Variables with normal distribution were expressed with mean and standard deviation. Quantitative variables without a normal distribution were expressed using the median and interquartile range (IQR). To compare two groups with quantitative variables, the Mann-Whitney test for comparisons without normal distribution.

To investigate the association between SB and snoring in non-apneic patients, two qualitative variables were used, justifying the use of the chi-square test to calculate the odds ratio (OR). Proportion data were presented in percentage form and along with the confidence interval (CI). The measure of the effect size of the variables, according to each test, was evaluated [27,28].

To evaluate the influence of snoring index, age, sex, BMI and anxiety regarding SB severity, a multinomial logistic regression was performed. The unadjusted model accepted variables with $p<0.02$. The overall evaluation of the model was performed

with the F-test, only models with a p-value <0.05 were considered significant. The variance inflation factor (VIF) was calculated to detect multicollinearity, values below five were considered to ensure the absence of multicollinearity between predictors.

The dependent variable of the study was definite SB and classified as absent, mild/moderate or severe. The independent variable was snoring. And adjustment variables were grouped respectively as: demographics (age, sex, height, weight); questionnaires (smoking, alcohol, and anxiety symptoms). Moreover, variables related to sleep setting were also used, such as: total sleep time (TST) in minutes, arousal index, sleep latency, rapid eyes movement (REM) sleep latency, sleep efficiency, percentage (%) of sleep stages (N1, N2, N3 and N4), REM (%), wake after sleep onset (WASO), total SB episodes/h, total bursts/h and episodes per burst. The variables included in this study and their categorization form are presented in Appendix D.

Results

Participants and descriptive data

A total of 1042 participants were assessed for eligibility. Finally, 502 individuals were part of the final sample with mean age of 36.4±11.8. Most of the sample was female individuals 63.94% (n=321). Figure 1 presents the flowchart of the participants. The characteristics of participants is represented in Table 1 using proportion data. The chi-square was not possible to be calculated since less than 80% of the cells were smaller than five. There was no difference regarding the characteristic's variables with SB and without SB (p>0.05).

Outcome data

Thirty-nine participants were detected with definite SB (7.8%; 95% CI: 5.5% to 10.5%), with 25 considered to have low-frequency SB (64.1%; 95% CI: 48.42% to 77.26%) and 14 to have high-frequency SB (35.9%; 95%: 22.74% to 51.58%). Snoring was identified in 402 individuals (80.08%; 95% CI: 73.36% to 83.34%).

Main results

The association between SB and snoring and the effect size was not significant ($p>0.05$; $V=0.171$). The difference regarding sleep structure variables were evaluated and can be seen at Table 2. Individuals with SB had a higher proportion of REM sleep.

Multinominal logistic regression models with SB severity as the dependent variable was performed. Snoring, anxiety classification, BMI classification, smoke and alcohol ingestion, sex and age were selected for inclusion at the unadjusted model. However, smoke and alcohol variables could not be included for assessment for the unadjusted model since p-value was $p>0.05$. At the adjusted model the association of patients with mild anxiety in the presence of mild SB was found ($p=0.02$). The effect size was considered small (<3.5). The unadjusted and adjusted model can be seen in Table 3.

In Table 4, the multinominal logistic regression model was performed evaluating the influence of sleep stages on the severity of SB. The unadjusted model was performed only with N1 and REM sleep ($x^2=9.65$; R^2 0.033 $p<0.05$). In the adjusted model, an association between the percentage of REM sleep was found in patients with mild SB ($p=0.009$). As in the previous regression, the effect size was also considered small.

Discussion

The main objective of this research was to investigate the possible association between SB and snoring in non-apneic adult patients. However, the findings diverged from expectations, revealing no discernible association between the two variables.

Previously studies have sought to associated SB with sleep breathing disorders, based on the explanation that the muscular contraction of SB is linked with respiratory events. Snoring occurs due to the narrowing of the oropharyngeal or nasopharyngeal space, where air passes turbulently through the posterior wall of the pharynx, uvula, soft palate and base of the tongue, producing the vibration of the upper airways. Moreover, this condition can lead to xerostomia, the sensation of dry mouth [14]. RMMA is an oromotor activity that may help reinstate airway patency following a disrupted respiratory event during sleep, including airway resistance. Also, is stated that the RMMA activity could happen to improve lubrication of oral mucosa during sleep; when the salivary flow rate is lower [29]. A study included a total of 207 individuals and investigated snoring through both questionnaire and the polysomnography exam. The

results revealed that patients identified as snorers were 2.67 times more likely to experience mucosal dryness compared to non-snorers [30]. Therefore, is theoretically assumed that these events might be associated [31].

Snoring has been studied for many years in the scientific community, with records of studies on snoring dating back to the 19th century, such as this case report written by the editor in the Southern Medical and Surgical Journal [32]. Snoring assessment can be performed in a subjective process, such as self-report questionnaires [15,33]; or objective methods, such as microphones [14]. However, there is still no consensus on its classification in objective assessments such as PSG. A recent study by Kim and colleagues [34] retrospectively analyzed two thousand PSG exams performed in a specialized clinic in South Korea. Snoring was assessed using a nasal airflow transducer. The study suggests that the snoring event be counted when the transducer pressure is <200 microbar. Therefore, a snoring episode is recorded when three consecutive events occur within a 10-second interval. A validation study is still required to enable the application of this method.

Cigarettes and alcohol are substances legally classified as psychoactive, impacting the central nervous system and exerting influence on the behavior, cognitive functions, and mood of those who partake in their consumption [35,36]. These substances have been previously associated with the presence of SB [37]. No discernible differences were observed between the groups exhibiting SB and those without regarding consume of alcohol and smoke. A study aimed to evaluate SB intensity in tobacco smokers and alcohol drinkers in 113 individuals [38]. However, alcohol drinkers did not present difference regarding SB episodes. Smokers presented a higher rate of SB episodes than nonsmokers.

Sex, age and BMI did not present a statistical significance difference within the groups with and without SB Previously studies also did not found difference regarding these variables [31,39]. Alternatively, a study performed by Smardz *et al.*, 2021 [8] evaluated the influence of sex and age on SB and snoring. With a sample of 127 participants evaluated via PSG, the results indicated male sex as a possible predisposing factor for the coexistence of SB and snoring.

The present study found that anxiety symptoms could influence the presence of mild SB. A previous SR had concluded that probably specific symptoms could be associated with SB [6]. Recent primary studies have also found this association [40,41]. Anxiety, similar to stress, is regulated through the central nervous system by

catecholamines. Exemples of catecholamines include norepinephrine, serotonin, dopamine. These substances, characterized as both hormones and neurotransmitters, exhibit several functions, including the control of motoneuron activity, regulation of sleep and modulation of heart rate [31]. Furthermore, there is a suggestion that neurotransmitters may play a role in the initiation of jaw movements [42].

The architecture of human sleep is divided into two main stages: NREM and REM [43]. REM sleep constitutes around 25% of the total sleep time [14]. This study detected that the amount of REM period was higher among the SB group and the REM period influenced the presence of mild SB. This finding conflicts with previouly finding that showed no difference within bruxers and no-bruxers [44]. Moreover, trigeminal motoneurons experience postsynaptic inhibition by glycine and GABA through neurons situated in the medulla, leadind to a period of lowest muscle tone during REM sleep [45].

The use of a type I PSG is an important point of this study. This particular subtype is the most thorough, necessitating the placement of electrodes on specific areas of the patient's body within a sleep laboratory or hospital environment, enabling the detection of various sleep disorders [46]. Moreover, is the reference test for detection of SB [47]. However, your use is limited regarding the high cost. As alternative methods for detection, such as clinical examination and questionnaire, are also acceptable your use is more frequent in research [48].

Prudent consideration should be taken when extrapolation the results of this study to a different population. One of the main restrictions of this study lies in the fact that it is restricted to the population of São Paulo, Brazil. The unique demographic, cultural, and socioeconomic characteristics of São Paulo may not be representative of other regions, necessitating caution in generalizing the results. Furthermore, the statistical power of the original EPISONO study was designed to estimate the prevalence of obstructive sleep apnea in the population, estimated at the time at 3%. Therefore, statistical power is not equivalent for the subsamples analyzed.

Conclusion

Within the confines of this study in a non-apneic population, there was no evidence of an association between sleep bruxism and snoring. The association with age, sex, body mass index, consumption of coffee and alcohol was also not found.

However, it seems that anxiety symptoms and the duration of the REM period may be associated with the occurrence of sleep bruxism in this non-apneic sample.

References

1. Lobbezoo F, *et al.* International consensus on the assessment of bruxism: Report of a work in progress. *J Oral Rehabil.* 2018;45(11);837-844.

2. Lobbezoo F, *et al.* Bruxism defined and graded: an international consensus. *J Oral Rehabil.* 2013;40(1);2-4.

3. Martynowicz H, et al. The co-occurrence of sexsomnia, sleep bruxism and other sleep disorders. *J Clin Med.* 2018;**7**(9);233.

4. Mayer P, et al. Sleep bruxism in respiratory medicine practice. *Chest.* 2016;149(1);262-271.

5. Polmann H, et al. Association between sleep bruxism and stress symptoms in adults: A systematic review and meta-analysis. *J Oral Rehabil.* 2021;48(5);621-631.

6. Polmann H, et al. Association between sleep bruxism and anxiety symptoms in adults: A systematic review. *J Oral Rehabil.* 2019;46(5);482-491.

7. Michalek-Zrabkowska M, et al. The relationship between simple snoring and sleep bruxism: A polysomnographic study. *I Int J Environ Res Public Health.* 2020;17(23);8960.

8. Smardz J, et al. Influence of age and gender on sleep bruxism and snoring in non-apneic snoring patients: A polysomnographic study. *J Sleep Res.* 2021;30(3);e13178.

9. da Costa Lopes AJ, et al. Is there an association between sleep bruxism and obstructive sleep apnea syndrome? A systematic review. *Sleep Breath.* 2020;24(913-921.

10. De Luca Canto G, *et al.* Sleep bruxism and sleep-disordered breathing: a systematic review. *J Oral Facial Pain Headache.* 2014;28(4);299-305.

11. Jokubauskas L, Baltrušaitytė A. Relationship between obstructive sleep apnoea syndrome and sleep bruxism: a systematic review. *J Oral Rehabil.* 2017;44(2);144-153.

12. Pauletto P, et al. Sleep bruxism and obstructive sleep apnea: association, causality or spurious finding? A scoping review. *Sleep.* 2022.

13. Koutsourelakis I, et al. Clinical and polysomnographic determinants of snoring. *J Sleep Res.* 2012;21(6);693-699.

14. AAMS *The International Classification of Sleep Disorders: (ICSD-3).* American Academy of Sleep Medicine; 2014.

15. Chung F, et al. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. *Chest.* 2016;149(3);631-638.

16. Palinkas M, et al. Nocturnal sleep architecture is altered by sleep bruxism. *Arch Oral Biol.* 2017;81,56-60.

17. van de Langenberg SC, et al. The multidimensionality of sleep in population-based samples: a narrative review. *J Sleep Res.* 2022;31(4);e13608.

18. Vandenbroucke JP, et al. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. *Annals of Internal Medicine.* 2007;147(8);W-163-W-194.

19. Von Elm E, et al. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *The Lancet.* 2007;370(9596);1453-1457.

20. Santos-Silva R, et al. Sao Paulo Epidemiologic Sleep Study: rationale, design, sampling, and procedures. *Sleep Medicine.* 2009;10(6);679-685.[3]

21. Iber C. The AASM manual for the scoring of sleep and associated events: Rules. *Terminology and Technical Specification.* 2007.

22. Ferrario V, et al. An electromyographic investigation of masticatory muscles symmetry in normo-occlusion subjects. *J Oral Rehabil.* 2000;27(1);33-40.

23. Rompré P, *et al.* Identification of a sleep bruxism subgroup with a higher risk of pain. *J Dent Res.* 2007;86(9);837-842.

24. Tufik S, *et al.* Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. *Sleep medicine.* 2010;11(5);441-446.

25. Group WAW. The alcohol, smoking and substance involvement screening test (ASSIST): development, reliability and feasibility. *Addiction.* 2002;97(9);1183-1194.

26. Cunha JA. *Manual da versão em português das Escalas Beck*. São Paulo: casa do psicólogo. 2001.

27. Normando D, Honório HM. *Bioestatística quase sem fórmulas*. 2023.

28. Sullivan GM, Feinn R. Using effect size—or why the P value is not enough. *J Grad Med Educ.* 2012;4(3);279-282.

29. Carra MC, et al. Overview on sleep bruxism for sleep medicine clinicians. *Sleep Med Clin.* 2015;10(3);375-384.

[3] Artigo disponível para leitura no Anexo A desse trabalho (p. 94).

30. Zhang C, et al. The role of dry mouth in screening sleep apnea. *Postgrad Med J.* 2021;97(1147);294-298.

31. Carra MC, et al. Sleep bruxism: a comprehensive overview for the dental clinician interested in sleep medicine. *Dent Clinic North Am.* 2012;56(2);387-413.

32. Snoring Prevented by Excision of the Uvula. *Northwest Med Surg J.* 1853;1(9);416.

33. Chiu H-Y, et al. Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: a bivariate meta-analysis. *Sleep Med Rev.* 2017;36:57-70.

34. Kim SG, et al. Definition of the snoring episode index based on the analyses of snoring parameters and the apnea hypopnea index. *Sci Rep.* 2022;12(1);6761.

35. Hajdusianek W, et al. Tobacco and Nervous System Development and Function—New Findings 2015–2020. *Brain Sci.* 2021;11(6);797.

36. Costardi JVV, et al. A review on alcohol: from the central action mechanism to chemical dependency. *Rev Assoc Med Bras.* 2015;61(4);381-387.

37. Ohayon MM, et al. Risk factors for sleep bruxism in the general population. *Chest.* 2001;119(1);53-61.

38. Frosztega W, et al. Polysomnographic assessment of effects of tobacco smoking and alcohol consumption on sleep bruxism intensity. *J Clin Med.* 2022;11(24);7453.

39. Palinkas M, et al. Analysis of the sleep period and the amount of habitual snoring in individuals with sleep bruxism. *Med Oral Patol Oral Cir Bucal.* 2019;24(6);e782-e786.

40. Flueraşu MI, et al. The epidemiology of bruxism in relation to psychological factors. *Int J Environ Res Public Health.* 2022;19(2);691.

41. Ekman A, et al. Association of health-related factors with self-reported sleep and awake bruxism in Northern Finland Birth Cohort 1966-a cross-sectional study. *CRANIO®.* 2023;1-11.

42. Lavigne G, et al. Neurobiological mechanisms involved in sleep bruxism. *Crit Rev Oral Biol Med.* 2003;14(1);30-46.

43. Eban-Rothschild A, et al. To sleep or not to sleep: neuronal and ecological insights. *Curr Opin Neurobiol.* 2017;44:132-138.

44. Zhu Y, *et al.* Sleep architecture as a candidate for phenotyping sleep bruxism: A narrative physiological review. *J Oral Rehabil.* 2024;51(1):87-102.

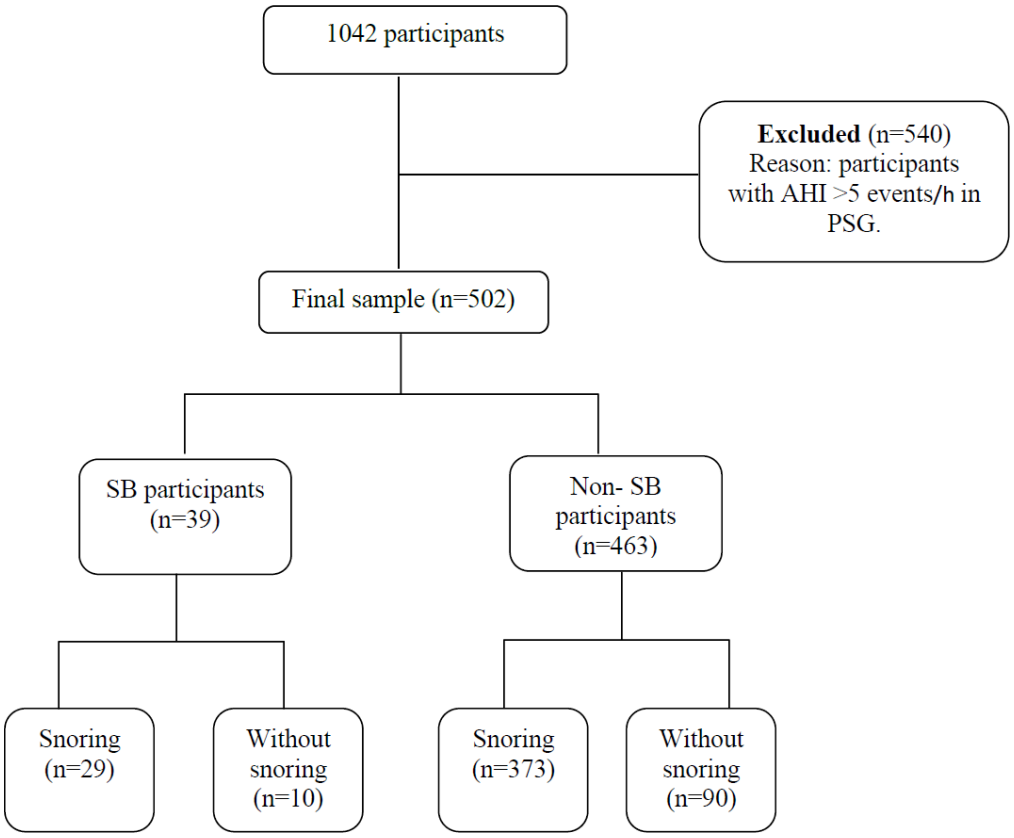
45. Peever J. Control of motoneuron function and muscle tone during REM sleep, REM sleep behavior disorder and cataplexy/narcolepsy. *Arch Ital Biol.* 2011;149(4);454-466.

46. de Abreu HF. *Prática em Medicina do Sono.* Thieme Revinter; 2020.

47. Casett E, et al. Validity of different tools to assess sleep bruxism: a meta-analysis. *J Oral Rehabil.* 2017;44(9);722-734.

48. Manfredini D, et al. Standardised tool for the assessment of bruxism. *J Oral Rehabil.* 2023;51(1):29-58.

Figure 1. Flowchart of participants



AHI: apnea-hypopnea index

SB: sleep bruxism

PSG: polysomnography

Table 1. Characteristics of participants.

		With SB n=39		Without SB n= 463					
		N	% (95% CI)	N	% (95% CI)	Total N	Measure of effect - OR (95% CI)	p-value	V-Cramer
Sex	**Female**	24	7.48 (5.08-10.89)	297	92.52 (89.11-94.92)	321			
	Male	15	8.29 (5.09-13.23)	166	91.71 (86.77-94.91)	181	0.89 (0.45-1.75	0.887	-0.01
BMI	**Underweight**	23	9.24 (6.24-13.48)	226	90.76 (86.52-93.76)	249			
	Normal*	11	6.21 (3.5-10.78)	166	93.79 (89.22-96.5)	177	0.65 (0.30-1.37)	0.340	-0.05
	Overweight	3	5.17 (1.77-14.14)	55	94.83 (85.86-98.23)	58	1.21 (0.32-4.51)	0.531 †	0.02
	Obese	2	11.11 (3.1-3.28)	16	88.89 (67.2-96.9)	18	0.53 (0.10-2.60)	0.342 †	-0.06
Age (yrs)	**<40**	29	8.68 (6.11-12.19)	305	91.32 (87.81-93.89)	334			
	>40	10	5.95 (3.26-10.61)	158	94.05 (89.39-96.74)	168	1.50 (0.71-3.16)	0.368	0.05
BAI	**Minimal***	25	7.18 (4.91-10.39)	323	92.82 (89.61-95.09)	348			
	Mild	9	9.09 (4.86-16.38)	90	90.91 (83.62-95.14)	99	0.74 (0.33-1.65)	0.610	-0.03
	Moderate	2	5.26 (1.45-17.28)	36	94.74 (82.72-98.55)	38	1.33 (0.30-5.89)	0.515 †	0.02
	Severe	3	17.75 (6.19-41.03)	14	82.35 (58.9-93.81)	17	0.34 (0.09-1.29)	0.122	-0.09
Smoke	**Yes**	9	4.97 (2.64-9.18)	172	95.03 (90.82-97.36)	181			

	No	22	8.24 (5.5-12.16)	245	91.76 (87.84-94.5)	267	0.58 (0.26-1.29)	0.250	-0.06
Alcohol	**Yes**	1	2.86 (0.51-16.62)	34	97.14 (85.46-99.49)	35			
	No	30	7.28 (5.15-10.2)	382	92.72 (89.8-94.85)	412	0.27 (0.03-2.09)	0.152 †	-0.07

Odds Ratio=OR; Body Mass Index=BMI; Beck Anxiety Inventory=BAI.

*Normal weight reference

*BAI minimal reference

† fisher test was used when the expected cell number was below five.

Table 2. Sleep Variables

	Sleep bruxism N= 39		**No sleep bruxism N =463**		
	Median	**IQR**	**Median**	**IQR**	**p-value**
TST (min)	363	306-424	351	300-398	0.142
Arousal index (n)	49	37-64	50	35.5-70	0.798
Sleep Latency	10.8	3.9-24.3	9.25	4.7-20.9	0.916
REM Sleep Latency	77.5	64.5-98	82	64.1-125	0.407
Sleep Efficiency	88.6	82.5-93.8	87.3	78.8-92.8	0.341
N1 (%)	2.8	1.7-4.45	3.3	2.2-5.18	0.154

N2 (%)	53.6	49.8-56.6	53.1	48.4-58.4	0.451
N3 e 4 (%)	21.4	16.7-27.4	23.7	18.2-28.1	0.325
REM (%)	22.4	18.1-25.9	19.2	15.3-22.4	**0.002**
WASO	29	19.2-48.2	40.2	20.5-68.9	0.256
Total episodes/h	3.3	2.3-4.5	0	0	<.001
Total bursts/h	11	6.44-14.4	0	0	<.001
Episodes per burst	3.58	3.58-3.95	0	0	<.001

Table 3. Multinomial logistic regression bruxism severity and variables.

Variables	**Unadjusted Odds Ratio (OR) - 95% CI**		**Adjusted Odds Ratio (OR) - 95% CI**	
	AIC 330; R^2 0.101 p=0.045		**AIC 319; R^2 0.054 p=0.023**	
	Sleep Bruxism	**p-value**	**Sleep Bruxism**	**p-value**
		Classification SB 1-0*		
Snoring[a]	1.10 (0.356-3.455)	0.856		
BAI				
1-0	3.6 (1.329-9.676)	0.012	**2.945 (1.184-7.327)**	**0.02**
2-0	1.72 (0.344-8.622)	0.508		
3-0	5.34 (1.012-28.203)	0.048		
BMI				

1-0	0.820 (0.322-2.088)	0.679
2-0	1.07 (0.281-4.062)	0.921
3-0	NA	NA
Sex[b]	1.399 (0.586-3.336)	0.449
Age[c]	1.026 (0.413-2.547)	0.956
		Classification SB 2-0*
Snoring[a]	0.5937 (0.180-1.950)	0.39
BAI		
1-0	NA	<0.01
2-0	NA	0.881
3-0	2.607 (0.285-23.814)	0.396
BMI		
1-0	0.820 (0.322-2.088)	0.679
2-0	1.07 (0.281-4.062)	0.921
3-0	NA	NA
Sex[b]	0.732 (0.230-2.337)	0.145
Age[c]	0.308 (0.063-1.498)	0.601

[*] Reference: no sleep bruxism; [a] Reference: no snoring; [b] Reference: female; [c] Reference: <40 years old. NA: values <0.000001.

Table 4. Multinomial logistic regression with sleep variables.

	Unadjusted Odds Ratio (OR) (95%CI)		Adjusted Odds Ratio (OR) (95%CI)	
	x^2=9.65; R^2 0.033 p<0.05		x^2=7.59; R^2 0.054 p<0.05	
Variables	**Sleep Bruxism**	**p-value**	**Sleep Bruxism**	**p-value**
		Classification SB 1-0*		
REM (%)	1.090 (1.023-1.160)	0.007	**1.087 (1.021-1.158)**	**0.009**
N1 (%)	1.034 (0.911 -1.173)	0.604		
		Classification SB 2-0*		
REM (%)	1.034 (0.946-1.131)	0.451		
N1 (%)	0.849 (0.647 -1.147)	0.239		

* Reference: no sleep bruxism

Appendix A. STROBE Statement—Checklist of items that should be included in reports of *cross-sectional studies*.

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	53
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	53
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	54
Objectives	3	State specific objectives, including any prespecified hypotheses	55
Methods			
Study design	4	Present key elements of study design early in the paper	55
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	55
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	55
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	56,57,58
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*56*
Bias	9	Describe any efforts to address potential sources of bias	-
Study size	10	Explain how the study size was arrived at	55
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe	Appendix C

		which groupings were chosen and why	
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	58
		(*b*) Describe any methods used to examine subgroups and interactions	58
		(*c*) Explain how missing data were addressed	-
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	-
		(*e*) Describe any sensitivity analyses	-
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	59
		(b) Give reasons for non-participation at each stage	59,67
		(c) Consider use of a flow diagram	67
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	68,69
		(b) Indicate number of participants with missing data for each variable of interest	-
Outcome data	15*	Report numbers of outcome events or summary measures	68
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	70,71,72,73
		(*b*) Report category boundaries when continuous variables were categorized	Appendix C
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a	-

		meaningful time period	
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	-
Discussion			
Key results	18	Summarise key results with reference to study objectives	60
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	62
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	60,61
Generalisability	21	Discuss the generalisability (external validity) of the study results	62
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	52

Appendix B – Ethics Committee Approval

UNIFESP
PAULISTA
ESCOLA MEDICINA

Universidade Federal de São Paulo
Escola Paulista de Medicina

Comitê de Ética em Pesquisa
Hospital São Paulo

São Paulo, 9 de junho de 2006.
CEP 0593/06

Ilmo(a). Sr(a).
Pesquisador(a) SÉRGIO TUFIK
Co-Investigadores: Augusto Taddei, Maria Laura Nogueira Pires, Celine Pompéia, Adriana Kauati, Marcia Pradella-Halinan
Disciplina/Departamento: Psicobiologia/Medicina e Biologia do Sono da Universidade Federal de São Paulo/Hospital São Paulo
Patrocinador: AFIP.

PARECER DO COMITÊ DE ÉTICA INSTITUCIONAL

Ref: Projeto de pesquisa intitulado: **"Epidemiologia do sono na cidade de São Paulo - EpiSono 2006 (versão 2006)".**

CARACTERÍSTICA PRINCIPAL DO ESTUDO: estudo epidemiológico.

RISCOS ADICIONAIS PARA O PACIENTE: risco mínimo, desconforto mínimo, envolvendo coleta de sangue.

OBJETIVOS: Traçar o perfil epidemiológico dos distúrbios de sono para a população adulta da cidade de São Paulo em 2006 e a tendência secular das prevalências a partir dos resultados dos inquéritos similares realizados em 1987 e 1995. Traçar o perfil epidemiológico dos distúrbios do sono para a população de crianças e adolescentes (1 até 19 anos de idade). Estudar associações entre o padrão e distúrbios de sono na população do município de São Paulo, e analisar as variações sócio demográficas, ciclo atividade/repouso, atividade e condicionamento físico, hábitos alimentares, variações bioquímicas, hematológicas, endócrinas, imunologicas e inflamatórias no sangue periférico, marcadores genéticos, disfunção sexual masculina, depressão , ansiedade e alcoolismo..

RESUMO: O estudo terá como base aplicação de questionários domiciliares, como realizado em 1987 e 1995. Serão realizados exames polissonográficos, actigráficos, hematológicos, bioquímicos e genéticos, medida de pressão arterial, peso e altura. Haverá avaliação do perfil epidemiológico dos distúrbios do sono para a população de crianças e adolescentes, através de questionários sobre o sono dirigido aos adolescentes e ou responsáveis pelas crianças/adolescentes dos domicílios sorteados. Os questionários serão aplicados nos domicílios dos voluntários, 3 questionários de sono, questionários complementares para avaliação de cronotipagem, depressão, ansiedade, disfunção erétil, atividade hormonal feminina e memória. Será realizado um pré-teste para 32 unidades amostrais..

FUNDAMENTOS E RACIONAL: Estudo epidemiológico, avaliando os distúrbios do sono da população de São Paulo, e correlação com dados demográficos e laboratoriais..

MATERIAL E MÉTODO: Estudo envolvendo grande número de pesquisadores, com infra-estrutura adequada para realização da pesquisa..

TCLE: Adequado, contemplando os itens da resolução 196/96.

DETALHAMENTO FINANCEIRO: AFIP - FAPESP- R$ 1669000,00.

CRONOGRAMA: 12 meses.

OBJETIVO ACADÊMICO: .

ENTREGA DE RELATÓRIOS PARCIAIS AO CEP PREVISTOS PARA: **04/06/2007** e **29/05/2008**.

O Comitê de Ética em Pesquisa da Universidade Federal de São Paulo/Hospital São Paulo **ANALISOU** e **APROVOU** o projeto de pesquisa referenciado.

Rua Botucatu, 572 - 1º andar – conj. 14 - CEP 04023-062 - São Paulo / Brasil
Tel.: (011) 5571-1062 - 5539.7162

Appendix C - Descriptive Statistics

Name	Type	Variable treatment
Definite Sleep Bruxism	Categorical (Absent=0 and Present=1)	Dependent Variable
RMMA/h	Categorical (Absent=0; Mild/Moderate=1; Severe=2)	Dependent Variable
Snoring	Categorical (Absent=0 and Present=1)	Independent Variable
Age (years)	Categorical (Less than 40 years=0 and Greater than 40 years=1)	Adjustment Variable
Sex	Categorical (Female; Male)	Adjustment Variable
BMI	Categorical (Underweigth= BMI<18.5; Normal Weight= BMI>18.5 to 24.9 kg/m²; Overweight= BMI ≥25 to 29.9 kg/m²; Obesity= BMI >30.0 kg/m²)	Adjustment Variable
Anxiety (BAI)	Categorical (Absent=0; Mild =1; Moderate =2; Severe=3)	Adjustment Variable
Smoking (ASSIST)	Categorical (Yes=0 and No=1)	Adjustment Variable
Alcohol (ASSIST)	Categorical (Yes=0 and No=1)	Adjustment Variable
TST	Continuous in minutes (min)	Adjustment Variable
REM	Continuous in percentage (%)	Adjustment Variable
Arousals index	Continuous in episodes (n)	Adjustment Variable
Sleep Latency	Continuous in minutes (min)	Adjustment Variable
REM Sleep Latency	Continuous in minutes (min)	Adjustment Variable
N 1	Continuous in percentage (%)	Adjustment Variable
N 2	Continuous in percentage (%)	Adjustment Variable
N 3 e 4	Continuous in percentage (%)	Adjustment Variable
WASO	Continuous in minutes (min)	Adjustment Variable
Total episodes/h	Continuous in episodes (n)	Adjustment Variable
Total burst/h	Continuous in episodes (n)	Adjustment Variable
Episodes per burst	Continuous in episodes (n)	Adjustment Variable

7 CONSIDERAÇÕES FINAIS

Esta tese proporcionou uma análise aprofundada dos fatores associados entre o bruxismo do sono e o ronco, utilizando dados de dois estudos distintos: um realizado no Hospital Baia Sul, focado em uma amostra não probabilística de indivíduos com indicação médica para polissonografia, e um segundo estudo com dados provenientes de uma amostra de base populacional realizado em São Paulo, o EPISONO. As principais informações de cada estudo estão sumarizadas no Quadro 1.

QUADRO 1 – PRINCIPAIS CARACTERÍSTICAS E RESULTADOS DE CADA ESTUDO

	Estudo Baia Sul	**Estudo EPISONO**
Características da amostra	Amostra não probabilística de indivíduos com suspeita de distúrbios do sono (n=61).	Dados provenientes de uma amostra de base populacional não apneica (n=502).
Avaliação varíaveis	Bruxismo do sono: AMMR na PSG. Ronco: microfones (n).	Bruxismo do sono: AMMR na PSG. Ronco: microfones (presença/ausência).
Associação bruxismo do sono e ronco	Não foi encontrada associação entre BS e ronco. Durante o período REM, o BS e o ronco/h apresentaram associação.	Não foi encontrada associação entre BS e ronco.
Associação bruxismo do sono e idade, sexo e IMC.	Não foi encontrada associação entre bruxismo do sono e idade, sexo e IMC.	
Variáveis relacionadas ao sono	Episódios de dessaturação apresentaram um tamanho de efeito médio em relação ao BS no período REM.	BS leve/moderado foi associado com a duração do sono REM.
Associação bruxismo do sono e sintomas de ansiedade, álcool e tabagismo	Esse desfecho não foi avaliado nesse estudo.	Sintomas de ansiedade leve foram associados com bruxismo do sono leve. Álcool e tabagismo também não foram associados ao bruxismo do sono.

Fonte: Elaboração própria.

Esses resultados reforçam a complexidade do bruxismo do sono, evidenciando que fatores objetivos, como o ronco, bem como fatores subjetivos, como sintomas de ansiedade,

podem desempenhar papéis na sua gênese. Importante notar que, devido à natureza dos estudos, não é possível inferir causalidade nos dados encontrados, sendo mais apropriado indicar associações de risco entre as variáveis.

Em síntese, esta tese contribui para a compreensão mais completa do bruxismo do sono, em duas populações distintas, destacando a influência de aspectos físicos e fatores psicológicos nessa condição.

REFERÊNCIAS

AAMS. **The International Classification of Sleep Disorders: (ICSD-3)**. American Academy of Sleep Medicine 2014.

ABE, Y. *et al.* Association of genetic, psychological and behavioral factors with sleep bruxism in a Japanese population. **Journal Sleep Research,** v. 21, n. 3, p. 289-96, Jun 2012.

AL-JEWAIR, T. S. *et al.* Prevalence and risks of habitual snoring and obstructive sleep apnea symptoms in adult dental patients. **Saudi medical journal,** v. 37, n. 2, p. 183, 2016.

ALTHUBAITI, A. Sample size determination: a practical guide for health researchers. **Journal of General and Family Medicine,** v. 24, n. 2, p. 72-78, 2023.

BERRY, R. B. *et al.* AASM scoring manual updates for 2017 (version 2.4). **American Academy of Sleep Medicine**, v. 13, p.665-666, 2017.

BERTOLAZI, A. N. *et al.* Validation of the Brazilian Portuguese version of the Pittsburgh sleep quality index. **Sleep medicine,** v. 12, n. 1, p. 70-75, 2011.

BERTOLAZI, A. N. *et al.* Portuguese-language version of the Epworth sleepiness scale: validation for use in Brazil. **Jornal Brasileiro de Pneumologia,** v. 35, p. 877-883, 2009.

BONNET, M. *et al.* EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. **Sleep,** v. 15, n. 2, p. 174-184, 1992.

BOUTROS, N. *et al.* The effects of severe bruxism on sleep architecture: a preliminary report. **Clinical Electroencephalography,** v. 24, n. 2, p. 59-62, 1993.

BUYSSE, D. J. Sleep health: can we define it? Does it matter? **Sleep,** v. 37, n. 1, p. 9-17, 2014.

CARRA, M. C. *et al.* Overview on sleep bruxism for sleep medicine clinicians. **Sleep Medicine Clinics,** v. 10, n. 3, p. 375-384, 2015.

CARRA, M. C.; HUYNH, N.; LAVIGNE, G. Sleep bruxism: a comprehensive overview for the dental clinician interested in sleep medicine. **Dental Clinics,** v. 56, n. 2, p. 387-413, 2012.

CASETT, E. *et al.* Validity of different tools to assess sleep bruxism: a meta-analysis. **Journal of Oral Rehabilitation,** v. 44, n. 9, p. 722-734, 2017.

CHIU, H.-Y. *et al.* Diagnostic accuracy of the Berlin questionnaire, STOP-BANG, STOP, and Epworth sleepiness scale in detecting obstructive sleep apnea: a bivariate meta-analysis. **Sleep Medicine Reviews,** v. 36, p. 57-70, 2017.

CHUNG, F.; ABDULLAH, H. R.; LIAO, P. STOP-Bang questionnaire: a practical approach to screen for obstructive sleep apnea. **Chest,** v. 149, n. 3, p. 631-638, 2016.

COUNTER, P.; WILSON, J. A. The management of simple snoring. **Sleep Medicine Reviews,** v. 8, n. 6, p. 433-441, 2004.

CUNHA, J. A. **Manual da versão em português das Escalas Beck**. São Paulo: casa do psicólogo, v. 171, 2001.

DA COSTA LOPES, A. J. *et al.* Is there an association between sleep bruxism and obstructive sleep apnea syndrome? A systematic review. **Sleep and Breathing,** v. 24, p. 913-921, 2020.

DE ABREU, H. F. **Prática em medicina do sono**. Thieme Revinter, 2020.

DE LUCA CANTO, G. *et al.* Sleep bruxism and sleep-disordered breathing: a systematic review. **J Oral Facial Pain Headache,** v. 28, n. 4, p. 299-305, Fall 2014.

DE OLIVEIRA, J. M. D. *et al.* Prevalence of Awake Bruxism: a systematic review. **Journal of Dentistry**, p. 104715, 2023.

DEARY, V. *et al.* Simple snoring: not quite so simple after all? **Sleep Medicine Reviews,** v. 18, n. 6, p. 453-462, 2014.

DUARTE, J. *et al.* Is there an association of genetic polymorphisms of the catechol-O-methyltransferase gene (rs165656 and rs174675) and the 5-hydroxytryptamine receptor 2A gene (rs4941573 and rs6313) with sleep bruxism in individuals with obstructive sleep apnea? **Archives of Oral Biology,** v. 133, p. 105315, 2022.

EBAN-ROTHSCHILD, A.; GIARDINO, W. J.; DE LECEA, L. To sleep or not to sleep: neuronal and ecological insights. **Current Opinion in Neurobiology,** v. 44, p. 132-138, 2017.

EKMAN, A. *et al.* Association of health-related factors with self-reported sleep and awake bruxism in Northern Finland Birth Cohort 1966-a cross-sectional study. **CRANIO®**, p. 1-11, 2023.

EMODI-PERLMAN, A. *et al.* Symptoms of Nocturnal Masticatory Muscle Activity among Women of Different Age Groups and Their Association to Obstructive Sleep Apnea-A Cross Sectional Study. **Journal of Clinical Medicine,** v. 11, n. 5, Feb 23 2022.

FERRARIO, V. *et al.* An electromyographic investigation of masticatory muscles symmetry in normo-occlusion subjects. **Journal of Oral Rehabilitation,** v. 27, n. 1, p. 33-40, 2000.

FLUERAŞU, M. I. *et al.* The epidemiology of bruxism in relation to psychological factors. **International Journal of Environmental Research and Public Health,** v. 19, n. 2, p. 691, 2022.

FRANKEN, P.; DIJK, D. J. Circadian clock genes and sleep homeostasis. **European Journal of Neuroscience,** v. 29, n. 9, p. 1820-1829, 2009.

GROUP, W. A. W. The alcohol, smoking and substance involvement screening test (ASSIST): development, reliability and feasibility. **Addiction,** v. 97, n. 9, p. 1183-1194, 2002.

GUO, S.; HUSSEY, D. L. Nonprobability sampling in social work research: Dilemmas, consequences, and strategies. **Journal of Social Service Research,** v. 30, n. 3, p. 1-18, 2004.

HASEGAWA, Y. *et al.* Is there a first night effect on sleep bruxism? A sleep laboratory study. **Journal of Clinical Sleep Medicine,** v. 9, n. 11, p. 1139-1145, 2013.

HOSOYA, H. *et al.* Relationship between sleep bruxism and sleep respiratory events in patients with obstructive sleep apnea syndrome. **Sleep and Breathing,** v. 18, p. 837-844, 2014.

HUANG, Z. *et al.* Associated factors of primary snoring and obstructive sleep apnoea in patients with sleep bruxism: A questionnaire study. **Journal of Oral Rehabilitation,** v. 49, n. 10, p. 970-979, Oct 2022.

HUANG, Z. *et al.* Associations between snoring and dental sleep conditions: A systematic review. **Journal of Oral Rehabilitation,** v. 50, n. 5, p. 416-428, May 2023.

IBER, C. The AASM manual for the scoring of sleep and associated events: Rules. **Terminology and Technical Specification**, 2007.

JENSEN, R. *et al.* Prevalence of oromandibular dysfunction in a general population. **Journal of Orofacial Pain,** v. 7, n. 2, 1993.

JOKUBAUSKAS, L.; BALTRUŠAITYTĖ, A. Relationship between obstructive sleep apnoea syndrome and sleep bruxism: a systematic review. **Journal of Oral Rehabilitation,** v. 44, n. 2, p. 144-153, 2017.

KATO, T. *et al.* Masseter EMG activity during sleep and sleep bruxism. **Archives Italiennes de Biologie,** v. 149, n. 4, p. 478-491, 2011.

KATO, T. *et al.* Sleep bruxism: an oromotor activity secondary to micro-arousal. **Journal of Dental Research,** v. 80, n. 10, p. 1940-1944, 2001.

KATO, T. *et al.* Age is associated with self-reported sleep bruxism, independently of tooth loss. **Sleep Breath,** v. 16, n. 4, p. 1159-65, Dec 2012.

KIM, S. G.; CHO, S.-W.; KIM, J.-W. Definition of the snoring episode index based on the analyses of snoring parameters and the apnea hypopnea index. **Scientific Reports,** v. 12, n. 1, p. 6761, 2022.

KLEITMAN, N. **Sleep and wakefulness**. University of Chicago Press, 1987.

KOSKENVUO, M. *et al.* Snoring as a risk factor for ischaemic heart disease and stroke in men. **British Medical Journal (Clinical Research Edition),** v. 294, n. 6563, p. 16-19, 1987.

KOUTSOURELAKIS, I. *et al.* Clinical and polysomnographic determinants of snoring. **Journal of Sleep Research,** v. 21, n. 6, p. 693-699, 2012.

LAVIGNE, G. *et al.* Research routes on improved sleep bruxism metrics: Toward a standardised approach. **Journal of Sleep Research,** v. 30, n. 5, p. e13320, 2021.

LAVIGNE, G. *et al.* Neurobiological mechanisms involved in sleep bruxism. **Critical Reviews in Oral Biology & Medicine,** v. 14, n. 1, p. 30-46, 2003.

LAVIGNE, G. *et al.* Rhythmic masticatory muscle activity during sleep in humans. **Journal of Dental Research,** v. 80, n. 2, p. 443-448, 2001.

LAVIGNE, G. J. *et al.* Sleep disorders and the dental patient: an overview. **Oral Surgery, Oral Medicine, Oral Pathology, Oral Radiology, and Endodontology,** v. 88, n. 3, p. 257-272, 1999.

LAVIGNE, G. J. *et al.* Genesis of sleep bruxism: motor and autonomic-cardiac interactions. **Archives of Oral Biology,** v. 52, n. 4, p. 381-384, 2007.

LOBBEZOO, F. *et al.* Bruxism defined and graded: an international consensus. **Journal of Oral Rehabilitation,** v. 40, n. 1, p. 2-4, 2013.

LOBBEZOO, F. *et al.* International consensus on the assessment of bruxism: report of a work in progress. **Journal of Oral Rehabilitation,** v. 45, n. 11, p. 837-844, 2018.

LOBBEZOO, F.; NAEIJE, M. Bruxism is mainly regulated centrally, not peripherally. **Journal of Oral Rehabilitation,** v. 28, n. 12, p. 1085-1091, 2001.

MACALUSO, G. M. *et al.* Sleep bruxism is a disorder related to periodic arousals during sleep. **Journal of Dental Research,** v. 77, n. 4, p. 565-573, 1998.

MALULY, M. *et al.* Polysomnographic study of the prevalence of sleep bruxism in a population sample. **Journal of Dental Research,** v. 92, n. 7_suppl, p. S97-S103, 2013.

MANFREDINI, D. *et al.* Epidemiology of bruxism in adults: a systematic review of the literature. **Journal of Orofacial Pain,** v. 27, n. 2, p. 99-110, 2013.

MANFREDINI, D. *et al.* Standardised tool for the assessment of bruxism. **Journal of Oral Rehabilitation**, 2023a.

MANFREDINI, D. *et al.* The bruxism construct: from cut-off points to a continuum spectrum. **Journal of Oral Rehabilitation,** v. 46, n. 11, p. 991-997, 2019.

MANFREDINI, D. *et al.* Standardized Tool for the Assessment of Bruxism (STAB). **Journal of Oral Rehabilitation**, 2023b.

MARTYNOWICZ, H. *et al.* The co-occurrence of sexsomnia, sleep bruxism and other sleep disorders. **Journal of Clinical Medicine,** v. 7, n. 9, p. 233, 2018.

MAYER, P.; HEINZER, R.; LAVIGNE, G. Sleep bruxism in respiratory medicine practice. **Chest,** v. 149, n. 1, p. 262-271, 2016.

MELO, G. *et al.* Bruxism: an umbrella review of systematic reviews. **Journal of Oral Rehabilitation,** v. 46, n. 7, p. 666-690, 2019.

MICHALEK-ZRABKOWSKA, M. *et al.* Effect of sleep bruxism intensity on blood pressure in normotensives. **Journal of Clinical Medicine,** v. 10, n. 6, p. 1304, 2021.

MICHALEK-ZRABKOWSKA, M. *et al.* The relationship between simple snoring and sleep bruxism: A polysomnographic study. **International Journal of Environmental Research and Public Health,** v. 17, n. 23, p. 8960, 2020.

MICHALEK-ZRABKOWSKA, M. *et al.* The Relationship between Simple Snoring and Sleep Bruxism: A Polysomnographic Study. **International Journal of Environmental Research and Public Health,** v. 17, n. 23, Dec 2 2020.

NEFF, T. A. Routine oximetry: a fifth vital sign? **Chest,** v. 94, n. 2, p. 227, 1988.

NOAL, R. B. *et al.* Ronco habitual e apnéia obstrutiva observada em adultos: estudo de base populacional, Pelotas, RS. **Revista de Saúde Pública,** v. 42, p. 224-233, 2008.

NORMANDO, D.; HONÓRIO, H. M. **Bioestatística quase sem fórmulas**. 2023.

O'BRIEN, L. M. *et al.* Snoring during pregnancy and delivery outcomes: a cohort study. **Sleep,** v. 36, n. 11, p. 1625-1632, 2013.

PALINKAS, M. *et al.* Analysis of the sleep period and the amount of habitual snoring in individuals with sleep bruxism. **Medicina Oral, Patologia Oral y Cirugia Bucal,** v. 24, n. 6, p. e782-e786, Nov 1 2019.

PALINKAS, M. *et al.* Analysis of the sleep period and the amount of habitual snoring in individuals with sleep bruxism. **Medicina Oral, Patologia Oral y Cirugia Bucal,** v. 24, n. 6, p. e782, 2019.

PALINKAS, M. *et al.* Nocturnal sleep architecture is altered by sleep bruxism. **Archives of Oral Biology,** v. 81, p. 56-60, 2017.

PALMER, L. J.; REDLINE, S. Genomic approaches to understanding obstructive sleep apnea. **Respiratory Physiology & Neurobiology,** v. 135, n. 2-3, p. 187-205, 2003.

PAULETTO, P. *et al.* Sleep bruxism and obstructive sleep apnea: association, causality or spurious finding? A scoping review. **Sleep**, 2022.

PELLEGRINO, G. M. *et al.* Effects of air stacking on dyspnea and lung function in neuromuscular diseases. **Archives of Physical Medicine and Rehabilitation,** v. 102, n. 8, p. 1562-1567, 2021.

POLMANN, H. *et al.* Association between sleep bruxism and anxiety symptoms in adults: A systematic review. **Journal of Oral Rehabilitation,** v. 46, n. 5, p. 482-491, 2019.

POLMANN, H. *et al.* Association between sleep bruxism and stress symptoms in adults: A systematic review and meta-analysis. **Journal of Oral Rehabilitation,** v. 48, n. 5, p. 621-631, 2021.

RANGANATHAN, P.; PRAMESH, C.; AGGARWAL, R. Common pitfalls in statistical analysis: logistic regression. **Perspectives in Clinical Research,** v. 8, n. 3, p. 148, 2017.

REUS, J. C. *et al.* Association Between Primary Headache and Bruxism: An Updated Systematic Review. **Journal of Oral Facial Pain Headache,** v. 35, p. 129-138, 2021.

RICH, J. *et al.* An epidemiologic study of snoring and all-cause mortality. **Otolaryngology--Head and Neck Surgery,** v. 145, n. 2, p. 341-346, 2011.

ROMPRÉ, P. *et al.* Identification of a sleep bruxism subgroup with a higher risk of pain. **Journal of Dental Research,** v. 86, n. 9, p. 837-842, 2007.

SANTOS-SILVA, R. *et al.* Sao Paulo Epidemiologic Sleep Study: rationale, design, sampling, and procedures. **Sleep Medicine,** v. 10, n. 6, p. 679-685, 2009.

SEIDELL, J. C.; FLEGAL, K. M. Assessing obesity: classification and epidemiology. **British Medical Bulletin,** v. 53, n. 2, p. 238-252, 1997.

SHIN, C. *et al.* Association of habitual snoring with glucose and insulin metabolism in nonobese Korean adult men. **American Journal of Respiratory and Critical Care Medicine,** v. 171, n. 3, p. 287-291, 2005.

SMARDZ, J. *et al.* Influence of age and gender on sleep bruxism and snoring in non-apneic snoring patients: A polysomnographic study. **Journal of Sleep Research,** v. 30, n. 3, p. e13178, 2021.

SNORING Prevented by Excision of the Uvula. **Northwest Med Surg J,** v. 1, n. 9, p. 416, Jan 1853.

STUGINSKI-BARBOSA, J. *et al.* Agreement of the International Classification of Sleep Disorders Criteria with polysomnography for sleep bruxism diagnosis: a preliminary study. **The Journal of Prosthetic Dentistry,** v. 117, n. 1, p. 61-66, 2017.

SUZUKI, Y. *et al.* Changes in oxygen and carbon dioxide in the genesis of sleep bruxism: a mechanism study. **Journal of Prosthodontic Research,** v. 64, n. 1, p. 43-47, 2020.

SVENSSON, P.; LAVIGNE, G. Clinical bruxism semantics beyond academic debates: Normo-and patho-bruxism as a new proposal. **J Oral Rehabil**, v. 47, n. 5, p. 547-8, 2020.

TAVARES, A. *et al.* **Medicina do sono**: diagnóstico e manejo. Porto Alegre: Artmed, 2022.

TUFIK, S. *et al.* Obstructive sleep apnea syndrome in the Sao Paulo epidemiologic sleep study. **Sleep Medicine,** v. 11, n. 5, p. 441-446, 2010.

VAN DE LANGENBERG, S. C.; KOCEVSKA, D.; LUIK, A. I. The multidimensionality of sleep in population-based samples: a narrative review. **Journal of Sleep Research,** v. 31, n. 4, p. e13608, 2022.

VANDENBROUCKE, J. P. *et al.* Strengthening the Reporting of Observational Studies in Epidemiology (STROBE): explanation and elaboration. **Annals of Internal Medicine,** v. 147, n. 8, p. W-163-W-194, 2007.

VON ELM, E. *et al.* The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. **The Lancet,** v. 370, n. 9596, p. 1453-1457, 2007.

WIECKIEWICZ, M. *et al.* Genetic basis of sleep bruxism and sleep apnea: response to a medical puzzle. **Scientific Reports,** v. 10, n. 1, p. 7497, 2020.

WINOCUR, E. *et al.* Self-reported bruxism-associations with perceived stress, motivation for control, dental anxiety and gagging. **Journal of Oral Rehabilitation,** v. 38, n. 1, p. 3-11, 2011.

YAP, A. U.; CHUA, A. P. Sleep bruxism: Current knowledge and contemporary management. **Journal of Conservative Dentistry: JCD,** v. 19, n. 5, p. 383, 2016.

YOUNG, D. *et al.* Response time of pulse oximeters assessed using acute decompression. **Anesthesia and Analgesia,** v. 74, n. 2, p. 189-195, 1992.

ZHANG, C. *et al.* The role of dry mouth in screening sleep apnea. **Postgraduate Medical Journal**, v. 97, n. 1147, p. 294-298, 2021.

ZICARI, A. M. *et al.* Cephalometric pattern and nasal patency in children with primary snoring: the evidence of a direct correlation. **PLoS One,** v. 9, n. 10, p. e111675, 2014.

ZUCCONI, M. *et al.* Craniofacial cephalometric evaluation in habitual snorers with and without obstructive sleep apnea. **Otolaryngology: Head and Neck Surgery,** v. 109, n. 6, p. 1007-1013, 1993.

APÊNDICE A – Memorial Descritivo

Graduação

Iniciei minha graduação em agosto de 2013 após a aprovação no vestibular para a Universidade Federal de Santa Catarina (UFSC). Semestre de inúmeras novidades e desafios, que com muito estudo e horas de anatômico foi finalizado com sucesso. Após a ambientação com a faculdade, percebi a importâncias das atividades extracurriculares. No início de 2014 realizei a seleção para o Estágio no Centro de Cirurgia e Traumatologia Bucomaxilofacial UFSC no Hospital Universitário, seguindo do Estágio no Núcleo de Atendimento a Pacientes com Deformidade Facial da UFSC. Também realizei um semestre de Italiano no Curso Extracurricular de Línguas Estrangeira na UFSC.

Na quinta fase, em 2015, entrei para a equipe do Centro Brasileiro de Pesquisas Baseadas em Evidências (COBE), o qual sou membro atuante até hoje. Dentro do COBE, realizei trabalhos de monitoria nos cursos de Revisão Sistemática. Realizei uma palestra no Encontro Acadêmico sobre a Importância da Pesquisa Baseada em Evidências no auditório principal da UFSC. Nesse período auxiliávamos nos cursos de extensão de Revisão Sistemática, organizávamos reuniões semanais para membros da equipe, onde eram apresentados artigos para discussão. Reuniões essas que já eram um treinamento de apresentação e confecção de slides, além de fala e postura diante de uma plateia. Sou e sempre serei grata ao treinamento que recebi da equipe COBE. A importância do trabalho em equipe, comprometimento, pontualidade são ensinamentos que levarei para sempre em minha vida. Em 2017, realizei o projeto para obtenção de bolsa PIBIC, após aprovação de projeto, me tornei a primeira bolsista sob orientação da professora Graziela De Luca Canto. Através do PIBIC, realizei uma revisão sistemática escrita em inglês. Apresentei o trabalho na reunião da Sociedade Brasileira de Pesquisas Odontológicas- SBPqO no formato de painel, e a versão final já no formato da revista *Jornal of Oral Rehabilitation* foi apresentada como meu trabalho de conclusão de curso.

No último ano de faculdade já estava decidida a seguir na pós-graduação. Sempre admirei muito a professora Graziela De Luca Canto e queria seguir com esse aprendizado. Realizei o processo seletivo Programa de Pós-Graduação em Odontologia, com Área de Concentração em Clínica Odontológica Nível Mestrado, da Universidade Federal de Santa Catarina no final do meu último semestre e fui aprovada.

Pós-Graduação

O período do mestrado teve início em agosto de 2018, com a boa notícia de ter sido contemplada com a bolsa da Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES) devido a pontuação obtida por ser bolsista PIBIC. Nos anos seguintes (2019, 2020, 2021 e 2023), fui aprovada em primeiro lugar nos editais de seleção de bolsa CAPES.

Em busca da educação continuada em relação à língua inglesa, realizei dois semestres do curso Inglês Sem Fronteiras na UFSC, sendo um semestre totalmente focado no inglês aplicada à área da saúde. Nessa época realizei a prova do Toefl ITP e obtive pontuação 587, obtendo assim, o nível B2. Também realizei o curso presencial da *British Council* na Unisul – Tubarão, uma imersão de práticas e aulas totalmente em inglês.

No ano de 2019 realizamos a coleta de dados do nosso macroprojeto de pesquisa sobre "Bruxismo do sono e apneia obstrutiva no Hospital Baia Sul em Florianópolis". Resultando em dois artigos publicados e um em processo de submissão:

- Duarte *et al.* Is there an association of genetic polymorphisms of the catechol-O-methyltransferase gene (rs165656 and rs174675) and the 5-hydroxytryptamine receptor 2A gene (rs4941573 and rs6313) with sleep bruxism in individuals with obstructive sleep apnea? **Archives of Oral Biology**, v. 133, p. 105315, 2022.
- Gaio *et al.* Association between genetic polymorphisms in the melatonin receptor type 1 A gene and sleep bruxism. **Archives of Oral Biology**, v. 144, p. 105565, 2022.

Em processo de submissão na revista *Brazilian Oral Research:*

- -Pauletto *et al.* Is there an occurrence pattern between sleep bruxism and obstructive sleep apnea?

Em processo de submissão na *Journal of the American Dental Association*:

- Réus e al. Association between sleep bruxism and primary headaches: a descriptive study

As atividades no COBE continuaram ativas com grupos de estudos semanais e nossos cursos extensivos. Além disso, durante a pós comecei a ministrar aulas durantes os nossos cursos extensivos e intensivos.

Os projetos iniciados ainda na graduação e que possibilitaram o trabalho em equipe com importantes autores internacionais, tais quais: Jeffrey P. Okeson (*University of Kentucky*), Gilles J. Lavigne (*Université de Montréal*, Bruce Dick e Carlos Flores-Mir da *University of Alberta*, Efraim Winocur (*Tel Aviv University*), David Gozal (*University of Missouri*). Dessa parceria foram publicados os seguintes artigos:

- Pauletto *et al.* Sleep Bruxism and Obstructive Sleep Apnea: Association, Causality or Spurious Finding? A Scoping Review. **Sleep**, 2022.
- Pauletto *et al.* Critical appraisal of systematic reviews of intervention in dentistry published between 2019-2020 using the AMSTAR 2 tool. **Evidence-Based Dentistry**, 2022.
- Reus *et al.* Association Between Primary Headache and Bruxism: An Updated Systematic Review. **Journal of Oral & Facial Pain and Headache**, 2021.
- Bernhardt *et al.* Diagnostic Accuracy of Screening Questionnaires for Obstructive Sleep Apnoea in Adults in different Clinical Cohorts: A Systematic Review and Meta-analysis. **Sleep and Breathing**, 2021.
- Sanglard *et al.* Evaluating pain, fear, anxiety or stress/distress using children's drawings in paediatric dentistry: a scoping review**. European Archives of Paediatric Dentistry** (online), 2021
- Reus *et al.* Association between primary headaches and temporomandibular disorders. **Journal of the American Dental Association**, 2021.
- Polmann *et al.* Association between sleep disordered breathing and symptoms of attention deficits in adults: a systematic review. **Sleep Medicine**, 2020.
- Polmann *et al.* Association between sleep bruxism and stress symptoms in adults: A systematic review and meta-analysis. **Journal of Oral Rehabilitation**, 2020. ***(Top downloaded paper 2021-2022-Wiley***)
- Polmann *et al.* Association between sleep bruxism and anxiety symptoms in adults: a systematic review. **Journal of Oral Rehabilitation**, 2019. (Top downloaded paper 2018-2019-Wiley)

- Polmann *et al.* Prevalence of dentofacial injuries among combat sports participants: a systematic review and meta-analysis. Dental Traumatology, 2019.

Durante o segundo semestre de 2019, organizamos a I Conferência Brasileira de Pesquisas Baseadas em Evidências (COBRAPE) na cidade de Florianópolis. Palestrantes nacionais e internacionais estiveram presentes, como o professor Carlos Flores e o professor David Moher (*University of Ottawa*) e Profa. Vanessa Garcia-Larsen (*The Johns Hopkins Bloomberg School of Public Health*).

Realizei a defesa da minha dissertação de Mestrado com o trabalho "*Association between sleep bruxism and stress symptoms: a systematic review*" de modo remoto, devido a pandemia da Covid-19. O artigo com autores do COBE (Jéssica Réus, Carla Massignan e minha orientadora Graziela De Luca Canto), a professora Junia Serra-Negra (Universidade Federal de Minas Gerais) e os autores internacionais Bruce Dick, Carlos Flores-Mir (ambos *University of Alberta*) e Gilles Lavigne (*Université de Montréal*) foi publicado logo em seguida e já foi referenciado acima.

Logo após a defesa do mestrado, ingressei no programa de doutorado na UFSC. Devido a pandemia, todas as atividades continuaram sendo realizadas de modo remoto. Nesse período, juntamente com toda a equipe COBE trabalhamos para finalizar o livro "Revisões Sistemáticas da Literatura: guia prático" e o livro o "Risco de Viés em Revisões Sistemáticas: Guia Prático", em ambos pude contribuir com coautoria de três capítulos. Além disso, participei da escrita do "Capítulo 14 – Perspectivas Futuras para as Revisões Sistemáticas" no livro "Fundamentos Das Revisões Sistemáticas em Saúde", do professor Heitor Marques Honório.

No mesmo ano publiquei um relato de caso sobre osteonecrose medicamentosa com a equipe de Odontologia Hospitalar do Hospital Santa Catarina em Blumenau:

- Polmann *et al.* A maxillary reconstruction after osteonecrosis with surgical biomodels: A case report. **Advances in Oral and Maxillofacial Surgery**, v. 4, p. 100174, 2021.

Em 2023, foi publicado o livro "Uma abordagem GRADE para avaliação da certeza da evidência em revisões sistemáticas", no qual tive o prazer de compartilhar autoria com a

professora Caroline Martins-Pfeifer e professora Cristine Miron Stefani no capítulo sobre o domínio três: “Evidência indireta”.

Assim como nos anos anteriores, permaneço como integrante ativa do grupo COBE. Atuando como docente em cursos online, como curso de Revisão Sistemática e de Revisão de Escopo. O grupo também me permitiu atuar como coorientadora de discentes da graduação, e auxiliar a construção de trabalhos à nível de Mestrado. Atualmente temos dois protocolos de revisão sistemática em fase de submissão:

- “Bruxism in completely edentulous patients: a scoping review protocol”, vinculado ao Trabalho de Conclusão de Curso da aluna de graduação Daniela Bianchini Orlandi.
- “Clear Aligner’s Adverse Effects: a Systematic Review Protocol”, vinculado ao Trabalho de Conclusão de Curso da mestranda Cintia Ronchi Lemos.

Atividades Clínicas

Como pós-graduanda da área de Clínica Odontológica, sempre entendi a necessidade da formação além acadêmica, também prática. Para isso, acompanhei a professora Beatriz Mendes nas práticas clínicas do CEMDOR. Fui bolsista do Centro de Especialidades Odontológicas da UFSC, onde atuava clinicamente na área de Endodontia fazendo 10h semanais. Ainda, realizei novamente estágio ambulatorial no HU-UFSC no Centro de Cirurgia e Traumatologia Bucomaxilofacial.

Realizei atualizações voltados para Clínica Odontológica:

- Atualização em Cirurgia Oral menor – 2021 (80h);
- Atualização em Periodontia - ênfase em cirurgia plástica periodontal - 2021 (120h);
- Capacitação CEMDOR – 2021 (36h);
- Aperfeiçoamento em prótese convencional e prótese sobre implante – 2023 (180h).

Em julho de 2022, obtive aprovação em um processo seletivo da Secretaria de Estado da Administração Prisional e Socioeducativa de Santa Catarina, iniciando minha atuação como Cirurgiã Dentista generalista na Penitenciária Industrial de Blumenau. Durante seis meses, pude realizar diversos atendimentos no âmbito da atenção primária.

Experiência da docência

Conforme mencionado anteriormente, tive experiências significativas na área da docência. Atuei como professora durante os cursos do COBE, somando a outras experiências prévias e durante a pós-graduação.

Em parceria com outras monitoras do COBE, organizei e ministrei dois minicursos da "Semana de Ensino, Pesquisa e Extensão" nos anos de 2016 e 2018, seguidos por um curso de verão promovido pela PROEX em 2019, além de um hands-on no I Meeting Odontológico focado em aprimoramento de busca científica. Em 2019, minha colega Patrícia Pauletto e eu fomos convidadas a ministrar um workshop Universidade Estadual do Oeste do Paraná em Cascavel. Na ocasião, ministramos um curso de 16h para uma turma de mestrado e doutorado da pós-graduação em Biociência e Saúde.

Desde 2021, atuo como professora do Curso Técnico Instituto Hermann Blumenau. À nível de graduação, atuei durante três semestres na Unisociesc-Blumenau, nas disciplinas de Clínica Integrada, Morfologia de Cabeça e Pescoço, assim como Técnicas Cirúrgicas. Entre outubro de 2022 e julho de 2023, atuei como professora substituta na UFSC, nas Clínicas I, II e III, contribuindo ativamente nas áreas de Oclusão, DTM, Dentística e Periodontia. Desde agosto de 2023, sou docente na Uniasselvi, campus Blumenau, nas disciplinas de Estomatopatologia teórica e clínica, e na disciplina teórica Semiologia e Diagnóstico Bucal.

Reflexão

Ao longo da minha trajetória acadêmica, tanto como graduanda quanto como pós-graduanda, busquei ampliar meu conhecimento de maneira interdisciplinar. Assim, participei de estágios, monitorias e cursos realizados em diversas áreas da Odontologia. Entretanto, meu foco principal foi a área da Disfunção Temporomandibular. O estudo dessa área traz a necessidade do estudo avançado de Anatomia de Cabeça e Pescoço, Materiais Dentários, Terapêutica Medicamentosa, bem como a necessidade do estudo aprofundado de técnicas de Semiologia e Diagnóstico Bucal e Imaginologia.

A minha graduação me permitiu uma base sólida sobre conhecimentos teórico-práticos em todas as áreas da Odontologia. A pós-graduação permitiu um aprendizado intenso sobre pesquisa, docência e atividades de extensão, além do aprimoramento de práticas clínicas. A participação como membro do COBE foi essencial para o desenvolvimento e lapidação dessas atividades. O curso de Odontologia, pelo seu conteúdo prático elevado, gera a necessidade de um docente que entende e sabe o que faz. Portanto, todas as atividades

descritas nesse memorial foram essenciais no meu desenvolvimento como docente e cirurgiã-dentista.

Após 11 anos, finalizo a minha formação na UFSC, com 13 artigos publicados, 6 capítulos de livro escritos, e com mais de 30 cursos extracurriculares na área de revisão sistemática, estatística, idiomas (inglês e italiano), oratória e construção de material didático. Termino esse período grata, por ter tido uma formação sólida, cem por cento adquirida em uma universidade pública de qualidade.

ANEXO A – Artigo do periódico "Sleep Medicine", de Santos-Silva *et al.*

Sleep Medicine 10 (2009) 679–685

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Special Section in Sleep Medicine

Sao Paulo Epidemiologic Sleep Study: Rationale, design, sampling, and procedures

Rogerio Santos-Silva [a,*], Sergio Tufik [a], Silvia G. Conway [a], Jose Augusto Taddei [b], Lia Rita A. Bittencourt [a]

[a] Discipline of Medicine and Biology of Sleep, Department of Psychobiology, Univ Fed Sao Paulo – UNIFESP, Rua Napoleao de Barros 925, 1o andar, CEP 04024-002, Sao Paulo/SP, Brazil
[b] Discipline of Nutritional and Metabolism, Department of Pediatrics – Universidade Federal de Sao Paulo – UNIFESP, Sao Paulo, Brazil

ARTICLE INFO

Article history:
Received 11 September 2008
Accepted 1 November 2008
Available online 18 February 2009

Keywords:
Sleep epidemiologic profile
Sleep disorders
Population of Sao Paulo, Brazil
Polysomnography
Actigraphy

ABSTRACT

Objectives: To present the rational design, sampling, and procedures utilized in an Epidemiologic Sleep Study carried out in 2007 to establish the epidemiologic profile of sleep disorders in the adult population of a large metropolitan city, Sao Paulo, Brazil.
Methods: A population-based survey adopting a probabilistic three-stage cluster sample of Sao Paulo was used to represent the population according to gender, age (20–80 years), and socioeconomic class. Questionnaires, actigraphy, polysomnography (PSG), and blood samples were collected to investigate associations between sleep patterns and disturbances according to social-demographic status, activity/rest cycle, physical activity habits, mood disturbances, memory complaints, sexual dysfunction in males, drug addiction, genetic markers, and anthropometric, clinical, biochemical, hematological, endocrine, immunologic, and inflammatory indicators.
Results: A total of 1101 questionnaires were administered at home. A total of 156 volunteers were substituted, who were equivalent to the remaining sample in terms of age, gender, and socioeconomic class. A total of 1042 volunteers underwent PSG recordings at a Sleep Institute, and the refusal rate was 5.4%.
Conclusion: The Sao Paulo Sleep Study is a pioneering investigation, incorporating and integrating up-to-date methodologies for understanding sleep profiles and sleep disorders in large populations. This study will provide reliable information for the planning of health policies and programs aimed to control such disorders and their consequences in the city of Sao Paulo and similar urban environments.

1. Introduction

Although sleep medicine has existed for only four decades, the specialty has given rise to novel investigations and clinical research activities. Investigation of sleep epidemiology has helped to promote social, labor, and public policies supporting the recognition of the impact of sleep disorders on society. Population-based surveys featuring random sampling are defined as the gold standard to describe sleep disorders in the population [1]. Rarely are such studies feasible, however, because of ethical, methodological, operational, technical, and/or financial constraints. The available estimated sleep disorder prevalence presents a number of methodological limitations [2,3]. Differences in sampling schemes, disparities in techniques used for monitoring sleep, and variability in sleep disorders definitions can alter disease prevalence and potentially preclude a comprehensive estimate of both symptomatic and asymptomatic disorders [4–10]. Hence, methodologically comprehensive and sound investigations into the epidemiology of sleep are still lacking in the literature. While some of the initial studies presented most, if not all, of the above limitations, relatively consistent estimates of disease prevalence across several population cohorts have emerged [11,12].

The Sao Paulo Epidemiologic Sleep Study was thus implemented to (1) establish the epidemiologic profile of sleep disorders in the adult population of Sao Paulo in 2007; (2) investigate the associations between the population's sleep patterns and disorders related to social-demographic status, activity/rest cycle, eating and physical activity habits, mood disturbances, memory performance, male sexual dysfunction, alcoholism, drug addiction, genetic markers, and anthropometric, clinical, biochemical, hematological, endocrine, immunologic, and inflammatory indicators; and (3) compare the results collected in the current study with those of the Sao Paulo sleep surveys carried out in 1987 and 1995 [13] in order to assess secular trends in sleep disorders. The present paper presents the rational design, sampling, and procedures used in the Sao Paulo Epidemiologic Sleep Study.

2. Methods

2.1. The population under investigation

The city of Sao Paulo is the largest in the southern hemisphere and is located at the center of one of the major metropolitan re-

* Corresponding author. Tel.: +55 11 21490155; fax: +55 11 55725092.
E-mail address: roger.ss@psicobio.epm.br (R. Santos-Silva).

1389-9457/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.sleep.2008.11.001

gions of the globe. According to the National Institute of Demographics and Statistics (IBGE) (www.ibge.gov.br), its population reached 10,886,518 inhabitants living within 1524 km^2 in January 2008, corresponding to a population density of 7233 inhabitants/km [2]. Practically all ethnicities are represented in the city inhabitants because the slave trade from Africa and migrations from Europe and Asia in the 18th and 19th centuries led to miscegenation. The mean population age is 31.1 years, and 53% are females. There are great discrepancies in income and 38% of the population has a very low income of less than US$15,000 per year.

The study protocol was approved by the Ethics Committee for Research of the Universidade Federal de Sao Paulo at the Hospital Sao Paulo (CEP 0593/06) and registered with ClinicalTrials.gov (Identifier NCT00596713).

2.2. Sampling procedures

A sample size of 1056 volunteers was defined in order to allow for prevalence estimates with 3% precision [14]. To obtain a representative sample of the inhabitants of Sao Paulo, we used a probabilistic three-stage cluster sampling technique [15]. In the first stage, in order to assure the representativeness of different levels of wealth, we proportionally selected, from the four homogenous socio-economical regions of Sao Paulo, 96 districts from the 1500 districts in which the city is divided by the IBGE for censuses purposes. Slums and shantytowns were excluded due to high criminal activity. To consider recent changes in the number of households in each of the selected sectors, we visited and recounted every one before the selection. Households were selected if they were permanently occupied private homes, so clinics, schools, and other commercial and non-commercial establishments were excluded. In the second stage, the selection of a given household was made by randomly picking the first home and subsequently skipping a specified number, relative to the total number of raffled homes divided by a fixed number, in order to select 11 households in each sector. For example, in a sector with 110 households in which the household numbered 5 was the first randomly selected, the other selected homes should be the homes numbered 15, 25, 35, 45, 55, 65, 75, 85, 95, and 105. Each apartment in an apartment building was considered a home, and counting was carried out from the upper floor to the lower floor. Finally, in the third stage of sampling, all eligible dwellers of each picked house were ranged from the youngest to the oldest, and the subject was selected by means of 96 pre-established random tables, which had the rank number to be chosen for each of the 11 households, from the 96 selected districts. Pregnant and lactating women, people with physical or mental impairments that prevent self-care, individuals below 20 or over 80 years old, and people who work every night were not included in the household drawing. Substitutes were chosen in the home next door, following the same random selection criteria described above, in the following instances: three unsuccessful attempts to contact the target individual, total refusal to participate, obstruction by a family member, or inability to participate for a specified reason (e.g., travel, agenda, hospitalization).

2.3. Data collection instruments

Data were collected by questionnaires and objective methods. The questionnaires were organized into two blocks: the home instrument (HI) and the institutional instrument (II) (Table 1).

At the time of selection, volunteers read and signed the informed consent form, then answered the HI (Table 1). If the volunteer agreed to visit the Sleep Institute, he or she received an actigraph along with a sleep diary to be filled out for at least 72 consecutive hours. On the scheduled visit date, a driver from the Sleep Institute picked the volunteer up at a place of his/her choice about 2 h before his/her habitual bedtime. At the sleep lab, the volunteer had a light dinner before institutional data (including the II and PSG) were collected. The habitual bedtime hour was observed, and blood samples for biochemical, hematological, and genetic assays were collected on the following morning. After blood collection, the actigraph and completed sleep diary were returned, the volunteer was given breakfast, and he or she was driven back to the place of his or her choice. The results of the exams were made available to each volunteer by a physician of the Sleep Institute, who coordinated any necessary clinical follow-up.

2.4. Staff training and field procedures

2.4.1. HI questionnaires

To collect the HI and gather volunteers for participation, the DATAFOLHA® Institute was hired. In order to minimize inter-observer variation, no more than 10 DATAFOLHA interviewers were used throughout the data collection period between July and December 2007. DATAFOLHA interviewers were trained by the Institute staff in an 8-h course on the principles of sleep disorders and application methodology of the HI, in order to ensure uniform understanding among the interviewers. Part of the training included 2 h of psychodrama focused on motivation that was conducted by a specialized psychologist. To clarify the purpose of the study and to incite the participation of the sample volunteers, each interviewer went into the field carrying folders and a DVD player with a multimedia video describing the Sleep Institute and the study protocol procedures, with an emphasis on the PSG, which is unknown to many in the population. The interviewers also informed all the volunteers of the personal gains from their participation, which included a full check up (Table 2), a PSG, a bag for carrying their personal belongings for the overnight stay at the sleep lab, and R$75 (~US$40) as a reward for their night spent at the sleep lab. The average time taken to complete the HI was 25 min.

2.4.2. II questionnaires and objective methods

To collect the II, a group of 10 psychologists, three physical education teachers, and six ENT physicians were also trained on the 8-h course in order to (1) standardize their data-gathering techniques, and (2) promote team integration in performing the institutional protocol. The average time taken to complete the II was 45 min.

A team of 12 experienced PSG technicians was also trained to receive the volunteers and perform sleep recording. All PSG scoring was done by four trained technicians. Two nursing assistants were trained to collect the samples of blood included in the Sao Paulo Sleep Study protocol (Table 2).

2.5. Polysomnography

A complete full-night PSG was performed on a digital system (EMBLA® S7000, Embla Systems Inc., Broomfield, CO, USA) at the Sleep Institute, an 80-bed sleep lab (www.sono.org.br). All recording sensors were fixed to the patient in a non-invasive manner using tape or elastic bands. The following physiological variables were monitored simultaneously and continuously: four channels for the electroencephalogram (EEG) (C3-A2, C4-A1, O1-A2, O2-A1), two channels for the electrooculogram (EOG) (EOG-Left-A2, EOG-Right-A1), four channels for the surface electromyogram (muscle of the submentonian region, anterior tibialis muscle, masseter region, and seventh intercostal space), one channel for an electrocardiogram (derivation V1 modified), airflow detection via two channels through a thermocouple (one channel) and nasal pressure (one channel), respiratory effort of the thorax (one channel) and of the abdomen (one channel) via x-trace belts, snoring

Table 1
Summary of the questionnaires included in the home instrument and institutional instrument.

	Category	Characteristics
Home instrument	Socio-economic and Demographics [24]	Validated and structured questionnaire with 15 questions to sort the social classes in the Brazilian population
	"UNIFESP" Sleep Questionnaire [13]	Validated questionnaire with 59 questions concerning occupational routine and sleep problems and habits, utilized in surveys in the city of Sao Paulo in 1987 and 1995
	Pittsburgh Sleep Quality Index – PSQI [25]	Portuguese version of a 9-question instrument validated in English, providing a sleep quality score
	Insomnia Severity Index [26]	Portuguese version of a 5-question instrument validated in English concerning insomnia symptoms, providing a score for insomnia severity
	Berlin Questionnaire [27]	Portuguese version of a 9-question instrument validated in English, assessing patient risk for sleep apnea
Institutional instrument	General Sleep – last 6 months [28]	Selection of 21 questions by a panel of sleep specialists to ask about sleep habits, behaviors during sleep, subjective perception of sleep, and physical manifestations of sleep
	International Restless Legs Scale – IRLS [29]	Portuguese version of a 5-question scale validated in English, providing a score for the presence and impact of symptoms
	Bruxism (Sleep Institute – unpublished)	Seven questions to assess complaints associated with face pain and tooth grinding
	Epworth Sleepiness Scale [30]	Scale to evaluate daytime somnolence with 8 questions that describe daily situations
	Chalder Fatigue Scale [31]	Portuguese version of a 14-question scale validated in English measuring physical and mental fatigue
	Morningness-eveningness Questionnaire [32]	Portuguese version of an English questionnaire with 19 questions concerning morning–evening routine preferences
	ASSIST – Alcohol Smoking and Substance Involvement [33]	Portuguese version of an 8-question instrument validated in English, assessing patient risk of addiction
	General health [28]	Selection of six questions concerning general health
	Cardiovascular Questionnaire [34]	Five-question questionnaire adapted from a validated in English questionnaire concerning cardiovascular symptoms
	Respiratory Questionnaire [35]	Portuguese version of an 18-question instrument validated in English that investigates pulmonary function
	WHOQOL-BREF quality of life assessment [36]	Portuguese-validated questionnaire with 26 questions, providing scores for four domains related to quality of life: physical health, psychological, social relationships, and environment, besides overall quality of life and general health
	Prospective and Retrospective Memory Questionnaire – PRMQ [37]	Portuguese version of a 16-question instrument validated in English that investigates prospective and retrospective complaints regarding short- and long-term memory, triggered by internal and external clues
	Beck Anxiety Inventory – BAI [38]	Portuguese-validated questionnaire with 21 anxiety symptoms providing a classification of anxiety severity
	Beck Depression Inventory – BDI [38]	Portuguese-validated questionnaire with 21 items of depression symptoms providing a classification of depression severity
	Women's Questionnaire (Sleep Institute – unpublished)	Nineteen questions concerning menstrual cycles
	Men's Questionnaire (Sleep Institute – unpublished)	Eight questions concerning sexual and erection problems
	International Physical Activity Questionnaire – IPAQ version 6 [39]	Portuguese version of an 8-question instrument validated in English concerning habitual physical activity
	Pre sleep – previous day and night [28]	Selection of 26 questions by a panel of sleep specialists concerning aspects of the day preceding the PSG night that could influence sleep parameters
	Ear, nose, and throat assessment (Sleep Institute – unpublished)	Selection of 20 questions by a panel of ear, nose, and throat specialists concerning complaints and physical evaluation of upper airways and facial bone structure
	Pos sleep [28]	Selection of 19 questions by a panel of sleep specialists concerning the PSG night, such as discomfort, pain, and sleep perception
	Technical report [28]	Twenty four questions and additional notes concerning the PSG recording, filled out by PSG technician over the entire course of the night

(one channel) and body position (one channel) via EMBLA sensors, and arterial oxygen saturation (SaO2) and pulse rate via an EMBLA oximeter. All PSG were performed and sleep stages visually scored according to standardized criteria for investigating sleep [16]. EEG arousals, sleep-related respiratory events, and leg movements were scored in accordance with the criteria established by the American Academy of Sleep Medicine Manual for Scoring Sleep and Associated Events [17]. Four percent of all PSG were randomly rescored by a registered PSG technologist (RPSGT) in order to guarantee that all PSG scoring had been correctly executed.

2.6. Actigraphy

Actigraphy was based on monitoring the level of activity within the 24 h established in the protocol. The procedure made use of a sensor, placed on the wrist like a standard watch, which was able to store information about motor activity and rest. The volunteers wore the actigraph (Actiwach®-64, Respironics Inc. Co., USA) for at least three consecutive days, and the data were analyzed afterwards using the Actiware® 5.0 software. Data analysis assessed all parameters found in the pattern of the activity/rest cycle. Throughout the period that the volunteers wore the actigraph, they filled out a sleep diary containing information regarding sleep and activity. These data were compared to the actigraphy recording.

2.7. Ear, nose, and throat assessment

Ear, nose, and throat (ENT) assessments were made by four trained ENT physicians and included the investigation of nose complaints and a physical exam of the upper airways and facial bone structure by oroscopy and anterior rhinoscopy [18].

2.8. Physical measurements

General physical measurements were made immediately before preparation for the PSG hook-up following recommended procedures and utilizing precise instruments. Measurements were taken by two trained physical education teachers and included body weight (kg), height (m), calculation of body mass index (BMI) using the formula weight/height [2]; circumferences (cm) of the neck, waste, and hip [19]. Skinfold thickness (mm) at three regions (chest, abdomen, and thigh for male subjects; triceps, suprailium, and thigh for female subjects) [20] and blood pressure (mmHg) [21] were also measured.

2.9. Biochemical and hematological assays

Approximately 45 mL of venous blood was collected, and serum and plasma were obtained by conventional centrifugation. Analy-

Table 2
Summary of the assayed analytes.

Analyte	Method	Equipment/reagents
Hemogram	Peroxidase [40]	Advia® 120/Siemens Healthcare Diagnostics Inc., USA
Hemosedimentation speed (HSS)	Changed Westergeen [40]	Vesmatic 20® – Diesse Inc., USA
Uric acid	Uricase – enzymatic colorimetric [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Creatinin	Jaffe – kinetic [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Glycemia	Hexoquinase – UV – enzymatic colorimetric [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Cholesterol	Esterase-oxidase –enzymatic colorimetric [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
HLD cholesterol	Selective inhibition – enzymatic colorimetric [41]	Advia 1650/2400/Kovalent, Brazil
LDL and VLDL Cholesterol	Friedewald formula [42]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Triglycerides	Glycerol 3-phosphate dehydrogenase (GPDH) – enzymatic colorimetric [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Sodium	Ise-direct [43]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Potassium	Ise-direct [43]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Calcium	Arzenazo III – enzymatic colorimetric [44]	Advia 1650/2400/Synermed Int. Inc., USA
Magnesium	Magon – xilidil blue – enzymatic colorimetric [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Iron	Ferene – colorimetric [41]	Advia® 1650/2400/Kovalent, Brasil
Glutamyl ossalacetic transaminasis	L-malate – changed IFCC – kinetic enzymatic [41]	Advia® 1650/2400/Diasys Diagnostic System, Germany
Glutamyl pyruvic transaminasis	L-lactate – changed IFCC – kinetic enzymatic [41]	Advia® 1650/2400/Diasys Diagnostic System, Germany
Gamma glutamyl transferase (γ-GT)	*p*-Nitroanilide – kinetic enzymatic [41]	Advia® 1650/2400/Siemens Healthcare Diagnostics Inc., USA
Gonad axis stimulating hormone (PRL)	Acrinidine ester – chemiluminescence [45]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Luteinizing hormone (LH)	Acrinidin ester – chemiluminescence [46]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Follicle-stimulant hormone (FSH)	Acrinidin ester – chemiluminescence [46]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
17β-estradiol	Acrinidin ester – chemiluminescence [46]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Progesterone	Acrinidin ester – chemiluminescence [47]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Total testosterone	Acrinidin ester – chemiluminescence [46]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Thyroid-stimulating hormone (TSH)	Acrinidin ester – chemiluminescence [48]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Free thyroxine (T4)	Acrinidin ester – chemiluminescence [48]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Ferritin	Acrinidin ester – chemiluminescence [49]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Folic acid	Acrinidin ester – chemiluminescence [49]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Vitamin B12	Acrinidin ester – chemiluminescence [49]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Carcinogenic antigen (CA) 125	Acrinidin ester – chemiluminescence [50]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Prostate specific antigen (PSA)	Acrinidin ester – chemiluminescence [51]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Homocysteine	Acrinidin ester – chemiluminescence [52]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Immunoglobulin E	Acrinidin ester – chemiluminescence [53]	Advia Centaur®/Siemens Healthcare Diagnostics Inc., USA
Insulin	Adamantyl dioxetane phosphate ester – chemiluminescence [54]	Immulite® 2000/Siemens Healthcare Diagnostics Inc., USA
Cortisol	Adamantyl dioxetane phosphate ester – chemiluminescence [55]	Immulite® 2000/Siemens Healthcare Diagnostics Inc., USA
Tumor necrosis factor-alpha (TNF-α)	Adamantyl dioxetane phosphate ester – chemiluminescence [56]	Immulite® 1000/Siemens Healthcare Diagnostics Inc., USA
Interleukin-6	Adamantyl dioxetane phosphate ester – chemiluminescence [57]	Immulite® 1000/Siemens Healthcare Diagnostics Inc., USA
Interleukin-1β	Adamantyl dioxetane phosphate ester – chemiluminescence [58]	Immulite® 1000/Siemens Healthcare Diagnostics Inc., USA
Total grelin	Radioimmunoassay [59]	LINCO Research Inc., USA
Leptin	Radioimmunoassay [59]	LINCO Research Inc., USA
Free testosterone	Radioimmunoassay [60]	Siemens Healthcare Diagnostics Inc., USA
C-reactive protein	Nephelometry [41]	IMMAGE® Beckman Coulter, USA

ses were assayed by the Medicina Laboratorial/Associacao Fundo Incentivo a Psicofarmacologia (Table 2).

2.10. Genetic assays

Blood samples were collected from all participants in the study, and DNA was extracted from white cells [22]. We are currently analyzing polymorphisms in genes related to sleep regulation, including clock genes. Among the genes studied were hypocretin receptors 1 and 2, *Bmal1*, *Per3*, *Per2*, *Per1 Clock*, Casein quinases ε and δ, and angiotensin converting enzyme. Additionally, a blood sample was drawn from every volunteer and placed in PAXgene tubes (Pre-analytix, Hombrechtikon, Switzerland) for immediate stabilization of RNA. Blood was drawn and stored in tubes according to a standard protocol. The total RNA will be used to access microarray-based gene expression profiles (Affymetrix Inc., Santa Clara, CA, USA) for the conditions of interest and to investigate the expression of specific candidate genes using real-time quantitative PCR (Applied Biosystems, Foster City, CA, USA).

2.11. Pre-test

In order to check for all procedures and verify that the planned activities could be executed adequately, a pre-test was completed on 45 volunteers 1 month before the data gathering for the study began. This pre-test included all procedures, from the selection of

volunteers to the analysis of data consistency. The pre-test allowed fine-tuning of the study protocol.

2.12. Questionnaires quality assessment

To verify the quality of HI responses, 30% of the volunteers were asked 10 questions from the HI again by phone. To verify the II answers, six selected questions were repeated to 10% of the volunteers by an independent and blinded interviewer.

2.13. Data handling

Data collected in the HI and II were typed into SPHINX® v5 software files (SphinxBrasil, Canoas, RS, Brazil). This provides filter criteria to ensure that entered data fell within a plausible range of variation. Data were double-entered by two typing experts on sleep data in order to reduce mistakes. After the double entry, both databases were compared for each entered variable. Any disagreement was corrected by consulting the actual questionnaires or exam sheets.

Descriptive statistics for every variable were generated to check for outliers, and corrections were applied where appropriate.

A final data bank with all data (a total of 856 variables plus one weight variable for sample expansion) was generated. Subfiles will be created from this to provide data for focused investigations into specific components of the sleep study.

2.14. Statistical analysis

Because the study involved structurally complex probabilistic sampling, inferential statistical methods should be adequate for the sampling plan. Classical statistical techniques do not apply to this set of data because independence among sample units cannot be assumed. The assessments made for variability and precision, as well as for intervals (reliability intervals), must employ methods like linearization by a Taylor series to avoid underestimation bias [15].

The techniques shall be described according to the various goals that are proposed at the start of the study. Multivariate techniques shall be employed in the analysis of the associations and interactions among several variables. Factorial analysis and multiple correspondence analyses shall be used to analyze latent and construed variables, such as somnolence and sleep architecture. These techniques include the identification and classification of groups of individuals, discriminate analysis, and hierarchal grouping of algorithms.

When comparing studies from each decade (1987, 1995, and 2007 surveys), pseudo-panel analysis techniques shall be employed since the same population is under investigation. These techniques shall be adopted in comparisons of averages or proportions of the results, thereby allowing for temporal analysis of the results.

In addition, descriptive methods will be employed in order to provide a complete, easy-to-read description so that the data collected in the epidemiologic survey can be understood in their entirety. All analysis will be performed utilizing the STATA 10 software (Stata Survey Data Reference Manual. STATA Corporation; Texas, 2007).

3. Results

Data gathering, including pre-test procedure, lasted from July 2nd to December 22nd, 2007. A total of 1101 HI questionnaires were applied (1056 sample volunteers plus 45 pre-test volunteers). To reach the total sample, 165 volunteers were substituted after three unsuccessful attempts to contact the target individual, total refusal to participate, obstruction by a family member, or inability to participate for a specified reason (e.g., travel, agenda, hospitalization). A test of homogeneity [23] comparing the three categories of sample individuals (original volunteers, pre-test volunteers, and substitutes) was performed for age ($p < 0.01$), gender ($p = 0.24$), and socioeconomic class ($p = 0.5$) compositions and showed no statistical significance (Table 3) except for the age composition of the small pre-test group, which was higher in the 20–39 years old class. Based on those results, we concluded that the substitutes did not introduce significant selection bias, and also the small pre-test sample could be considered as units to compose the final sample. A total of 1042 volunteers underwent PSG at the Sleep Institute (1008 volunteers plus 34 pre-test volunteers), with a very low refusal rate of 5.4%. Age ($p = 0.11$), gender ($p = 0.55$), socioeconomic class ($p = 0.38$), and Pittsburgh Sleep Quality Index ($p = 0.65$) distributions were not statistically different between volunteers who accepted and refused PSG recording.

Applying the generated sample weight, we reach the distribution by gender, age group and socioeconomic class for the population of Sao Paulo which matched the demographic projections for the city inhabitants in 2007 derived from the 2000 city census.

The random rescoring of 4% of all PSG recordings showed an agreement rate of 93.3 ± 5.1%, Kappa 0.91 ± 0.03, which guaranteed PSG scoring reliability.

A total of 561 volunteers agreed to wear the actigraph for at least three consecutive days before the PSG night. The refusal rate

Table 3
Distributions of proportions and 95% CI for the three categories of final sample individuals by age group, gender, and socioeconomic class.

	Volunteers ($n = 891$)	Pre-test volunteers ($n = 45$)	Substitute volunteers ($n = 165$)	Total ($n = 1101$)
Ages[*]				
20–29 years	24.91 (22.29; 27.73)	**33.89** (**27.88**; **40.48**)	23.73 (18.61; 29.75)	25.15 (22.81; 27.66)
30–39 years	24.67 (21.37; 28.29)	**29.95** (**25.99**; **34.24**)	20.31 (16.33; 24.95)	24.21 (21.36; 27.32)
40–49 years	21.48 (19.58; 23.51)	5.422 (1.901; 14.5)	24.11 (19.52; 29.38)	21.13 (18.84; 23.62)
50–59 years	15.48 (12.82; 18.56)	12.01 (10.36; 13.88)	16.69 (12.16; 22.48)	15.51 (13.2; 18.13)
60–69 years	9.336 (7.251; 11.94)	14.36 (10.82; 18.81)	5.72 (3.40; 9.44)	8.99 (7.18; 11.2)
70–80 years	4.12 (2.515; 6.699)	4.366 (2.138; 8.71)	9.447 (5.722; 15.21)	5.002 (3.329; 7.451)
Gender[**]				
Female	54.13 (49.93; 58.26)	45.77 (42.62; 48.96)	53.41 (46.2; 60.48)	53.61 (49.88; 57.29)
Male	45.87 (41.74; 50.07)	54.23 (51.04; 57.38)	46.59 (39.52; 53.8)	46.39 (42.71; 50.12)
Socioeconomic class[#]				
A	10.43 (8.362; 12.94)	7.161 (3.776; 13.16)	13.84 (8.417; 21.91)	10.83 (8.675; 13.44)
B	40.64 (37.58; 43.78)	47.82 (34.01; 61.97)	40.16 (32.58; 48.24)	40.91 (38.08; 43.79)
C	40.74 (37.86; 43.69)	36.91 (24.42; 51.44)	40.24 (29.95; 51.46)	40.48 (37.11; 43.94)
D/E	8.186 (6.603; 10.11)	8.111 (6.601; 9.929)	5.767 (3.356; 9.734)	7.789 (6.341; 9.534)

Pearson Chi-Square test for homogeneity, p value: [*]$Chi^2 = 23.6688$ $p < 0.01$. [**]$Chi^2 = 1.4070$ $p = 0.24$. [#]$Chi^2 = 4.2451$ $p = 0.5$.

for this procedure reached high proportions (50.9%), which may hinder the representativeness for the population of Sao Paulo in estimates regarding the patterns of activity/rest cycle by actigraphy.

4. Discussion

The Sao Paulo Epidemiologic Sleep Study is a pioneering investigation incorporating and integrating up-to-date methodologies to provide greater understanding of sleep profiles and sleep disorders in large populations. This study will provide reliable information for the planning of health policies and programs aimed to control such disorders and their consequences in the city of Sao Paulo and similar urban environments.

The use of objective assessments of sleep patterns and disorders by PSG and actigraphy in a representative sample from one of the major cities of the globe, along with the description of the secular trends provided by previous surveys using the same questionnaire, will permit the establishment of associations between the prevalence of sleep disorders and major environmental and population behavior patterns over the last three decades. Such information may also allow for predictions of the future prevalence of sleep disorders in different ecological and environmental scenarios.

Acknowledgments

We would like to thank the Associaçao Fundo de Incentivo a Psicofarmacologia (AFIP) and the Fundacao de Apoio a Pesquisa do Estado de Sao Paulo (FAPESP) for their financial support in the current study, and Fernando Antonio Basili Colugnati for statistical analyses support.

References

[1] Deaton A. The analysis of household surveys: a microeconomic approach to development policy. Washington, DC: The International Bank for Reconstruction and Development/The World Bank; 1997.
[2] Punjabi NM. The epidemiology of adult obstructive sleep apnea. Proc Am Thorac Soc 2008;5:136–43.
[3] Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev 2002;6:97–111.
[4] Bixler EO, Vgontzas AN, Have T, Tyson K, Kales A. Effects of age on sleep apnea in men. Am J Respir Crit Care Med 1998;157:144–8.
[5] Bixler EO, Vgontzas AN, Lin H, Ten Have T, Rein J, Vela-Bueno A, et al. Prevalence of sleep-disordered breathing in women: effects of gender. Am J Respir Crit Care Med 2001;163:608–13.
[6] Udwadia ZF, Doshi AV, Lonkar SG, Singh CI. Prevalence of sleep-disordered breathing and sleep apnea in middle-aged urban Indian men. Am J Respir Crit Care Med 2004;169:168–73.
[7] Ip MSM, Lam B, Lauder IJ, Tsang KW, Chung KF, Mok YW, et al. A community study of sleep-disordered breathing in middle-aged Chinese men in Hong Kong. Chest 2001;119:62–9.
[8] Ip MSM, Lam B, Tang LCH, Lauder IJ, lp TY, Lam WK. A community study of sleep-disordered breathing in middle-aged Chinese women in Hong Kong: prevalence and gender differences. Chest 2004;125:127–34.
[9] Bearpark H, Elliott L, Grunstein R, Cullen S, Schneider H, Althaus W, et al. Snoring and sleep apnea. A population study in Australian men. Am J Respir Crit Care Med 1995;151:1459–65.
[10] Durán J, Esnaola S, Rubio R, Iztueta Á. Obstructive sleep apnea-hypopnea and related clinical features in a population-based sample of subjects aged 30 to 70 ys. Am J Respir Crit Care Med 2001;163:685–9.
[11] Quan SF, Howard BV, Iber C, Kiley JP, Nieto FJ, O'Connor GT, et al. The sleep heart health study: design, rationale, and methods. Sleep 1997;20:1077–85.
[12] Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342:1378–84.
[13] Pires MLN, Benedito-Silva AA, Mello MT, Del Giglio S, Pompeia C, Tufik S. Sleep habits and complaints of adults in the city of São Paulo, Brazil, in 1987 and 1995. Braz J Med Biol Res 2007;40:1505–15.
[14] Marques RM, Berquó ES. Considerações sobre os modelos causais. Cebrap 1975;11:89–121.
[15] Kish L. Survey sampling. New York: John Wiley & Sons Inc.; 1965.
[16] Rechtschaffen A, Kales A. A manual of standardized terminology: techniques and scoring system for sleep stages of human subjects. Los Angeles: Brain Information Service/Brain Research Institute; 1968.
[17] Iber C, Ancoli-Israel S, Chesson Jr A, Quan S. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester: American Academy of Sleep Medicine; 2007.
[18] Ridley MB. Aesthetic facial proportions. In: Pape ID, Nachlis NE, editors. Facial plastic and reconstructive surgery. St. Louis: Mosby – Year Book; 1992.
[19] Heyward VH. Advanced fitness assessment & exercise prescription. Champaign: Human Kinetics; 2006.
[20] Siri WE. Body composition fluid spaced and density. In: Brozek J, Hanschel A, editors. Techniques for measuring body composition. Washington, DC: Natl. Acad. Sci.; 1961.
[21] American College of Sports Medicine. ACSM's guidelines for exercise testing and prescription. American College of Sports Medicine; 2005.
[22] Miller VT, Nath R, Kwaan HC, Nishiura B. Reproducibility of two in vivo tests of platelet function. Thromb Res 1988;52:507–15.
[23] Kleinbaum DG, Kupper LL, Muller KE, Nizam A. Applied regression analysis and other multivariable methods. Pacific Grove: Brooks/Cole Publishing Company; 1998.
[24] Associação Brasileira de Empresas de Pesquisa – ABEP. Critério de Classificação Econômica Brasil (CCEB); 2003.
[25] Buysse DJ, Reynolds 3rd CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh sleep quality index: a new instrument for psychiatric practice and research. Psychiatry Res 1989;28:193–213.
[26] Morin CM. Insomnia: psychological assessment and management. New York: Guilford Press; 1993.
[27] Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin questionnaire to identify patients at risk for the sleep apnea syndrome. Am Intern Med 1999;131:485–91.
[28] Bittencourt LRA, Silva RS, Conway SG. Laboratório do sono – Estrutura física e pessoal, técnica polissonográfica, questionário de sono e banco de dados. Sao Paulo: Associacao Fundo de Incentivo a Psicofarmacologia – AFIP; 2005.
[29] Abetz L, Arbuckle R, Allen RP, Garcia-Borreguero D, Hening W, Walters AS, et al. The reliability, validity and responsiveness of the international restless legs syndrome study group rating scale and subscales in a clinical-trial setting. Sleep Med 2006;7:340–9.
[30] Johns MW. A new method for measuring daytime sleepiness: the epworth sleepiness scale. Sleep 1991;14:540–5.
[31] Chalder T, Berelowitz G, Pawlikowska T, Watts L, Wessely S, Wright D, et al. Development of a fatigue scale. J Psychosom Res 1993;17:147–53.
[32] Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness–eveningness in human circadian rhythms. Int J Chronobiol 1976;4:97–110.
[33] WHO ASSIST Working Group. The alcohol, smoking and substance involvement screening test (ASSIST): development, reliability and feasibility. Addiction 2002;97:1183–94.
[34] Wang TH, Bhatt DL, Fox KA, Steinhubl SR, Brennan DM, Hacke W, et al. An analysis of mortality rates with dual-antiplatelet therapy in the primary prevention population of the CHARISMA trial. Eur Heart J 2007;28:2200–7.
[35] Ferris BG. Epidemiology standardization project (American Toracic Society). Am Rev Respir Dis 1978;118:1–120.
[36] Skevington SM, Lotfy M, O'Connell KA. The World Health Organization's WHOQOL-BREF quality of life assessment: psychometric properties and results of international field trial – a report from the WHOQOL group. Qual Life Res 2004;13:299–310.
[37] Crawford JR, Henry JD, Ward AL, Blake J. The prospective and retrospective memory questionnaire (PRMQ): latent, structure, normative data, and discrepancy analysis for proxy-ratings. Br J Clin Psychol 2006;45:83–104.
[38] Cunha JA. Manual da versão em português das Escalas Beck. Sao Paulo: Casa do Psicologo; 2001.
[39] Craig CL, Marshall AL, Sjöström M, Bauman AE, Booth ML, Ainsworth BE, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc 2003;35:1381–95.
[40] Wintrobe MM. Hematologia Clinica. Buenos Aires: Intermedica; 1969.
[41] Tietz NW. Clinical guide to laboratory tests. Philadelphia: WB Saunders Company; 1995.
[42] Friedewald WT, Levi RI, Fredrickson DS. Estimation of the concentration of low density lipoproteins cholesterol in plasma without use of the use of the ultracentrifuge. Clin Chem 1972;18:499–502.
[43] Eisenman G. Glass electrodes for hydrogen and other captions. Principles and practice. New York: Marcel Dekker Inc.; 1967.
[44] Jacobs DS, DeMott WR, Oxley DK. Laboratory test handbook. Cleveland: Lexi-Cop Inc.; 1996.
[45] Ashby CD. Prolactin. In: Kaplan LA, Presce AJ, editors. Methods in clinical chemistry. St. Louis: CV Mosby; 1987.
[46] Kicklighter EJ, Norman RJ. The gonads. In: Kaplan LA, Presce AJ, editors. Clinical chemistry: theory, analysis and correlation. St. Louis: CV Mosby; 1989.
[47] Chattoraj SC, Watts NB. Endocrinology. In: Tietz NW, editor. Fundamentals of clinical chemistry. Philadelphia: WB Saunders; 1987.
[48] Chen IW, Sperling MI. Thyroxine. In: Kaplan LA, Presce AJ, editors. Clinical chemistry: theory analysis and correlation. St. Louis: CV Mosby; 1989.
[49] Mieale JB. Laboratory medicine: hematology. St. Louis: CV Mosby; 1982.
[50] Schwartz MK. Cancer markers. In: De Vita VT, Hellman S, Rosenberg SA, editors. Cancer: principals and practice of oncology. JB Lippincott Company; 1993.
[51] National Committee for Clinical Laboratory Standards – NCCLS. Primary reference preparations used to standardize calibration of immunochemical

assays for serum prostate antigen (PSA) approved guideline. Wayne, PA: NCCLS; 1997.
[52] Ueland PM, Refsum H, Stabler SP, Malinow MR, Andersson A, Allen RH. Total homocysteine in plasma or serum: methods and clinical applications. Clin Chem 1993;39:1764–79.
[53] Kjelman NIM, Johansson SGO, Roth A. Serum IgE levels in healthy children by a sandwich technique (PRIST). Clin Allergy 1976;6:51–9.
[54] Dods RF. Diabetes mellitus. In: Kaplan LA, Presce AJ, editors. Clinical chemistry: theory, analysis and correlation. St. Louis: CV Mosby; 1996.
[55] Pudek MR. Adrenal hormones. In: Kaplan LA, Presce AJ, editors. Clinical chemistry: theory analysis and correlation. St. Louis: CV Mosby; 1989.
[56] Vilcek J, Lee TH. Tumor necrosis factor. New insights into the molecular mechanisms of its multiple actions. J Biol Chem 1991;266:7313–6.
[57] Hirano T, Akira S, Taga T, Kishimoto T. Biological and clinical aspects of interleukin-6. Immunol Today 1990;11:443–9.
[58] Lomedico PT, Gubler U, Hellmann CP, Dukovich M, Giri JG, Pan YC, et al. Cloning and expression of murine interleukin-1 cDNA in *Escherichia coli*. Nature 1984;312:458–62.
[59] Feldman H, Rodbard D. Mathematical theory of radioimmunoassay. In: Odell WD, Doughaday WH, editors. Principles of competitive protein-binding assays. Philadelphia: JB Lippincott Company; 1971.
[60] McCann D, Kirkish L. Evaluation of free testosterone in serum. J Clin Immunol 1985;8:234–6.