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Katedra i Klinika Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii
Klinicznej Uniwersytetu Medycznego we Wrocławiu

Ocena wpływu wybranych używek na nasilenie bruksizmu sennego oraz architekturę snu w badaniach polisomnograficznych

Weronika Frosztęga

ROZPRAWA DOKTORSKA

Cykl publikacji powiązanych tematycznie

PROMOTOR

dr. hab. Helena Martynowicz, prof. UMW

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Mojej promotorce, dr. hab. Helenie Martynowicz, prof. UMW, pragnę złożyć najszczersze podziękowania za inspirację, wiarę w moje możliwości, wsparcie w procesie twórczym, chęć dzielenia się wiedzą a także za możliwość poszerzania horyzontów.

Ponadto pragnę podziękować moim przyjaciołom, na których zawsze mogłam liczyć i którzy nigdy we mnie nie zwątpili w procesie twórczym.

„Kto chce zapalać innych, sam musi płonąć.” – Ludwik Hirszfeld

Pracę dedykuję mojej Mamie. Dziękuję za nieustanne wsparcie i motywację do działania.

Spis treści

1. Cykl prac stanowiących pracę doktorską

1) Frosztęga W, Więckiewicz M, Nowacki D, Michałek-Zrąbkowska M, Poręba R, Wojakowska A, Kanclerska J, Mazur G, Martynowicz H

Polysomnographic Assessment of Effects of Tobacco Smoking and Alcohol Consumption on Sleep Bruxism Intensity.

Journal of Clinical Medicine, 2022, vol. 11, nr 24, art.7453 [13 s.], DOI:10.3390/jcm11247453

IF= 3,9 Pkt. MEiN: 140,00

2) Frosztęga W, Więckiewicz M, Nowacki D, Poręba R, Lachowicz G, Mazur G, Martynowicz H

The effect of coffee and black tea consumption on sleep bruxism intensity based on polysomnographic examination.

Heliyon, 2023, e16212 [10 s.], DOI:10.1016/j.heliyon.2023.e16212

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3) Frosztęga W, Więckiewicz M, Gać P, Lachowicz G, Poręba R, Mazur G, Martynowicz H

The effect of cadmium on sleep parameters assessed in polysomnographic studies: a case–control study.

Journal of Clinical Medicine, 2023, vol. 12, nr 12, art.3899 [12 s.], DOI:10.3390/jcm12123899

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2. Wykaz skrótów

SB	Sleep Bruxism	Bruksizm senny
OSA	Obstructive sleep apnea	Obturacyjny bezdech senny
PSG	Polysomnography	Polisomnografia
BEI	Bruxism episode index	Wskaźnik epizodów bruksizmu
REM	Rapid eye movement	Faza szybkich ruchów gałek ocznych
NREM	Non-rapid eye movement	Faza wolnych ruchów gałek ocznych
AHI	Apnea-hypopnea index	Wskaźnik bezdechów i spłyceń oddychania
ODI	Oxygen desaturation index	Wskaźnik desaturacji
PLMS	Periodic limb movement disorder	Okresowe ruchy kończyn podczas snu
SL	Sleep latency	Latencja snu
WASO	Wake after sleep onset	Czuwanie wtrącone
SE	Sleep efficiency	Wydajność snu
AI	Arousal index	Wskaźnik wzbudzeń
HR	Heart rate	Częstość akcji serca
IF	Impact factor	Współczynnik wpływu

3. Omówienie rozprawy doktorskiej

3.1 Wstęp

Sen jest neurofizjologicznym procesem charakteryzującym się obniżoną aktywnością umysłową i fizyczną. Funkcja snu nie została jeszcze całkowicie poznana. Ustalono, że sen jest niezbędny do uzupełnienia energii, utrzymania stabilności synaptycznej, zachowania funkcji immunologicznych i usuwania odpadów neurotoksycznych. Zarówno odpowiednia jakość snu jak i czas jego trwania są niezbędne do zachowania dobrostanu psychicznego, fizycznego i społecznego.

Sen jest uporządkowanym zjawiskiem składającym się z 4 lub 5 powtarzających się cyklów. Jeden cykl snu trwa zazwyczaj pomiędzy 45 a 120 minut, średnio 90 minut i składa się z następujących po sobie faz snu non-REM (*rapid eye movements;* szybkie ruchy gałek ocznych): N1, N2 i N3 oraz fazy snu REM. Przejście ze stanu czuwania do snu N1 jest nazywane zasypianiem, przy czym zaśnięcie jest definiowane jako pojawienie się co najmniej 15 sekund snu w 30 sekundowej składce polisomnograficznej. Faza snu N1 jest najpłytszą z faz snu, której towarzyszą wolne ruchy gałek ocznych i stanowi 5-10% całkowitego czasu snu. W trakcie tej fazy pojawiają się kilkusekundowe okresy snu, które się stopniowo wydłużają, a okresy czuwania stopniowo się skracają. Przejście w fazę snu N2 zachodzi w przeciągu kilku minut. Charakteryzuje się ona postępującym spadkiem napięcia mięśniowego i charakterystycznymi zmianami w zapisie EEG, tj. wrzecion snu i kompleksów K. Faza snu N2 trwa ponad połowę całkowitego czasu snu. Faza snu N3 nazywana jest snem głębokim, wolnofalowym, trwającym do 20% całkowitego czasu snu. Faza ta jest niezbędna do skutecznej regeneracji organizmu, naprawy materiału genetycznego i odnowy komórkowej. Następnie fale wolne zanikają i pojawia się faza snu szybkich ruchów gałek ocznych (REM), zazwyczaj po 90-120 minutach snu. Charakterystyczne dla tej fazy jest pojawienie się atonii mięśniowej, nieregularnego rytmu oddechowego, zmian rytmu tętna, wartości ciśnienia tętniczego i występowanie marzeń sennych. Sen REM obejmuje 20-25% całkowitego czasu snu.

Pomiędzy fazami snu, nieodłącznym zjawiskiem w trakcie snu są tzw. wzbudzenia, występujące fizjologicznie do 5 razy na godzinę. Wzbudzenie jest wzrostem częstotliwości fal mózgowych trwającym między 3 a 15 sekund zwykle z towarzyszącym wzrostem częstości

rytmu serca. Wskaźnik wzbudzeń jest w istocie wyrazem fragmentacji snu, która w świetle ostatnich badań stanowi nowy czynnik ryzyka sercowo-naczyniowego.

U młodszych osób wybudzenia są krótsze, często nie pozostawiające śladów pamięciowych. Natomiast osoby starsze doświadczają dłuższych wybudzeń, które są przez nie pamiętane i mogą trwać nawet 30-45 minut. Wybudzenia podobnie jak wzbudzenia są również a markerami fragmentacji snu.

Jakość i ilość snu pełnią niezwykle istotną rolę w utrzymaniu homeostazy organizmu. Niedobór snu, zazwyczaj definiowany jako czas snu poniżej 6 godzin na dobę, prowadzi do zwiększenia aktywności współczulnej i niedostatecznego nocnego obniżenia ciśnienia krwi, co sprzyja rozwojowi nadciśnienia tętniczego. Ponadto, deprywacja snu związana jest z przyspieszeniem rozwoju procesów miażdżycowych, upośledzeniem tolerancji glukozy i wrażliwości na insulinę.

Rezultatem pogorszenia jakości snu są zaburzenia metaboliczne, wzrost apetytu na pokarmy wysokoenergetyczne, wzrost wydzielania tzw. hormonów stresu (amin katecholowych, kortyzolu), otyłość, i w konsekwencji wzrost ryzyka sercowo-naczyniowego. Zaburzenia snu dotyczą nawet 2 miliardów populacji generalnej. Do najczęstszych zaburzeń snu zaliczamy bezdech senny oraz bruksizm senny. Ze względu na ich częste rozpowszechnienie w społeczeństwie, coraz większą uwagę przykłada się do diagnostyki i leczenia zaburzeń snu. Bruksizm senny jest zaburzeniem ruchowym występującym w trakcie snu, które dotyczy nawet 8% populacji. Ze względu na niską rozpoznawalność tego zaburzenia oraz ze względu na częste występowanie masek tego schorzenia pod postacią bólów głowy, bezsenności czy przewlekłego zmęczenia, problem ten jest niedoszacowany. Patofizjologia bruksizmu sennego, ze względu na jego złożoną etiologię jest nadal niepewna i niedostatecznie zbadana. Ze względu na rosnące znaczenie bruksizmu sennego w medycynie, w 2013 roku międzynarodowy zespół ustalił nowy konsens dotyczący definicji bruksizmu sennego jako „powtarzającą się aktywność mięśni narządu żucia, która charakteryzuje się zaciskaniem, zgrzytaniem zębami lub wypychaniem lub usztywnianiem żuchwy”. W następnych latach definicja ta uległa ewolucji, ukazując bruksizm senny nie jako zaburzenie, a jako zachowanie ruchowe zagrożone pewnymi konsekwencjami klinicznymi u zdrowych osób. Konsekwencje bruksizmu sennego związane są ze ścieraniem się zębów, zaburzeniami funkcji stawu skroniowo-żuchwowego czy bólami głowy. Jednakże oprócz stomatologicznych konsekwencji, obserwuje się także zaburzenia ogólnoustrojowe takie jak zaburzenia snu, wzrost ciśnienia

tętniczego czy zaburzenia rytmu serca. Najnowsze badania wskazują na częste współwystępowanie bruksizmu i bezdechu sennego. Szacuje się, że aż około 50 % pacjentów z bezdechem sennym cierpi również na bruksizm senny.

W Polsce problem obturacyjnego bezdechu sennego dotyczy 2.5 miliona ludzi. Jest to schorzenie polegające na wielokrotnie powtarzających się epizodach obturacji górnych dróg oddechowych podczas snu prowadzących do spadków stężenia tlenu we krwi, wzrostu częstości akcji serca i ciśnienia tętniczego oraz powtarzających się wzbudzeń skutkujących fragmentacją snu. Czynniki ryzyka bezdechu sennego obejmują przede wszystkim otyłość, wiek, płeć męską, stan po menopauzie, powiększenie migdałków podniebiennych, przerost języczka, zwiększony obwód kołnierzyka, retro- i mikrognację, makroglosję oraz deformacje twarzoczaszki. Najpoważniejszymi powikłaniami bezdechu sennego jest nadciśnienie tętnicze, udar mózgu, zawał serca, zaburzenia rytmu serca oraz wypadki komunikacyjne spowodowane zaśnięciem za kierownicą.

Diagnostyka bruksizmu sennego jest skomplikowaną procedurą. Prawdopodobną diagnozę można postawić na podstawie zebrania dokładnego wywiadu lekarskiego, często z pomocą ankiet. Jednakże, aby postawić definitywną diagnozę tego zaburzenia ruchowego, niezbędne jest zastosowanie badania instrumentalnego, optymalnie badania polisomnograficznego, uznanego jako złoty standard w diagnostyce bruksizmu sennego. Jest to badanie czasochłonne i skomplikowane, oparte na rejestrowaniu zaburzeń snu przez całą noc i wymagające opisania wyników przez wykwalifikowanego i doświadczonego lekarza polisomnografistę. Badanie to obejmuje elektroencefalografię, elektrookulografię, elektrokardiografię i elektromiografię mięśnia podbródkowego/nadgnykowego, piszczelowego przedniego oraz mięśni żwaczy i mięśni skroniowych. Analizowany jest zapis elektromiograficzny, obraz kamery oraz zapis audio, w celu identyfikacji odgłosów zgrzytania zębami. Ponadto polisomnografia obejmuje analizę przepływu oddechowego, wysiłku oddechowego, pulsoksymetrię, aktywność ruchową i pozycję ciała.

Używki to substancje niebędące lekami charakteryzujące się wpływem na organizm człowieka poprzez działanie na ośrodkowy układ nerwowy. Używki można podzielić na legalne i nielegalne. Kawa, czarna herbata, alkohol i papierosy zaliczane są do legalnych substancji wpływających na układ nerwowy człowieka. Pomimo podziału ze względu na legalność substancji, należy pamiętać o zagrożeniach wynikających z możliwości uzależnienia się od konkretnej substancji jak i o ryzyku przedawkowania.

Picie kawy i czarnej herbaty jest powszechne i często związane jest z uwarunkowaniami kulturowymi. Ponad 80% Polaków deklaruje regularne spożycie czarnej herbaty i kawy. Zgodnie z raportem Głównego Urzędu Statystycznego z 2019 roku, do codziennego palenia papierosów przyznaje się 21% Polaków. W ostatnich latach obserwuje się tendencję spadkową odsetka palaczy, jednakże problem ten dotyczy nadal ponad 1/5 społeczeństwa.

Alkohol jest szeroko rozpowszechnioną substancją psychoaktywną w społeczeństwie. Polska należy do krajów z najwyższą średnią konsumpcją według raportu WHO. Ze względu na szerokie rozpowszechnienie stosowania używek wśród Polaków i ich potwierdzone działanie psychoaktywne, w tej rozprawie doktorskiej postanowiono zbadać ich wpływ na bruksizm senny i architekturę snu. Ponadto, ze względu na fakt, iż największe środowiskowe narażenie na kadm związane jest z paleniem papierosów jak i również zanieczyszczeniem żywności, zbadano wpływ tego pierwiastka na strukturę snu i zgrzytanie zębami.

Używki są poznanym czynnikiem ryzyka bruksizmu sennego. Tymczasem większość wcześniejszych badań opierała się na badaniach ankietowych, czyli metodach nieinstrumentalnych. Niemniej jednak to badanie polisomnograficzne jest uznane za „złoty standard" w ostatecznym rozpoznaniu bruksizmu sennego i z jego pomocą można obiektywnie ocenić strukturę snu pacjenta zgodnie z międzynarodowym konsensusem specjalistów ds. medycyny snu. Niniejsze badania oparto na badaniach polisomnograficznych, spełniając tym samym ostateczne wymagania rozpoznania bruksizmu sennego.

3.2 Cel główny pracy

Głównym celem badań przeprowadzonych w ramach rozprawy doktorskiej jest ocena wpływu wybranych używek na nasilenie bruksizmu sennego i ocena architektury snu z użyciem badania polisomnograficznego.

3.3 Cele szczegółowe pracy

3.3.1 Ocena wpływu palenia tytoniu na architekturę snu, w tym fragmentację snu oraz nasilenie bruksizmu sennego.

3.3.2 Ocena wpływu spożywania alkoholu, kawy i herbaty na architekturę snu i nasilenie bruksizmu sennego.

3.3.3 Ocena wpływu kadmu na architekturę snu, parametry oddechowe oraz nasilenie bruksizmu sennego.

3.4 Materiały i metody

Grupę badaną we wszystkich analizach stanowiły osoby pełnoletnie, spełniające kryteria włączenia do badania. Pacjenci zostali skierowani przez lekarzy stomatologów do Laboratorium Snu Uniwersytetu Medycznego im. Piastów Śląskich we Wrocławiu celem potwierdzenia diagnozy bruksizmu sennego. Pacjenci po zapoznaniu się z informacją wyrazili świadomą i pisemną zgodę na udział w badaniu.

Przeprowadzono całonocne badanie polisomnograficzne między godziną 22:00 a 6:00 z uwzględnieniem naturalnego rytmu dobowego pacjenta, zgodnie z wytycznymi Amerykańskiej Akademii Medycyny Snu (AASM). Badanie PSG obejmowało nagranie obrazu i dźwięku oraz zapis elektroencefalograficzny, elektrokardiograficzny, elektrookulograficzny, elektromiograficzny, analizę pozycji ciała i wysiłku oddechowego. Dodatkowo, pacjenci wypełnili kwestionariusze w postaci ankiet papierowych otrzymanych przy przyjęciu do szpitala. W ankietach zawarte zostały pytania dotyczące nawykowo stosowanych używek takich jak alkohol, papierosy, kawa i czarna herbata. Z badania zostali wyłączeni pacjenci spełniający odpowiednie dla poszczególnych publikacji kryteria wyłączenia. Następnego dnia po zakończeniu badania polisomnograficznego, od pacjentów pobrano krew żylną i próbkę moczu w celu dalszych analiz. Analizę lipidogramu, jonogramu i innych parametrów przeprowadzono zgodnie ze standardami laboratorium Uniwersyteckiego Szpitala Klinicznego we Wrocławiu.

Niniejsze badanie przeprowadzono zgodnie z Deklaracją Helsińską i po uzyskaniu zgody przez Komisję Etyki Uniwersytetu Medycznego we Wrocławiu (nr KB-790/2022).

W tabelach zbiorczych dane zbiorcze opisywano, podając wartość średnią oraz odchylenie standardowe (SD) oraz medianę i zakres międzykwartylowy. Obliczenia statystyczne wykonano z wykorzystaniem pakietu “Dell Statistica 13” (Dell Inc., Tulsa, OK, USA).

3.5 Wyniki

W pierwszej pracy oryginalnej pt. „Polysomnographic assesment of effects of tobacco smoking and alcohol consumption on sleep bruxism intensity" dokonano oceny wpływu palenia papierosów i picia alkoholu na nasilenie bruksizmu sennego. Zbadano grupę 133 pacjentów przyjętych do Kliniki Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii Klinicznej Uniwersytetu Medycznego we Wrocławiu celem przeprowadzenia badania polisomnograficznego. Pacjenci wypełnili ankietę dotyczącą ich nawykowego spożywania alkoholu i palenia papierosów. Dodatkowo, od pacjentów pobrano próbki krwi żylnej celem oceny stężenia elektrolitów i lipidogramu. Jest to pierwsze badanie wykorzystujące polisomnografię na dużej grupie badawczej (n=133) do analizy wpływu używek na bruksizm senny i architekturę snu. Żadne wcześniej przeprowadzone badanie nie badało elektromiograficznych fenotypów bruksizmu sennego oraz wpływu wzbudzeń i pozycji ciała podczas snu u osób deklarujących palenie papierosów i spożywanie alkoholu. W niniejszym badaniu palacze wykazywali wyższą aktywność epizodów mieszanych bruksizmu sennego niż osoby niepalące. Stwierdzono, że występują istotne różnice w parametrach snu u palących papierosy względem niepalących. Ponadto zauważono istotnie podwyższone stężenie trójglicerydów w surowicy krwi jak i obniżone stężenie magnezu i żelaza u palaczy. U pacjentów deklarujących spożywanie alkoholu nie zauważono statystycznie istotnych różnic w parametrach snu i badaniach laboratoryjnych.

W drugiej pracy oryginalnej pt. „The effect of coffee and black tea consumption on sleep bruxism intensity based on polysomnographic examination" dokonano oceny wpływu kawy i czarnej herbaty na nasilenie bruksizmu sennego oraz na architekturę snu. Do Kliniki Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii Klinicznej przyjęto 106 pacjentów celem przeprowadzenia badania polisomnograficznego. Pacjenci wypełnili ankietę dotyczącą ich nawyków związanych z piciem kawy i czarnej herbaty. Dodatkowo, od pacjentów pobrano próbki krwi żylnej celem oceny stężenia elektrolitów, białka C-reaktywnego (CRP) i lipidogramu. Według naszej najlepszej wiedzy jest to pierwsze badanie badające wpływ nawykowego spożycia kawy i czarnej herbaty na architekturę snu i bruksizm senny przy użyciu PSG z zapisem audiowizualnym. W oparciu o wyniki badania polisomnograficznego ustalono,

że pacjenci deklarujący picie kawy intensywniej zgrzytają zębami w porównaniu do pacjentów, którzy nie piją kawy. Jest to pierwsze badanie polisomnograficzne, w którym stwierdzono, że spożycie kawy jest skorelowane ze zwiększoną intensywnością bruksizmu podczas snu. Dodatkowo ustalono, że kawa spożywana nawykowo nie ma istotnego wpływ na architekturę snu. Nie stwierdzono zwiększonej ilości wzbudzeń u osób pijących kawę, co świadczy o podobnej ciągłości snu w obu badanych grupach. Co więcej, ilość snu głębokiego, najistotniejszego z punktu widzenia efektywności regeneracji oraz snu REM, istotnego dla konsolidacji pamięci, była statystycznie taka sama w grupie pijącej kawę i grupie kontrolnej. Ponadto, w omawianej pracy, nie zaobserwowano zmian w intensywności zgrzytania zębami i parametrach snu u pacjentów deklarujących picie czarnej herbaty.

W trzeciej pracy oryginalnej pt. „The effect of cadmium on sleep parameters assessed in polysomnographic studies: a case-control study" dokonano oceny wpływu środowiskowego narażenia na kadm na bruksizm senny i architekturę snu. 44 pacjentów przyjęto do Kliniki Chorób Wewnętrznych, Zawodowych, Nadciśnienia Tętniczego i Onkologii Klinicznej celem badania polisomnograficznego. Dodatkowo, pacjentom pobrano krew żylną i mocz celem oceny stężenia kadmu we krwi i w moczu. Według naszej najlepszej wiedzy jest to pierwsze badanie dotyczące wpływu kadmu na bruksizm senny, parametry snu i parametry oddechowe z użyciem polisomnografii. Ustalono, że narażenie na kadm nie jest czynnikiem ryzyka bruksizmu sennego. Narażenie na kadm wpływa jednak negatywnie na architekturę snu, powodując jej fragmentację i skrócenie fazy REM snu. Ponadto narażenie na kadm wpływa na parametry oddechowe. W rezultacie nasze badanie pokazało, że środowiskowe narażenie na kadm może zwiększać ryzyko rozwoju obturacyjnego bezdechu sennego.

3.6 Wnioski

3.6.1 Ocena wpływu potencjalnych czynników ryzyka na intensywność bruksizmu sennego:

1) Palenie papierosów oraz picie kawy stanowią czynniki ryzyka bruksizmu sennego, w przeciwieństwie do czarnej herbaty i alkoholu, które nie wpływają na intensywność zgrzytania zębami podczas snu.

2) Narażenie na kadm nie jest czynnikiem ryzyka bruksizmu sennego.

3.6.2 Ocena wpływu używek i kadmu na architekturę snu:

1) Palenie papierosów zmienia architekturę snu zwiększając ilość wzbudzeń i tym samym nasilając jego fragmentację.
2) Nawykowe spożywanie czarnej herbaty, kawy i alkoholu nie powoduje istotnych zaburzeń struktury snu.
3) Kadm powoduje ograniczenie trwania fazy snu REM oraz nasila fragmentację snu.
4) Kadm jest niezależnym czynnikiem ryzyka zaburzeń oddychania podczas snu, podobnie jak wiek, płeć i palenie tytoniu.

Przeprowadzone badania wchodzące w skład cyklu publikacji tematycznie ze sobą powiązanych bazują na całonocnym badaniu polisomnograficznym. Nowatorstwo tych badań polega na możliwości obiektywnego i definitywnego rozpoznania bruksizmu sennego oraz pozwala na zbadanie jego fenotypów elektromiograficznych. Wyniki powyższych badań poszerzają wiedzę o patofizjologii bruksizmu sennego oraz pozwalają na lepsze poznanie zaburzeń architektury snu u pacjentów deklarujących stosowanie używek takich jak kawa, czarna herbata, alkohol i papierosy. Wyniki badań mają znaczenie nie tylko poznawcze, lecz również mogą mieć wpływ na opracowanie w przyszłości nowych metod leczenia bruksizmu sennego. Wyniki badań mogą również przyczynić się do opracowania nowych zaleceń dla pacjentów z zaburzeniami snu w celu poprawy komfortu i jakości snu. Pacjentom z rozpoznanym bruksizmem sennym warto niewątpliwie zalecać ograniczenie spożywania kawy. Dowiedziono jednak, że pacjenci z zaburzeniami snu takimi jak obturacyjny bezdech senny czy chrapanie mogą kontynuować nawykowe i regularne picie kawy, gdyż nie zaburza to ich architektury snu.

Dodatkowym atutem badań była możliwość oceny fragmentacji snu oraz zburzeń oddychania podczas snu. Obturacyjny bezdech senny jest uznanym czynnikiem ryzyka sercowo-naczyniowego. W ostatnich latach dowiedziono, że również fragmentacja snu jest powiązana ze śmiertelnością zarówno całkowitą jak i z przyczyn sercowo-naczyniowych, szczególnie u kobiet. Wskazane jest więc poznanie przyczyn fragmentacji snu w celu ograniczenia tego ryzyka. Wyniki dysertacji wskazały po raz pierwszy na kadm jako czynnik ryzyka fragmentacji snu i bezdechu sennego. Badania te są niezwykle istotne ze względu na

wysokie rozpowszechnienie środowiskowego narażenia na kadm oraz rosnące rozpowszechnienie obturacyjnego bezdechu sennego w populacji europejskiej.

Warto zauważyć, iż wyniki dysertacji wytyczają nowe kierunki badań. Niewątpliwie warto określić ilościowo liczbę filiżanek kawy, które powodują bruksizm senny oraz podjąć badania nad wpływem na sen różnych rodzajów kawy i metod jej zaparzania. Wyniki wskazujące na wpływ kadmu na czas trwania fazy REM wskazują również na konieczność badań nad procesami pamięciowymi oraz procesowaniem emocjonalnym u osób narażonych na działanie kadmu. Podsumowując, przedstawione wyniki badań mają charakter nowatorski, istotnie poszerzają wiedzę z zakresu medycyny snu oraz zarówno mają znaczenie praktyczne dla codziennej praktyki lekarskiej jaki i wskazują na nowe, interdyscyplinarne kierunki badań naukowych.

4. Publikacje wchodzące w skład rozprawy doktorskiej

4.1 Artykuł pierwszy

Journal of *Clinical Medicine*

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Article

Polysomnographic Assessment of Effects of Tobacco Smoking and Alcohol Consumption on Sleep Bruxism Intensity

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Abstract: Background: Sleep bruxism (SB) is a common sleep-related movement behavior with a complex etiology. A recent hypothesis suggests psychoactive substance usage, tobacco smoking, and alcohol intake are risk factors for SB. This study aimed to evaluate SB intensity in tobacco smokers and alcohol drinkers. Methods: A total of 133 adults underwent full-night audio- and video-polysomnography, and the polysomnograms were evaluated using the American Academy of Sleep Medicine guidelines. The study group was divided into smoker and nonsmoker groups as well as drinker and non-drinker groups. Results: The results of the polysomnographic analysis confirmed that tobacco smoking has a significant effects on SB. Tobacco smokers showed increased bruxism intensity (5.50 ± 4.71 vs. 3.83 ± 3.26, $p < 0.05$), especially the mixed phenotype (0.93 ± 1.00 vs. 0.59 ± 0.59, $p < 0.05$), in the N1 sleep stage (22.84 ± 20.45 vs. 15.66 ± 13.60, $p < 0.05$) and the nonsupine position (4.93 ± 5.56 vs. 2.50 ± 2.31, $p < 0.05$). They also showed a higher number of bruxism episodes with arousal compared with nonsmokers (2.91 ± 2.83 vs. 1.61 ± 1.49, $p < 0.05$), indicating increased sleep fragmentation. However, no significant effect of alcohol on SB intensity was observed, and the bruxism episode index was similar in alcohol drinkers and nondrinkers. In addition, electrolyte disturbances and lipid disorders were evaluated. Compared with nonsmokers, tobacco smokers showed a higher concentration of plasma triglycerides (177.67 ± 106.9 vs. 129.18 ± 65.61) and lower levels of iron and magnesium (96.68 ± 43.58 vs. 123.83 ± 52.36 and 1.85 ± 0.22 vs. 1.96 ± 0.21, respectively). Conclusions: In summary, this study showed that tobacco smoking, but not alcohol consumption, is related to bruxism intensity and lipid and electrolyte disturbances in individuals with sleep disorders.

Keywords: sleep bruxism; polysomnography; alcohol; tobacco; smoking; iron; magnesium

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1. Introduction

Sleep bruxism (SB) is a major sleep-related movement behavior with a complex etiology and an uncertain and insufficiently understood pathophysiology [1].Various causes of SB have been reported, among which genetic contribution is one of the primary subjects of research [2]. Furthermore, the autonomic nervous system has been reported to play a role in SB genesis [3]. The prevalence of SB is estimated between 8% and 31.4% [4]. To date, many attempts have been made to establish a comprehensive definition of bruxism that covers all aspects of this extensive topic; thus, the definition has been evaluated taking into account the growth of knowledge on this subject.

As bruxism has become an emerging problem worldwide and attracted research interest in the medical field, Lobbezoo et al. established a new definition of bruxism, which was extended without the prior restrictions of earlier definitions [5]. They defined SB as

"a masticatory muscle activity during sleep that is characterized as rhythmic (phasic) or non-rhythmic (tonic) and is not a movement disorder or a sleep disorder in otherwise healthy individuals". A possible sleep bruxism diagnosis can be based only on a positive self-report, and a probable bruxism outcome is based on a positive clinical inspection with or without a positive self-report. To consider the outcome as definite, results need to be based on positive instrumental assessment, with or without a positive self-report and/or positive clinical inspection. In general, SB is considered not a medical condition in healthy individuals but more as a harmful or protective behavior, depending on its health outcomes [5]. According to the International Classification of Sleep Disorders, the third edition, bruxism is defined as a "sleep-related movement disorder characterized by teeth grinding or clenching associated with an excessive sleep arousal activity" [6]. No significant association between gender and SB has been observed since bruxism affects females and males equally; thus, gender should be not considered a risk factor for SB [7,8].

Symptoms of SB such as jaw clenching and tooth grinding are risk factors for several health problems [9]. Masticatory muscle activity can lead to masticatory muscle hypertrophy, indentations on the tongue or lip, linea alba on the inner cheek, damage to dental hard tissues (e.g., cracked teeth), repetitive failures of restorative work/prosthodontic constructions, mechanical wear of teeth, masticatory muscle pain, and/or morning headache [9,10]. However, some studies suggest that SB and temporomandibular disorders are less related [11–13]. Recently, an association between simple snoring and SB has been reported [14].

SB episodes can be analyzed using polysomnographic examination—the gold-standard tool for SB diagnosis—which is based on night video and audio recordings, along with bioelectric signals from electroencephalograms, electromyography, electrocardiograms, and airflow detectors [15,16].

Cigarettes and alcohol are legal psychoactive substances that affect the central nervous system (CNS) and can also affect the behavior, cognitive functions, and mood of individuals who consume them. Alcohol contains ethanol, which is a CNS depressant that acts as a gamma-aminobutyric acid receptor agonist and an N-methyl-D-aspartate receptor antagonist. Tobacco products contain nicotine, which is an acetylcholine agonist that can stimulate or depress the CNS depending on the amount consumed [4]. The most recent hypotheses of SB etiology imply a putative role of the central and autonomic nervous systems in the development of oromandibular activity during sleep [1]. Tobacco smoking can lead to significant health problems, and tobacco smokers are more likely to experience sleep-related disorders such as poor sleep quality, insomnia, and sleep apnea [17]. A wide-range cohort study of a Finnish adult population reported smoking as an independent risk factor for weekly bruxism, defined as bruxism that occurred frequently within a week [18]. Moreover, smoking is a well-established risk factor for premature mortality and morbidity [19]. In the most recent Global Burden of Disease study published in *The Lancet* in 2019, the major risk factor for death in countries with a middle to high socio-demographic index is the usage of tobacco products, which causes, among other effects, high systolic blood pressure, dietary risks, overweight, and high fasting plasma glucose levels. The primary risk factors have changed from 1990 to 2019, but the pattern remains comparable. In the 25–49 year age group, alcohol use is the most common risk factor, but smoking has become a less significant risk factor and has steadily declined, mainly due to widespread government actions (taxation, regulatory policies for tobacco smoking) that resulted in a behavior change in populations [20]. The association between SB and the usage of legal psychoactive substances has been previously demonstrated [21]. Recently, Michalek-Zrabkowska et al. reported that young individuals with SB tend to have a high cardiovascular risk [22]. Cardiovascular risk is attributable to several modifiable and nonmodifiable risk factors. Tobacco consumption is classified as a modifiable risk factor. Huge efforts are required to change the hazardous habits of patients, including encouraging them to quit smoking [23–25].

An unhealthy lifestyle, including the consumption of stimulants, can lead to significant health problems that affect the general health of patients and is a risk factor for bruxism.

Based on this knowledge and due to the lack of data on the cause–effect relationship, the effects of psychoactive substances on SB intensity were hypothesized in this study. The null hypothesis was that increased bruxism intensity occurs in tobacco smokers and alcohol drinkers compared with controls. The aim of the study was to investigate the relationship between bruxism intensity in tobacco smokers and alcohol drinkers using polysomnographic assessments. An additional aim of the study was to evaluate the lipid profile and concentrations of electrolytes and iron in blood samples of tobacco smokers and alcohol drinkers.

2. Materials and Methods

This was a prospective, observational study carried out on 133 adult Caucasian individuals in the Sleep Laboratory of the Department and Clinic of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at Wroclaw Medical University. This study was approved by the Ethical Committee of Wroclaw Medical University (no. KB-790/2022). All patients signed voluntary informed consent prior to their participation in the study.

Among the 133 participants, 62% (n = 82) used legal stimulants, including tobacco (n = 24) and alcohol (n = 77). Those who consumed both alcohol and tobacco contributed to 14% of the study group (n = 19). Alcohol drinkers who did not smoke contributed to 44% of the study group, and smokers who did not drink contributed to 4% of the study group. The following comorbidities were observed among the participants: myocardial infarction (n = 7), stroke history (n = 6), hypertension (n = 52), diabetes (n = 24), and ischemic heart disease (n = 10). The characteristics of the study group are presented in Table 1.

Table 1. The characteristics of the study group.

Parameter	Total (n = 133, %)	Smokers (n = 24, %)	Nonsmokers (n = 109, %)	Alcohol Drinkers (n = 77, %)	Nondrinkers (n = 56, %)
Myocardial infarction	7, 5%	5, 20.8%	2, 1.83%	5, 6.5%	2, 3.5%
Stroke	6, 4.5%	4, 16.6%	2, 1.83%	4, 5.2%	2, 3.5%
Hypertension	52, 39%	13, 54.2%	39, 35.7%	32, 41.5%	20, 35.7%
Diabetes	24, 18%	7, 29.2%	17, 15.6%	16, 20.7%	8, 14.3%
Ischemic heart disease	10, 7.5%	4, 16.6%	6, 5.5%	6, 7.8%	4, 7.1%

2.1. Inclusion and Exclusion Criteria

Among 292 patients admitted to the Sleep Laboratory due to suspicion of SB and/or sleep apnea between May 2020 and December 2021, 133 patients were included in the study group based on the following inclusion and exclusion criteria. The inclusion criteria included adults over 18 years of age and the provision of voluntary informed consent to be part of this study. The exclusion criteria were as follows: presence of neurological disorders and/or neuropathic pain, severe respiratory and cardiac insufficiency, active inflammation, confirmed active malignancy, treatments affecting muscle function and sleep architecture, severe mental disorders, cognitive disability, and lack of compliance during the study. The study design is presented in Figure 1.

2.2. Study Methods and Design

All patients underwent PSG examination under medical prescription, completed the self-reported questionnaire regarding the usage of legal stimulants such as alcohol drinking and tobacco smoking, and were medically examined. Lifetime smoking was estimated in pack-years, i.e., the number of years a full pack of cigarettes (20 cigarettes) was smoked per day. Smoking status was categorized as smoker or nonsmoker. There were no former

smokers in the study group, and all of the smokers were current smokers. Patients were classified as alcohol drinkers or nondrinkers based on self-reporting of any amount of alcohol consumption. Patients were divided into four groups: smokers $n = 24$, nonsmokers $n = 109$, alcohol drinkers $n = 77$, and non-drinkers $n = 56$. The group of patients who declared no legal stimulant usage consisted of 51 patients.

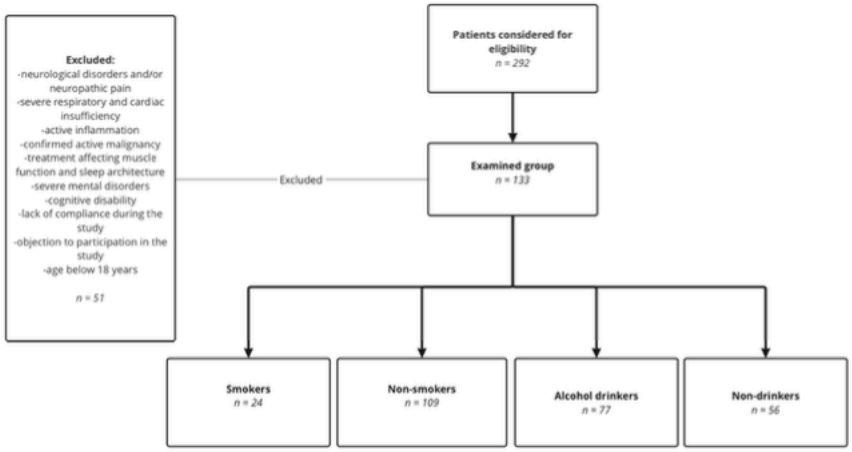

Figure 1. Flowchart showing the study design.

To confirm SB diagnosis and investigate sleep architecture, an instrumental approach was followed using video-polysomnography (PSG) with a NoxA1 (NOX Medical, Reykjavík, Iceland) device. Recordings were made between 22:00 and 06:00, in accordance with the natural circadian rhythm of the patients. Electromyographic electrodes were placed according to the recommendations of the American Academy of Sleep Medicine (AASM). The PSG examination included video and audio recording, along with electrocardiographic, electroencephalographic, electrooculographic, and electromyographic recordings (origin signal from the chin and masseter muscles), body position detection, and thoracic and abdominal breathing activity. Saturation level (SpO2%), pulse, and plethysmography data were recorded using a NONIN WristOx2 3150 pulse oximeter (Nonin Medical Inc., Plymouth, MN, USA). The recordings were stored using Noxturnal software (Nox Medical, Reykjavík, Iceland). The obtained PSG recordings were analyzed and interpreted in 30 s epochs in accordance with the guidelines for sleep scoring by a qualified physician in the Sleep Laboratory [26].

Rhythmic activities of masseter muscles occurring at least 3 s after the previous muscle activity were recognized as SB episodes. These episodes were frequently accompanied by specific movements in the orofacial region and grinding sounds. The bruxism episode index (BEI) was used to measure the bruxism intensity by counting the number of bruxism episodes per hour of sleep. Three phenotypes of SB were distinguished using electromyographic assessments: (1) phasic, characterized by $\geq$3 bursts of muscle contractions at 1 Hz frequency; (2) tonic, characterized by a contraction that lasts >2 s; and (3) mixed, including both phasic and tonic movements [27]. After overnight polysomnographic examinations, blood samples were obtained from the patients by venipuncture at 7 a.m., after 12 h of overnight fasting, which were analyzed at the Main Laboratory of Wroclaw Medical University. Lipid profile analysis and other laboratory tests were conducted in accordance with the standard laboratory protocols of Wroclaw University Teaching Hospital.

The sample size was evaluated using a sample size calculator based on the following standard assumptions: population size, 3,000,000; population proportion, 8%; confidence

level, 0.95; and maximum error, 5%. The required group size was found to be 114. Thus, a larger group (n = 133) was recruited in the present study.

2.3. Data Analysis

Statistical analysis of the data was carried out using the statistical analysis program Statistica 13.3 (Statsoft, Krakow, Poland). The data are presented as the mean ± standard deviation. Differences between the groups were analyzed using Student's t-test or analysis of variance (ANOVA) in the case of parametric data and the Mann–Whitney U test or Kruskal–Wallis ANOVA in the case of nonparametric data. Correlations were evaluated using Pearson correlation coefficients. A p value < 0.05 was considered to be statistically significant.

3. Results

The average age of the study population was 47.89 ± 16.57 years, with women comprising 45% (n = 60) of the study group and men comprising 55% (n = 73). The mean pack-years in the smoker group was 13.60 ± 2.77. The polysomnographic parameters are presented in Tables 2 and 3.

Table 2. Sleep bruxism parameters differentiated based on the usage of legal drugs (alcohol and tobacco).

Parameter	Smokers	Nonsmokers	p	Alcohol Drinkers	Nondrinkers	p
Bruxism episode index (BEI) (n/h)	**5.50 ± 4.71**	**3.83 ± 3.26**	**0.045**	4.07 ± 3.38	4.26 ± 3.96	0.750
Phasic episodes (n/h)	2.88 ± 3.02	1.89 ± 2.27	0.051	2.13 ± 2.23	2.01 ± 2.69	0.370
Tonic episodes (n/h)	1.70 ± 1.31	1.34 ± 1.27	0.130	1.32 ± 1.09	1.53 ± 1.51	0.779
Mixed episodes (n/h)	**0.93 ± 1.00**	**0.59 ± 0.59**	**0.039**	0.62 ± 0.69	0.71 ± 0.72	0.538
BEI supine (n/h)	8.02 ± 8.62	6.74 ± 11.25	0.291	5.70 ± 5.83	8.75 ± 15.05	0.999
BEI nonsupine (n/h)	**4.93 ± 5.56**	**2.50 ± 2.31**	**0.002**	3.20 ± 3.71	2.58 ± 2.50	0.488
BEI N1 (n/h)	**22.85 ± 20.46**	**15.67 ± 13.61**	**0.042**	17.72 ± 15.38	16.10 ± 15.31	0.414
BEI N2 (n/h)	5.34 ± 5.45	3.91 ± 4.20	0.250	3.97 ± 3.87	4.46 ± 5.22	0.912
BEI N3 (n/h)	2.05 ± 2.29	1.58 ± 1.94	0.0540	1.73 ± 2.23	1.59 ± 1.70	0.660
BEI REM (n/h)	3.54 ± 2.50	3.12 ± 2.67	0.340	3.00 ± 2.43	3.48 ± 2.89	0.470
Bruxism with arousal (n/h)	**2.91 ± 2.84**	**1.61 ± 1.49**	**0.000006**	1.84 ± 1.96	1.86 ± 1.73	0.833

BEI: bruxism episode index, REM: rapid eye movement, Statistically significant values are shown in bold (p < 0.05).

Table 3. Polysomnographic evaluation of the study group.

Parameter	Smokers	Nonsmokers	p	Alcohol Drinkers	Nondrinkers	p
AHI (n/h)	21.23 ± 26.79	19.52 ± 22.74	0.811	17.28 ± 21.14	23.28 ± 26.00	0.270
ODI (n/h)	21.11 ± 26.23	17.56 ± 20.10	0.861	16.68 ± 19.90	20.28 ± 23.00	0.580
Snore (%)	26.84 ± 24.30	19.49 ± 20.23	0.246	23.01 ± 23.00	17.85 ± 18.10	0.501
PLMS index (n/h)	8.33 ± 13.30	7.96 ± 18.05	0.552	10.10 ± 21.40	5.21 ± 8.50	0.084
SL (min)	18.81 ± 29.75	17.99 ± 18.90	0.460	15.32 ± 13.52	21.96 ± 28.10	0.210
REM latency (min)	97.80 ± 68.10	101.70 ± 80.00	0.899	89.51 ± 56.60	116.42 ± 98.00	0.218
WASO (min)	60.03 ± 47.11	67.12 ± 64.25	0.804	**56.71 ± 60.23**	**78.20 ± 61.32**	**0.007**

Table 3. *Cont.*

Parameter	Smokers	Nonsmokers	*p*	Alcohol Drinkers	Nondrinkers	*p*
SE (%)	79.73 ± 16.81	81.85 ± 13.74	0.581	**83.13 ± 15.00**	**79.21 ± 13.16**	**0.013**
N1 (% of TST)	7.23 ± 5.70	6.71 ± 6.50	0.647	6.53 ± 5.80	7.17 ± 7.00	0.795
N2 (% of TST)	46.19 ± 12.72	50.43 ± 23.60	0.264	47.27 ± 10.51	52.90 ± 31.43	0.498
N3 (% of TST)	24.00 ± 10.10	26.67 ± 27.03	0.701	23.32 ± 8.20	30.10 ± 36.71	0.181
REM (% of TST)	22.60 ± 8.93	22.58 ± 9.93	0.650	22.90 ± 7.50	22.18 ± 12.21	0.345
AI (n/h)	9.55 ± 7.76	6.75 ± 6.34	0.063	7.23 ± 7.05	7.30 ± 6.19	0.732

Statistically significant values are shown in bold ($p < 0.05$).

Major differences were observed between the smoker and nonsmoker groups. The PSG examination showed that smokers had a statistically significantly higher BEI than nonsmokers. Bruxism episodes were more frequent in smokers during the night in non-rapid eye movement sleep, especially during the N1 sleep stage and in the nonsupine position, compared with nonsmokers. The frequency of mixed episodes was also increased in smokers. The number of bruxism episodes with arousal was significantly higher in smokers than in nonsmokers (Table 2).

Statistically significant positive correlations were observed between pack-years and BEI ($r = 0.61$, $p = 0.002$), phasic BEI ($r = 0.62$, $p = 0.002$), mixed BEI ($r = 0.44$, $p = 0.033$), tonic BEI ($r = 0.42$, $p < 0.041$), and bruxism with arousal ($r = 0.50$, $p = 0.012$).

A statistically significantly higher plasma triglyceride (TG) content was observed among smokers compared with nonsmokers; however, no significant differences were observed between alcohol drinkers and nondrinkers. Noticeable changes were observed in the electrolyte and blood composition of smokers, which were characterized by lower magnesium (Mg) and iron (Fe) levels in the blood. No statistical differences were observed in sodium, potassium, calcium, total cholesterol, low-density lipoprotein, and high-density lipoprotein levels in smokers compared with nonsmokers. The blood parameters are presented in Table 4.

Table 4. Comparison of blood parameters regarding tobacco smoking and alcohol drinking.

Parameter	Smokers	Nonsmokers	*p*	Alcohol Drinkers	Nondrinkers	*p*
Mg [mmol/L]	**1.85 ± 0.22**	**1.96 ± 0.21**	**0.042**	1.95 ± 0.21	1.93 ± 0.23	0.417
Fe [µg/dL]	**96.68 ± 43.58**	**123.83 ± 52.36**	**0.041**	121.55 ± 48.87	113.46 ± 55.15	0.408
Na [mmol/L]	139.92 ± 1.72	139.90 ± 2.35	0.688	139.90 ± 2.35	139.92 ± 1.71	0.703
K [mmol/L]	4.31 ± 0.26	4.29 ± 0.31	0.685	4.29 ± 0.28	4.30 ± 0.33	0.913
Ca [mmol/L	9.32 ± 0.31	9.33 ± 0.31	0.752	9.31 ± 0.28	3.36 ± 0.34	0.216
Total cholesterol [mg/dL]	212.73 ± 56.63	196.80 ± 46.31	0.154	204.52 ± 49.00	193.16 ± 47.55	0.148
LDL [mg/dL]	124.86 ± 47.20	112.60 ± 39.16	0.317	119.38 ± 40.66	108.33 ± 40.48	0.154
HDL [mg/dL]	54.59 ± 16.42	57.43 ± 15.64	0.459	56.84 ± 15.94	56.98 ± 15.64	0.804
TG [mg/dL]	**177.68 ± 106.96**	**129.18 ± 65.61**	**0.016**	143.69 ± 76.02	130.81 ± 78.39	0.066

TG: triglycerides, Mg: magnesium, Fe: iron, Na: sodium, K: potassium, Ca: calcium, LDL: low-density lipoprotein, HDL: high-density lipoprotein, statistically significant values are shown in bold ($p < 0.05$).

4. Discussion

Although many research studies on SB are available in the literature, the majority of studies are based only on non-instrumental approaches using self-reported or telephone surveys [18,26,28–33].

In an international consensus, Lobbezoo et al. established that an instrumental approach for PSG assessment is the gold-standard for "definite" diagnosis of SB [5]. Non-instrumental approaches such as questionaries can only determine a "possible" diagnosis and further confirmation using clinical investigation and PSG examination is required [34]. The present study was based on PSG examinations, thus fulfilling the "definite" SB diagnosis requirements.

4.1. Effects of Smoking on SB

The most important finding of this study was the higher BEI in smokers compared with nonsmokers. Taking into account the electromyographic phenotype of episodes, a higher number of mixed bruxism episodes was observed in smokers compared with nonsmokers. As reported in a previous study, bruxism episodes are strongly associated with the sleep stages of non-rapid eye movement sleep, including the N1 and N2 stages, which are light sleep stages [35]. To the best of our knowledge, this study is the first research showing that tobacco smoking increases BEI during the N1 stage of sleep and in the nonsupine sleep position.

According to the AASM guidelines, arousals are "sleep perturbations characterized by a transient increase (for 3–15 s) in electroencephalography fast wave activity, with or without an increase in EMG activity and cardiac rhythm" [35,36]. Sleep arousal can be classified as respiratory arousal, which is associated with respiratory events, and movement arousal, which is accompanied by body movements (SB, PLM). Several SB mechanisms have been reported to date, and, among many etiological concepts, arousal is considered a trigger for RMMA [26,37]. Arousal in the context of SB is highly associated with the term "sleep fragmentation," along with wake after sleep onset (WASO) [38]. The impact of SB on sleep quality remains a subject of research, and many studies suggest that SB does not directly influence sleep quality or that it slightly lowers sleep quality [39,40]. In the present study, smokers showed an increased intensity of bruxism with arousal, suggesting increased sleep fragmentation, which is a novel and interesting finding. Very few research studies have used diagnoses based on or supported by instrumental approaches [41–43]. Moreover, no study has investigated the electromyographic phenotype and influence of arousal and body position during sleep in smokers and drinkers. Lavigne et al. established that smokers grind their teeth more frequently than nonsmokers in a polysomnographic study carried out on a Canadian population [44]. In the present study, smokers showed a higher mixed muscle activity (mixed episodes) than nonsmokers. These findings are in accordance with those of previous studies, pointing out that more than 88% of SB episodes confirmed using vPSG were of phasic or mixed type [45,46].

To the best of our knowledge, this is the first study to use PSG in a large study group (n = 133) to analyze SB-related movements and sleep architecture in smokers and alcohol drinkers. These results support the findings of previous studies, indicating that SB can be related to smoking [7,18,26,44,47–53]. However, some studies have failed to establish the association between these factors. Wincour et al. reported that no correlation between smoking, drinking, and SB in Israeli adolescents. Their study was limited by a small smoker group and the fact that alcohol consumption is the lowest in Israel among OECD countries [33]. Another study reported a negative association between tobacco smoking and SB but a positive association with awake bruxism among Dutch adolescents [30].

In hypertensive patients, the risk of SB tends to be increased with concomitant smoking and they experience a high number of bruxism episodes [33]. Martynowicz et al. stated that along with BEI, other risk factors for increased BEI include a high body mass index, a lower mean oxygen saturation (SpO2), and a higher percentage of SpO2 < 90% [54]. A recent study indicated that levels of inflammation markers were significantly increased by SB [22]. Furthermore, inflammation in the endothelium and atherosclerosis development due to the deleterious influence of SB was reported to be a risk factor for hypertension [22]. Many researchers have reported the influence of smoking on inflammation. The proinflammatory influence of smoking on increased levels of inflammation markers and cytokines has also

been reported [55–57]. Thus, hypertension and smoking are risk factors for SB and lead to increased inflammation, which is associated with the risk of cardiovascular diseases.

A previous study on a large group of patients with SB confirmed that SB impairs sleep architecture, affects the total sleep time, NREM N3 time, NREM sleep latency, sleep efficiency (SE), and increases the index of microarousals [58]. Furthermore, another study provided further knowledge about differences in sleep structure [59]. In the present study, a significantly higher number of bruxism episodes were observed in smokers in the nonsupine position (BEI nonsupine). The influence of sleep position on SB has rarely been discussed in previous studies, although one study investigated the influence of sleep position on SB occurrence [60]. Recently, Michalek-Zrabkowska et al. reported the dependence of sleep position on SB. The nonsupine position has been found to be correlated with a higher number of bruxism episodes and desaturation [14]. To the best of our knowledge, no other study has investigated the relationship between sleep position and bruxism episodes in smokers.

Several studies have reported the deleterious effects of tobacco on general health. A previous study investigated the influence of tobacco smoking on iron homeostasis dysregulation [61]. Another recent study reported a lower iron content due to smoking [62]. Smoking is a known and underestimated risk factor for iron deficiency anemia, which is more frequent among light smokers and depends on the smoking exposure time (duration of smoking) [63]. Exposure to tobacco smoke is one of the major risk factors of chronic obstructive pulmonary disease (COPD) [64]. Approximately 50% of heavy smokers tend to develop COPD [65]. This study indicated that the prevalence of nonanemic iron deficiency was higher in COPD patients due to increased levels of inflammation markers. COPD patients tend to have lower blood oxygen levels with no coexisting airflow obstruction [66]. Therefore, in the present study, the lower blood iron content observed in smokers compared with nonsmokers is in accordance with the findings of previous studies.

The effect of smoking on dyslipidemia is a well-researched topic. Increased serum lipid profiles, especially TG, are strongly correlated with obesity and smoking, which is consistent with the findings of the present study [65,67–69].

The finding that the magnesium content was lower in smokers is consistent with the findings of previous studies [70,71]. This can be explained by the fact that smokers consume lower amounts of fruits, vegetables, cereals, and dairy. As a result, their magnesium intake could be lower than in nonsmokers [72]. An inverse relationship between inflammation markers and magnesium content in smokers has also been reported in previous studies [70]. Thus, these results are in agreement with the findings of the present study.

4.2. Effect of Alcohol Intake on SB

In the present study, no significant differences in bruxism intensity and sleep architecture were observed between alcohol drinkers and nondrinkers. It is well established that alcohol consumption has adverse health effects on health and sleep [73,74]. Alcohol drinkers are at risk of cardiovascular diseases, type 2 diabetes, dementia, cancers, alcoholic liver disease, malnutrition, and several other associated diseases [74]. Alcohol makes falling asleep easier but, on the other hand, disrupts sleep architecture, triggers insomnia, and leads to natural circadian rhythm changes. In individuals with preexisting breathing-related disorders, alcohol consumption worsens respiratory events and lowers the oxygen saturation level [74,75]. Alcohol affects nocturnal sleep parameters such as reduced sleep onset latency, WASO, slow wave sleep in N3, and REM sleep [76]. Only a few studies have investigated the effect of alcohol intake in SB patients using PSG examinations [33]. Holanda et al. reported that alcohol consumption was strongly correlated with SB. The findings of Itani et al. supported the correlation between alcohol intake and smoking habits with SB in a research survey [26]. However, slight differences in WASO and SE were observed between drinkers and nondrinkers, which could be attributable to more consolidated sleep in the first hours of the night [68]. Therefore, alcohol, through sleep consolidation in the first hours of the night, may eliminate arousals and reduce SB. In

contrast, in the latter part of the night, alcohol could show the opposite effect and promote SB. However, this hypothesis needs further research.

4.3. Study Strengths

This study included a large study sample of 133 patients. Furthermore, this study was based on polysomnography, which is the "gold-standard tool" for SB diagnosis according to Lobbezoo et al. [5]. Moreover, this study measured blood parameters, which added to the characterization of the study population. To the best of our knowledge, this is the first study to use PSG evaluations to determine SB intensity in smokers and drinkers.

4.4. Limitations

There were a few limitations to this study. The small size of the smoker group is correlated with a higher risk of errors than in a larger sample group. In addition, patients were admitted to the Sleep Laboratory with no adaptive night before the avPSG examination due to the organization of the Polish health service and the limited capabilities of the laboratory. The group of nonsmokers could include alcohol drinkers, which may cause bias.

5. Conclusions

1. Tobacco smokers have a higher bruxism intensity, especially the mixed phenotype, in N1 sleep and in the nonsupine position.
2. Tobacco smokers have a higher number of bruxism episodes with arousal than non-smokers, which suggests increased sleep fragmentation.
3. Smokers with comorbid sleep-related disorders tend to have electrolyte disturbances and lipid disorders.
4. Alcohol consumption has no significant influence on bruxism parameters.

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Data Availability Statement: The data supporting the findings of this study are available on request from the corresponding author and are not publicly available due to privacy or ethical restrictions.

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Research article

The effect of coffee and black tea consumption on sleep bruxism intensity based on polysomnographic examination

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ABSTRACT

Background: Sleep bruxism (SB) is a common behavior that can result in various clinical consequences on human health. Risk factors for SB include among others emotional stress, anxiety, tobacco smoking, and excessive alcohol consumption. Coffee and black tea are among the most commonly consumed beverages worldwide. This study explores the influence of coffee and black tea consumption on bruxism intensity, as observed in polysomnographic examination.
Methods: Polysomnographic examination with simultaneous camera recording was conducted in 106 adult subjects. The results were evaluated according to guidelines set out by the American Academy of Sleep Medicine (AASM). The study group was divided according to habitual stimulant usage, as declared by the participants in a self-reported questionnaire. Four groups were identified: coffee drinkers versus non-drinkers and black tea drinkers versus non-drinkers.
Results: The bruxism episode index (BEI) was increased in coffee-drinkers as opposed to non-drinkers (4.59 ± 3.44 vs. 2.87 ± 1.50, $p = 0.011$). Sleep fragmentation, measured according to the arousal index, was comparable in coffee drinkers and non-drinkers. Electrolyte and lipid levels were similar in coffee drinkers and non-drinkers. Habitual black tea intake did not affect sleep architecture or bruxism intensity.
Conclusions: The study showed that habitual coffee consumption is a risk factor for the increased intensity of sleep bruxism. Neither coffee nor tea consumption is related to sleep fragmentation in habitual drinkers. Coffee and tea intake does not affect electrolyte and lipid concentrations. Caution should therefore be recommended in drinking coffee in people with sleep bruxism.

1. Introduction

Various definitions of bruxism have been discussed over a number of decades. The term "la bruxomanie" was first coined at the beginning of the twentieth century by Marie Pietkiewicz [1]. In 2013 Lobbezoo et al. defined sleep bruxism (SB) as a "repetitive jaw-muscle activity characterized by clenching or grinding of the teeth and/or bracing or thrusting of the mandible" [2]. In 2018

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Lobbezoo et al. updated the definition, distinguishing between two separate definitions for awake bruxism and sleep bruxism [3]. Rather than being referred to as a disorder, the term bruxism was now defined as a behavior at risk of certain clinical consequences in healthy individuals. Moreover, diagnostic techniques for sleep bruxism were divided into instrumental (polysomnography (PSG), as a gold standard tool in bruxism diagnosis in sleep laboratory and surface electromyography with or without heart rate (HR) recording at home) and non-instrumental (self-reports and clinical inspection findings) [3] Sleep bruxism is a common phenomenon worldwide, with a prevalence of 8–13% in the general population [4]. Risk factors for SB have previously been examined and include (among others), emotional stress, tobacco smoking, excessive alcohol consumption, sleep apnea and anxiety disorders [5]. Clinical manifestations of SB may include tooth wear, masticatory muscle pain, and headache [6,7].

Coffee and black tea are some of the most frequently consumed beverages worldwide. The consumption patterns vary between countries, due to cultural traditions/backgrounds and habits ingrained in society. Norway is the leader in per capita coffee consumption in Europe [8] It has been established, that drinking caffeinated beverages has gained in popularity over the last decade and about 85% of the U.S. population drinks one or more caffeinated beverages a day [9]. Furthermore, the last few years have been dominated by the ongoing COVID-19 pandemic, which has also left its mark on dietary behaviors, including caffeine consumption [10].

The two most prominent sources of caffeine are coffee and black tea [11]. Caffeine, namely 1,3,7-trimethylxanthine, is a purine alkaloid occurring naturally in coffee beans [12]. Caffeine is rapidly absorbed, has a high bioavailability and has biological effects on the human body via its blockage of the widely distributed adenosine receptors (A1 and A2A). Ultimately it leads to the stimulation of the respiratory, renal, cardiovascular, gastrointestinal and central nervous systems, as well as adipose tissue [13–15]. Adenosine in general promotes sleep. Due to the blockage of these receptors, caffeine intake acts as a stimulus and promotes wakefulness/has a positive influence on fatigue, reaction time, enhances attention and improves athletic performance [16–18]. It has been reported that the risk of developing Parkinson's disease, dementia, Alzheimer disease, type 2 diabetes, chronic liver cirrhosis as well as apnea in premature infants is significantly reduced with caffeine consumption [15]. Caffeine ($\geq$100 mg) is also widely used as a co-analgetic, increasing analgesic potential in pain management [19].

While the standard size of a cup of coffee may vary, it is estimated that a single cup of coffee provides about 100 mg of caffeine, while a cup of black tea contains about 55 mg of caffeine [13,20]. A caffeine overdose is associated with anxiety, tremulousness and sleeping difficulties [21]. The estimated fatal dose of caffeine is about 10–14 g [16,22]. It is worth noting though, that caffeine is not only found in coffee and black tea. It also occurs naturally in various plants such as cocoa beans, guarana berries and yerba mate leaves. Artificially, it is added to energy drinks.

Besides the caffeine content, coffee is also a rich source of micronutrients including nicotinic acid, niacin, vitamin E, magnesium and potassium. The average micronutrient quantity however varies considerably depending on the coffee brewing method [13].

Caffeine has been the subject of research in the past and has been shown to be a risk factor for developing sleep bruxism. However previous studies were predominantly based on questionnaires or self-reports, and had no possibility of diagnosing definite bruxism, or assessing its intensity. Moreover, the consumption of black tea and its compound theanine, has as yet not been investigated in the context of SB. To the best of our knowledge, there are no research papers investigating the impact of coffee and tea consumption on the intensity of sleep bruxism using polysomnographic assessment with camera recording, being gold standard tool for used in SB diagnosis [3]. The aim of this study is to define the effect of habitual coffee and black tea consumption on sleep bruxism intensity and alterations in sleep architecture.

2. Materials and methods

2.1. Participants

This was a prospective observational case-control study. The study was conducted in the Sleep Laboratory at the Department and Clinic of Internal Medicine, Occupational Diseases, Hypertension and Clinical Oncology at Wroclaw Medical University. All patients were referred to the Sleep Laboratory because of a suspicion of a sleep disorder. The study was approved by the Ethics Committee at Wroclaw Medical University (approval no. KB-790/2022). All procedures were performed in accordance with the Declaration of Helsinki. Voluntary informed consent (signed) was obtained from the participants preceding the start of the study.

After fulfilling specific inclusion and exclusion criteria requirements, 106 patients were included in the study group. The inclusion criteria were as follows: age >18 years and providing written informed consent to participate in the study. Subjects were excluded from the study if they: presented neurological disorders and/or neuropathic pain, active inflammation, confirmed active malignancy, severe respiratory and cardiac insufficiency, had treatments affecting muscle function and sleep structure, had severe mental disorders or cognitive disability, were pregnant, or if there was a lack of compliance during the study.

Patients were divided into groups based on their declaration of coffee and black tea consumption respectively. Four groups of patients were identified: coffee drinkers versus coffee non-drinkers and black tea drinkers versus black tea non-drinkers.

At admission, patients completed the self-reported questionnaire. Questions about coffee and black tea consumption were evaluated. The questionnaire included a question about the number of cups of coffee or black tea that was consumed on average in a day (between 1 and 10 cups).

The sample size was calculated using an online calculator (https://www.calculator.net/sample-size-calculator.html). With a margin of error of 5% and confidence level of 95%, the minimal sample size was set at 80. With a study group consisting of 106 subjects, the required criterion had been met. Fig. 1 presents a flowchart of the study design.

2.2. Polysomnography

Patients underwent a previously prescribed polysomnographic (PSG) examination. Video polysomnography was performed with a Nox A1 (NOX Medical, Reykjavík, Iceland) device. Patients were recorded between 22:00 and 6:00, taking into account the wishes and habits of the patient, in order to maintain the natural circadian rhythm. Electromyographic electrodes were attached as recommended by the American Academy of Sleep Medicine (AASM) guidelines [23]. The examination included audio and video recordings together with electrocardiographic, electroencephalographic, electrooculographic, electromyographic recordings, body position detection and thoracic and abdominal breathing activity. A NONIN WristOx2 3150 pulse oximeter (Nonin Medical Inc., Plymouth, MN, USA) was used to measure saturation level (SpO2%), pulse, and plethysmography data. Breathing, sleep bruxism (SB) and sleep parameters were collected. Sleep parameters were assessed and classified according to standard AASM criteria [23]: non-REM 1 sleep stage (N1), non-REM 2 sleep stage (N2), non-REM 3 sleep stage (N3), REM sleep stage, arousal index (AI), sleep latency (SL), sleep efficiency (SE), apnea-hypopnea index (AHI), periodic limb movement disorder (PLMD), oxygen desaturation index (ODI) and snore. SB parameters were assessed: bruxism episode index (BEI), phasic bruxism, tonic bruxism, and mixed bruxism. The classification of sleep bruxism was based on the number of bruxism episodes per hour of sleep (BEI) and assigned as irrelevant (BEI <2), mild to moderate (BEI 2–4) and severe (BEI >4) [24].

At 7 a.m., after the conclusion of the PSG examination, blood parameters were obtained by venipuncture preceded by 12 h of overnight fasting. Blood samples were analyzed at the Main Laboratory at Wroclaw Medical University. Laboratory tests were performed according to the standard laboratory protocols at Wroclaw University Teaching Hospital.

2.3. Statistics

The database, gathered from 106 individuals that met the inclusion criteria, was analyzed with Statistica 13.3 (Statsoft, Poland). Variables are presented as a mean and standard deviation. First, the data was characterized by the analysis of the distribution and the variance equality. For variables that had met the parametric criteria, classic parametric analyses were used for the evaluation of the difference between two groups for independent variables (T-test). In case data had not met the criteria of a standard parametric test, nonparametric, relevant alternatives were utilised for independent samples (such as: Mann–Whitney *U* test or two sample Kolmogorov–Smirnov test). The method of data analysis was determined by meeting the statistical criteria for the relevant test. Statistical significance was recognized for a p-value <0.05.

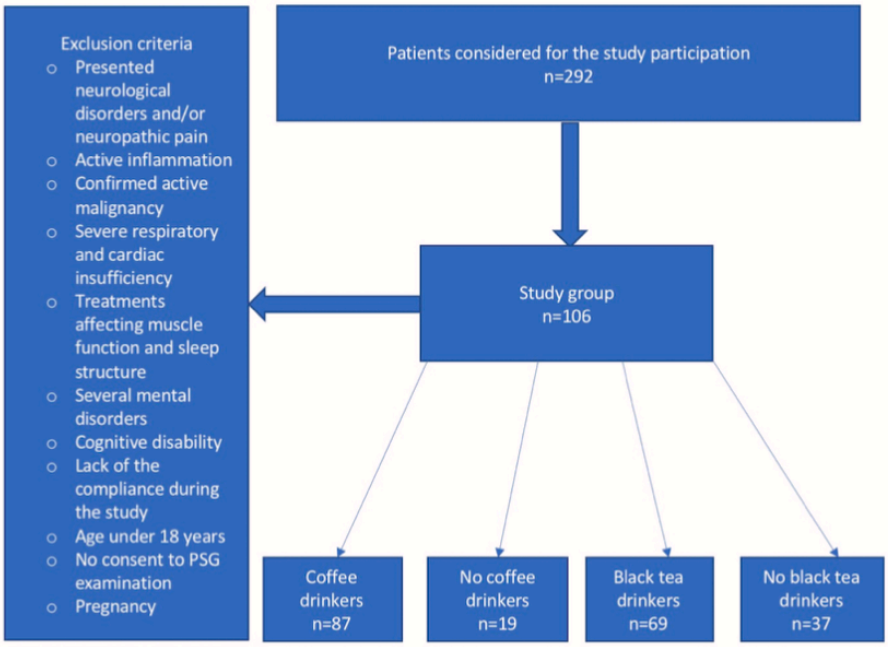

Fig. 1. Flowchart presenting the study design.

3. Results

Total of 292 patients were admitted to the sleep laboratory between May 2020 and December 2021. Among them, total of 106 adults were included in the study group. The average age of the study group was 48.18 ± 16.26 years. 44% of the participants were female (n = 47), and 56% were male (n = 59). Comorbidities observed in the study group included myocardial infarction (MI), stroke, arterial hypertension, diabetes and ischemic heart disease. Data on the prevalence of comorbidities in the study group is provided in Table 1. The polysomnographic and bruxism parameters of the entire study group are presented in Table 2.

The sleep bruxism parameters are presented in Table 3. The bruxism episode index (BEI), BEI in N1 (non-rapid eye movement sleep stage 1), BEI in N3 (non-rapid eye movement sleep stage 3) and BEI in rapid eye movement (REM) sleep stage was increased in coffee drinkers compared to non-drinkers. There were no significant differences in bruxism parameters between black tea drinkers and non-drinkers.

The polysomnographic parameters in each studied group, are presented in Table 4. N2 (non-rapid eye movement sleep stage 2) sleep stage duration was decreased in coffee drinkers compared to non-drinkers. A decreased duration of wake after sleep onset (WASO) was observed in coffee drinkers. The arousal index was similar in coffee drinkers and non-drinkers. All sleep parameters were comparable in black tea drinkers and non-drinkers.

The electrolyte, lipid and CRP concentrations remained similar in all the studied groups (Table 5).

4. Discussion

4.1. Rationale for conducting a study looking at the effect of coffee and black tea consumption on sleep parameters

To our knowledge, this is the first study investigating the influence of coffee and black tea intake on sleep architecture using PSG with camera recording. In our study, all patients underwent a single night of audio-video-PSG, a gold standard clinical diagnostic tool for definite SB diagnosis. Previous questionnaire-based studies on bruxism can only suggest a possible bruxism diagnosis, but not confirm it, in accordance with the Lobbezoo et al. consensus [3]. To our knowledge, there are no studies in the available literature investigating the effect of habitual coffee and black tea consumption on sleep parameters. There are however a few studies investigating the effects of coffee consumption right before bedtime [25].

It is generally believed that coffee consumption can worsen sleep parameters and that it possibly favors arousals. However, no recent study supports this hypothesis in habitual drinkers, therefore the aim of this study was to evaluate the effect of habitual coffee and black tea intake on sleep architecture.

4.2. The effect of coffee consumption on SB intensity

The patients included in the study declared habitual psychoactive substance use. This is associated with increasing tolerance/resistance for caffeine. Tolerance can develop in about a week of regular use [16,22]. It has previously been suggested that moderate black tea and coffee intake of about 3–4 cups a day, was not associated with any side effects on human health [26]. On the contrary, the consumption of black tea and coffee in these quantities may even be beneficial [27,28]. Its protective effect on the cardiovascular system, liver diseases, diabetes and gastrointestinal disorders has been a subject of interest. Most studies support results suggesting that moderate, and even heavy, coffee consumption, was not associated with a higher cardiovascular risk [29–31]. This is however the first study stating that coffee consumption is correlated with increased sleep bruxism intensity. So far, no study on SB was performed with the use of PSG examination. Up until now, only questionnaires have been used to investigate the usage and effects of stimulative substances on human health. This research indicates the probable influence of coffee consumption on the intensity of teeth grinding. On the other hand, despite increased sleep bruxism parameters, according to our study coffee does not disturb sleep architecture or electrolyte concentrations, including that of magnesium and potassium. This topic requires further investigation in order to establish the possible complications of coffee-induced teeth grinding, including temporomandibular disorders (TMD) and tooth wear [32].

4.3. The effect of coffee consumption on sleep architecture

Several authors have correlated coffee and black tea intake with sleep disturbances. However, no study has ever investigated sleep architecture changes and sleep bruxism in relation to coffee and tea consumption. To our best knowledge, the majority of the previous

Table 1
The prevalence of comorbidities in the entire study group.

Parameter	Total (*n* = 106)	Coffee drinkers (*n* = 87)	No coffee drinkers (*n* = 19)	Black tea drinkers (*n* = 69)	No black tea drinkers (*n* = 37)
Myocardial infarction	6	5	1	2	4
Stroke	5	4	1	3	2
Arterial hypertension	42	33	9	27	15
Diabetes	19	15	4	11	8
Ischemic heart disease	7	5	2	3	4

Table 2
The polysomnographic and sleep bruxism parameters in the entire study group (n = 106).

Parameter	Mean value ± SD
AHI (n/h)	21.10 ± 24.07
ODI (n/h)	19.30 ± 21.86
Snore (%)	21.59 ± 21.46
PLMS index (n/h)	8.13 ± 18.14
SL (min)	19.42 ± 22.97
REM latency (min)	102.112 ± 76.27
WASO (min)	62.90 ± 49.89
SE (%)	82.39 ± 11.93
N1 (% of TST)	6.52 ± 5.68
N2 (% of TST)	50.42 ± 23.82
N3 (% of TST)	26.97 ± 27.42
REM (% of TST)	22.67 ± 10.22
AI (n/h)	10.85 ± 17.25
Average Sp02 (%)	92.58 ± 4.74
Minimal Sp02 (%)	81.87 ± 8.88
Sp02 duration <90% (%)	10.61 ± 17.25
Bruxism episode index (BEI) (n/h)	4.29 ± 3.25
Phasic BEI (n/h)	2.05 ± 2.37
Tonic BEI (n/h)	1.38 ± 1.19
Mixed BEI (n/h)	0.68 ± 0.69
N1 BEI (n/h)	16.34 ± 10.61
N2 BEI (n/h)	4.79 ± 4.13
N3 BEI (n/h)	2.10 ± 1.98
REM BEI (n/h)	3.42 ± 2.37
Bruxism with arousal (n/h)	2.00 ± 1.821

AHI, apnea-hypopnea index; ODI, oxygen desaturation index; PLMS, periodic limb movements syndrome; SL, sleep latency; WASO, wake after sleep onset, SE, sleep efficiency; N1, non-rapid eye movement sleep stage 1; N2, non-rapid eye movement sleep stage 2; N3, non-rapid eye movement sleep stage 3; REM: rapid eye movement; TST, total sleep time; AI, arousal index; BEI, bruxism episode index; Sp02; oxygen blood saturation, SD; standard deviation; min, minutes; n/h, number/hour.

Table 3
Sleep bruxism parameters in the studied groups based on polysomnographic examination.

Parameter	Coffee drinkers	No coffee drinkers	*p*	Black tea drinkers	No black tea drinkers	*p*
Bruxism episode index (BEI) (n/h)	4.59 ± 3.44	2.87 ± 1.50	**0.011**	3.95 ± 2.44	4.91 ± 4.34	>0.05
Phasic BEI (n/h)	2.17 ± 2.56	1.47 ± 1.05	>0.05	1.75 ± 1.59	2.59 ± 3.34	>0.05
Tonic BEI (n/h)	1.36 ± 1.09	1.44 ± 1.61	>0.05	1.33 ± 1.26	1.47 ± 1.06	>0.05
Mixed BEI (n/h)	0.68 ± 0.69	0.65 ± 0.70	>0.05	0.63 ± 0.62	0.76 ± 0.82	>0.05
N1 BEI (n/h)	17.05 ± 10.42	13.10 ± 11.14	< **0.025**	15.74 ± 9.49	17.46 ± 12.50	>0.05
N2 BEI (n/h)	5.03 ± 4.21	3.73 ± 3.67	>0.05	4.46 ± 3.14	5.41 ± 5.52	>0.05
N3 BEI (n/h)	2.29 ± 2.08	1.22 ± 1.09	**0.003**	1.78 ± 1.53	2.69 ± 2.53	>0.05
REM BEI (n/h)	3.56 ± 2.22	2.80 ± 2.98	**0.019**	3.34 ± 2.51	3.58 ± 2.13	>0.05
Bruxism with arousal (n/h)	2.05 ± 1.91	1.76 ± 1.37	>0.05	1.96 ± 1.86	2.07 ± 1.78	>0.05

BEI, bruxism episode index; N1, non-rapid eye movement sleep stage 1; N2, non-rapid eye movement sleep stage 2; N3, non-rapid eye movement sleep stage 3; REM: rapid eye movement; n/h, number/hour; statistically significant values are shown in bold ($p < 0.05$).

studies based on PSG examination were concentrated on the effect of accidental caffeine intake (administered before bedtime) on sleep architecture. Furthermore, these studies were frequently conducted after sleep deprivation. Moreover, no previous study was ever performed on a large scale [25].

Sleep fragmentation is classified as an interruption in sleep that involves arousals and/or awakenings [33]. Sleep fragmentation impacts neuroendocrine pathways and is a risk factor for various diseases including, among others, cardiovascular, metabolic and mood issues [34,35]. Arousals are linked with excessive somnolence during the day, cognitive performance deficits and mood alterations. In our study, coffee is not significantly associated with an increased arousal-index. Moreover, the index of bruxism associated arousals were similar in coffee drinkers and non-drinkers. This indicates that bruxism has no effect on sleep fragmentation. WASO (wake after sleep onset) was decreased in coffee drinkers, which confirms the beneficial effect of coffee on the continuity of sleep. Thus, habitual drinking of coffee does not appear to promote sleep fragmentation. However, previous studies have shown that accidental drinkers have a lower resistance threshold and are more likely to develop side effects associated with caffeine overdose, including sleep problems [16].

Table 4
Polysomnographic evaluation of the studied groups.

Parameter	Coffee drinkers	No coffee drinkers	*p*	Black tea drinkers	No black tea drinkers	*p*
AHI (n/h)	21.30 ± 24.11	20.21 ± 24.52	>0.05	21.25 ± 22.44	20.84 ± 27.15	>0.05
ODI (n/h)	19.73 ± 22.30	17.36 ± 20.19	>0.05	19.22 ± 20.22	19.44 ± 24.87	>0.05
Snore (%)	21.92 ± 21.37	20.11 ± 22.37	>0.05	21.58 ± 22.22	21.60 ± 20.30	>0.05
PLMS index (n/h)	8.60 ± 19.61	6.00 ± 8.91	>0.05	9.23 ± 21.75	6.10 ± 8.01	>0.05
SL (min)	19.54 ± 23.68	18.87 ± 20.00	>0.05	19.99 ± 25.20	18.37 ± 18.46	>0.05
REM latency (min)	98.48 ± 69.40	118.58 ± 102.57	>0.05	100.11 ± 77.12	105.80 ± 75.60	>0.05
WASO (min)	57.94 ± 43.07	85.33 ± 70.50	**0.029**	67.41 ± 50.12	54.60 ± 49.04	>0.05
SE (%)	83.20 ± 10.63	78.71 ± 16.44	>0.05	81.39 ± 11.86	84.22 ± 11.99	>0.05
N1 (% of TST)	6.31 ± 5.62	7.43 ± 6.01	>0.05	7.26 ± 6.24	5.15 ± 4.20	>0.05
N2 (% of TST)	48.02 ± 17.90	61.30 ± 40.15	**0.011**	49.48 ± 23.82	52.14 ± 24.04	>0.05
N3 (% of TST)	27.56 ± 29.68	24.30 ± 13.28	>0.05	24.72 ± 10.19	31.10 ± 44.18	>0.05
REM (% of TST)	22.91 ± 7.29	21.59 ± 18.75	>0.05	22.61 ± 11.30	22.78 ± 8.02	>0.05
AI (n/h)	10.52 ± 16.20	12.33 ± 21.85	>0.05	10.74 ± 16.99	11.04 ± 17.95	>0.05
Average Sp02 (%)	92.51 ± 5.10	92.88 ± 2.68	>0.05	92.19 ± 5.53	93.28 ± 2.69	>0.05
Minimal Sp02 (%)	82.02 ± 9.04	81.21 ± 8.31	>0.05	81.58 ± 8.12	82.41 ± 10.22	>0.05
Sp02 duration <90% (%)	10.41 ± 16.68	11.55 ± 20.11	>0.05	11.33 ± 17.34	9.29 ± 17.24	>0.05

AHI, apnea-hypopnea index; ODI, oxygen desaturation index; PLMS, periodic limb movements syndrome; SL, sleep latency; WASO, wake after sleep onset; SE, sleep efficiency; N1, non-rapid eye movement sleep stage 1; N2, non-rapid eye movement sleep stage 2; N3, non-rapid eye movement sleep stage 3; REM: rapid eye movement; TST, total sleep time; AI, arousal index; BEI, Sp02; oxygen blood saturation, SD; standard deviation; min, minutes; n/h, number/hour; statistically significant values are shown in bold ($p < 0.05$).

Table 5
The concentration of electrolytes, CRP, lipids and serum uric acid in the studied groups.

Parameter	Coffee drinkers	No coffee drinkers	*p*	Black tea drinkers	No black tea drinkers	*p*
Mg [mmol/l]	1.94 ± 0.21	2.04 ± 0.18	>0.05	1.95 ± 0.20	1.97 ± 0.22	>0.05
Na [mmol/l]	140.10 ± 2.19	140.00 ± 1.29	>0.05	140.07 ± 2.15	140.09 ± 1.87	>0.05
K [mmol/l]	4.31 ± 0.30	4.3 ± 0.23	>0.05	4.30 ± 0.25	4.38 ± 0.35	>0.05
Ca [mmol/l]	9.28 ± 0.26	9.31 ± 0.43	>0.05	9.28 ± 0.28	9.31 ± 0.34	>0.05
Total cholesterol [mg/dl]	204.53 ± 44.66	197.16 ± 63.24	>0.05	204.62 ± 50.26	200.37 ± 45.82	>0.05
LDL [mg/dl]	118.15 ± 38.91	119.32 ± 48.57	>0.05	119.60 ± 40.83	116.09 ± 41.10	>0.05
HDL [mg/dl]	56.80 ± 16.12	53.53 ± 13.76	>0.05	56.00 ± 14.75	56.43 ± 17.41	>0.05
TG [mg/dl]	145.21 ± 84.66	121.26 ± 53.59	>0.05	139.21 ± 63.22	142.66 ± 103.62	>0.05
CRP [mg/l]	2.79 ± 4.81	2.57 ± 2.38	>0.05	3.17 ± 5.24	1.96 ± 2.19	>0.05
Creatinine [mg/dl]	0.93 ± 0.15	0.87 ± 0.11	>0.05	0.92 ± 0.14	0.92 ± 0.16	>0.05
Uric acid [mg/dl]	5.39 ± 1.53	5.24 ± 0.79	>0.05	5.33 ± 1.53	5.42 ± 1.19	>0.05

Mg: magnesium, Na: sodium, K: potassium, Ca: calcium, LDL: low-density lipoprotein, HDL: high-density lipoprotein, TG: triglycerides, CRP: *C*-reactive protein, mg/dl, milligram/deciliter; mg/L; milligram/liter.

On the other hand, other polysomnographic studies investigating the influence of caffeine on daytime recovery sleep structure, have revealed that caffeine does in fact impact sleep patterns. According to one such study, sleep efficiency, sleep duration, slow-wave sleep and rapid eye movement sleep (REM) were decreased. However, a great limitation of this study was a small study group (n = 24). Moreover, caffeine was given in pills, and PSG was conducted after an entire night of sleep deprivation [36], thus the aim and methodology were different from our study. Salin-Pascual et al. demonstrated that patients suffering from insomnia (n = 6) had a significantly longer sleep latency and less total sleep time in the multiple sleep latency test (MSLT), compared to non-insomniac volunteers after caffeine administration [37]. A questionnaire and diary based survey of 1498 individuals in a French middle-aged working population did not find a significant relationship between total sleep time and daily caffeine intake [38].A survey performed on 515 adults proved an association between poor sleep quality and coffee consumption, however no objective method of sleep estimation was conducted [39].

Several studies conducted in the past on animal models revealed, that caffeine decreased NREM (non-rapid eye movement sleep) and REM sleep stage duration. However, the study was not based on the habitual/regular caffeine influence on sleep architecture, focusing rather on the effects of coffee administered prior to the planned sleep [40].

Numerous studies examining sleep difficulties in military personnel have been published. Consumption of caffeinated products in this study group decreased the participants sleep duration and made it more difficult to fall asleep. It is however worth noting, that these studies were based on self-reported questionnaires without PSG examination [41].

Past studies have shown that a high overall consumption of caffeine, especially in the late afternoon and evening, alters sleep structure, ultimately causing a reduction in both the REM stage of sleep and in total sleep time [42]. Skarupke et al. in a large questionnaire-based German study group of adolescents between the ages of 11–17 years, established that coffee consumption can be associated with complaints of insomnia [43]. The study was conducted on adolescents, which may suggest that the effect of coffee consumption on sleep structure may be age dependent. However, several previous studies presented similar results. A cross-sectional questionnaire study conducted on an Australian study group also suggested that habitual coffee consumption decreases sleep duration,

but does not affect its quality [44]. A small PSG-based study investigated the impact of caffeine intake on nighttime sleep. It concluded that sleep architecture did not significantly differ between patients that consumed caffeine, or a placebo or those with withdrawal conditions [45]. Another PSG-based study by Youngberg et al. investigated sleep architecture in habitual moderate (up to 4 cups a day) coffee consumers among primary insomnia patients and good sleepers. No significant differences in sleep parameters were observed between the two study groups [46]. Thus, the result of the Youngberg study is in agreement with our results.

4.4. The effect of black tea consumption on sleep architecture

In addition to caffeine, black tea, is also a major theanine source. Due to its similar structure to glutamate and the glutamine neurotransmitter, this amino acid acts antagonistically on glutamate receptors [47]. It has been reported that black tea consumption has a favorable effect on neurocognitive function. The combined caffeine and theanine effect, has been the subject of numerous studies, since both have an influence on neurotransmitter pathways [48]. Caffeine alone is known to have stimulative properties, while theanine has a relaxing effect, promoting calmness and improving cognitive performance [48,49]. Jang et al. reported that small doses of theanine can partially counteract the effects of caffeine on sleep in rats [50]. In our study, black tea drinkers had similar bruxism intensity and sleep architecture as non-drinkers. Therefore, black tea consumption can be recommended even in patients with sleep disorders.

4.5. The effect of coffee and black tea on serum concentrations of electrolytes, lipids, CRP and uric acid

Caffeine is a purine alkaloid, a natural xanthine derivative. Purine metabolic pathways in general lead to uric acid production. A Japanese epidemiological study demonstrated a clear inverse relationship between coffee consumption and serum uric acid levels [51]. However, a meta-analysis conducted by Zang et al. showed no significant difference between the highest and the lowest coffee intake categories in terms of the uric acid level [52]. On the other hand Park et al. demonstrated that coffee has a significant lowering effect on serum uric acid [53].Thus, the effect of coffee consumption on the concentration of serum uric acid remains controversial. In our study, coffee consumption did not impact serum uric acid concentration.

Previously, the influence of caffeine on *C*-reactive protein has been considered. In a recent meta-analysis by Moua et al. no statistically significant associations were observed between CRP concentration and coffee consumption in 61,047 participants [54]. In our study, changes in CRP concentrations were also not statistically significant. The result indicates no effect of coffee and tea consumption on the inflammatory process.

It should be kept in mind, that coffee and caffeine vary and are two separate compounds. Coffee is a complex mixture that in addition to caffeine, includes about 1000 other compounds that also impact human health. Trigonelline, one of the main coffee alkaloids along with cafestol, kahweol and chlorogenic acid, is known for its strong anti-inflammatory properties. Other compounds include nicotinic acid, magnesium and potassium [12,14,29]. Potassium and magnesium levels in our study remained in the similar ranges in coffee and black tea drinkers compared to non-drinkers. Thus, our results dispel the myth regarding electrolyte depletion, including magnesium deficiency, in coffee drinkers and are in accordance with previous studies revealing that the diuretic property of caffeine that induces magnesium loss, is compensated by coffee intake itself, due to the high concentration of magnesium in coffee [55].

There are many misconceptions about including coffee and tea as part of a daily balanced diet. However, based on our study results, even patients with sleep disorders can consume coffee on a daily basis, however caution is recommended in sleep bruxers. Nevertheless, excessive daily caffeine intake may lead to physical and psychological dependence, and it should be taken into consideration in choosing healthy dietary choices [56]. Recent findings emerge concerns about disadvantageous influence of COVID-19 pandemic and it should be as well taken into consideration when discussing SB [57,58].

4.6. Study strengths

It is remarkable therefore that no polysomnographic study has investigated the role of coffee and black tea consumption on sleep bruxism intensity previously. The strengths of this study include a relatively large study group (n = 106), as well as an additional assessment of electrolyte and lipid panels. All 106 patients underwent an entire night of PSG examination with camera recording, a gold standard tool used in definite SB diagnosis [3]. In addition, PSG examination was performed with the use of video recording that allows to analyze patient's nocturnal behavior, correlate behavior with neuropsychologic parameters and detect epileptiform activity [59].

4.7. Study limitations

However, there are also several study limitations. The study group of coffee non-drinkers was small (n = 19). The surveys did not include questions about the type of coffee roasting, caffeine content or information about the method of preparation (e.g. brewed, filtered or boiled coffee), which can influence the results [60]. Patients were divided in four groups regarding coffee and tea drinking habits as mentioned before. However, there are some patients who drink both coffee and tea.

5. Conclusions

1. The bruxism episode index is increased in coffee drinkers compared to non-drinkers, thus coffee drinking may be considered a risk factor for definite sleep bruxism.
2. Habitual black tea consumption does not affect sleep bruxism intensity and sleep architecture.
3. Arousal levels, sleep latency and sleep efficiency are similar in coffee drinkers and non-drinkers. Coffee consumption is not related to sleep fragmentation in habitual coffee drinkers.
4. Habitual coffee and tea consumption does not influence CRP, serum uric acid, electrolyte and lipid concentrations in sleep disorder patients.

Author contribution statement

Weronika Frosztega: conceived and designed the experiments; wrote the paper.
Mieszko Wieckiewicz: conceived and designed the experiments; performed the experiments; wrote the paper.
Helena Martynowicz: conceived and designed the experiments; performed the experiments; analyzed and interpreted the data; contributed reagents, materials, analysis tools or data; wrote the paper.
Dorian Nowacki and Rafal Poreba analyzed and interpreted the data;
Gabriella Lachowicz and Grzegorz Mazur: contributed reagents, materials, analysis tools or data; wrote the paper.

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Institutional review board statement

The study was conducted according to the guidelines of the Declaration of Helsinki and approved by the Ethics Committee at Wroclaw Medical University (ID: KB-790/2022).

Informed consent statement

Informed consent was obtained from all subjects involved in the study.

Data availability statement

The data that supports the findings of this study is available on request from the corresponding author. The data is not publicly available due to privacy or ethical restrictions.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2023.e16212.

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4.3 Artykuł trzeci

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The Effect of Cadmium on Sleep Parameters Assessed in Polysomnographic Studies: A Case–Control Study

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Abstract: Cadmium is a heavy metal that accumulates in the body due to environmental and occupational exposure. The main form of environmental exposure to cadmium is related to cigarette smoking. The primary aim of this study was to evaluate the effect of cadmium on numerous sleep parameters with the use of polysomnography. The secondary aim of this study was to investigate if environmental exposure to cadmium is a risk factor for the intensity of sleep bruxism (SB). Methods: A total of 44 adults underwent a full night of polysomnographic examination. The polysomnograms were assessed according to guidelines set out by the American Academy of Sleep Medicine (AASM). The concentration of cadmium in the blood and urine was determined spectrophotometrically. Results: The polysomnographic examination confirmed that cadmium, age, male gender and smoking status are independent risk factors for an increase in the apnea–hypopnea index (AHI). Cadmium alters sleep architecture by favoring sleep fragmentation and decreasing the duration of the rapid eye movement (REM) phase of sleep. However, cadmium exposure is not a risk factor for the development of sleep bruxism. Conclusions: In summary, this study demonstrates that cadmium affects sleep architecture and is a risk factor for the development of obstructive sleep apnea; however, it does not affect sleep bruxism.

Keywords: cadmium; sleep architecture; polysomnography; REM sleep stage; obstructive sleep apnea (OSA); sleep bruxism (SB)

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1. Introduction

Cadmium is a widespread heavy metal that is present naturally in the Earth's crust [1]. Its biological half-life within the body, after environmental exposure, is estimated to be about 20 years [2]. In the last century, the industrial sector has most frequently used cadmium in the coating of iron and steel to prevent corrosion. Nowadays, this sector utilizes cadmium in the manufacture of batteries, pigments, coatings, plating substances and stabilizers for plastic. However, beyond the manufacturing sector, the most common form of exposure to cadmium is by means of inhalation and ingestion. Occupational exposure to cadmium relates to processes involving the heating of cadmium-containing materials [1].

Tobacco plants are known for absorbing heavy metals from the soil through their roots, accumulating them within their leaves which are ultimately used in the production of cigarettes. The single major significant source of cadmium exposure for the general population is tobacco smoking [3,4]. It has been established that smokers tend to have elevated

cadmium concentrations in the blood, compared to their non-smoking counterparts [5,6]. It is worth noting, though, that non-smokers are also exposed to high quantities of cadmium that is present in water and food. This is particularly true of populations consuming diets that are high in rice and wheat content [5].

The kidneys are the major site of cadmium accumulation in the body. This in turn leads to nephrotoxicity and renal tubular damage, causing numerous negative health outcomes [3,7]. Cadmium has also been found to be neurotoxic. The recent literature states that cadmium has a strictly dose-dependent effect on neurons: Cadmium can gradually cause cell injury, cell death and organ failure at high doses. On the other hand, it can modulate specific mechanisms at low doses without significantly harming cells [8]. Neurodegenerative disorders, such as Alzheimer's disease, Parkinson's disease, amyotrophic lateral sclerosis, multiple sclerosis and myalgic encephalomyelitis, have previously been linked with cadmium-dependent neurotoxicity [9].

The symptoms of poisoning depend on the level of cadmium in the blood and may result in acute and chronic intoxication. It has been determined that cadmium is a type I carcinogen and acts as a proinflammatory cytokine inducer, leading to a chronic inflammatory response [3]. Cadmium exposure has been linked to the development of numerous illnesses, including osteoporosis [10], depressive symptoms [11,12], smoking-induced cardiovascular diseases [13] and pulmonary diseases [3]. Recently, cadmium exposure from tobacco smoking has been linked with type 2 diabetes mellitus [14]. Direct prolonged exposure to cadmium is known to be a major etiological factor of itai-itai disease (otherwise known as "ouch-ouch" disease) in Japanese female residents living near cadmium-contaminated rivers. Severe spine and joint pain, softening of the bones and kidney failure were the main findings in these patients. Several studies were carried out after reports of itai-itai disease came to light, in order to determine the levels of cadmium exposure that are a health threat [7,15]. Due to its adverse effects on human health, cadmium usage has been restricted worldwide under numerous regulations [16].

Worldwide culture-associated smoking habits have brought the attention of the scientific community to the substances present in cigarettes, ultimately raising environmental and health concerns. No studies have been published investigating the possible influence of cadmium on sleep architecture (rapid eye movement (REM), non-rapid eye movement (nREM)), respiratory function (apnea–hypopnea index (AHI) and saturation parameters) and movement disorders (bruxism episode index (BEI)). Due to the lack of research in this regard, the primary aim of this study was to evaluate the influence of cadmium on sleep architecture, by utilizing polysomnographic examination. The secondary aim of this study was to establish if exposure to cadmium increases the likelihood of developing obstructive sleep apnea (OSA) and if cadmium itself is a risk factor for sleep bruxism (SB).

2. Materials and Methods

2.1. Participants

This was a prospective, observational study of a total of 44 adults. The patients were admitted to the Department of Internal Medicine and Occupational Diseases, Hypertension and Clinical Oncology at Wroclaw Medical University, Poland, in order to undergo polysomnographic examination. The patients were referred to the sleep laboratory for examination, due to a suspicion that they may have a sleep disorder. These 44 subjects were admitted to the department between December 2020 and May 2021. Inclusion criteria were as follows: age over 18 years, written informed consent to polysomnographic examination and urine/blood sample collection. Patients were excluded from the study if they had neurological disorders and/or neuropathic pain, active inflammation, confirmed active malignancy, present or past occupational exposure to cadmium, severe respiratory and cardiac insufficiency, treatments affecting muscle function and sleep structure, severe mental disorders, cognitive disability and a lack of compliance during the study. All study participants declared no occupational cadmium exposure throughout their lifetime. The study was approved by the Ethics Committee at Wroclaw Medical University (approval

no. KB-790/2022). Voluntary written informed consent was obtained from all patients prior to commencing the study. This study made use of the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist [17].

2.2. Polysomnography

All subjects (n = 44) underwent polysomnographic investigation with a NoxA1 (NOX Medical, Reykjavík, Iceland) device. The recording was conducted between 22:00 and 6:00, in accordance with the patient's natural circadian rhythm. Electromyographic electrodes were placed in line with guidelines set out by the American Academy of Sleep Medicine (AASM) [18]. Audio and video recordings together with electrocardiographic, electroencephalographic, electro-oculographic and electromyographic recordings were included, along with body position detection and thoracic and abdominal breathing activity. To measure saturation (SpO_2%), pulse and plethysmography data, a WristOx2 3150 pulse oximeter (Nonin Medical Inc., Plymouth, MN, USA) was used. The respiratory, sleep bruxism (SB) and sleep parameters were gathered. Sleep parameters were obtained and classified pursuant to standard AASM criteria: non-REM 1 sleep stage (N1), non-REM 2 sleep stage (N2), non-REM 3 sleep stage (N3), REM sleep stage, arousal index (ArI), sleep latency (SL), wake after sleep onset (WASO), sleep efficiency (SE), apnea–hypopnea index (AHI), oxygen desaturation index (ODI) and snoring. SB parameters were also assessed: bruxism episodes index (BEI), phasic bruxism, tonic bruxism and mixed bruxism. A constant burst episode sustained over 2 s was categorized as a tonic episode. An episode including three or more bursts lasting over 2 s was categorized as phasic, and an episode showing the characteristics of both tonic and phasic episodes was categorized as a mixed episode of SB. SB episodes were defined as the rhythmic movements of the masseter muscles that occurred at least three seconds after the previous muscle movement. EMG activity had to be at least twice the amplitude of the background EMG. The bruxism episodes index (BEI) was measured by counting the number of bruxism episodes per hour of sleep. Phenotypes of bruxism were distinguished as follows: phasic, tonic and mixed [18]. The number of bruxism episodes per hour of sleep was used to categorize sleep bruxism and assigned as irrelevant (BEI < 2), mild to moderate (BEI 2–4) and severe (BEI > 4) [19].

2.3. Sample Collection and Determination of Blood and Urine Cadmium Concentration

Fasting venous blood samples from the ulnar vein and urine samples were obtained at 7:00 a.m., after twelve hours of overnight fasting. These blood samples were collected into polyethylene terephthalate (PET) plastic tubes (Becton, Dickinson and Company; Franklin Lakes, NJ, USA) with K_2EDTA. Blood samples were stored at −70 °C until subsequent analyses were performed. Blood and urine samples were analyzed at the Main Laboratory of Wroclaw Medical University. Laboratory tests were performed according to the standard laboratory protocols of Wroclaw Medical University Teaching Hospital. The blood concentration of cadmium was determined by atomic absorption spectrophotometry with the use of a SOLAAR M6 (Thermo Elemental Ltd., London, UK) in an electrographite cuvette at λ = 228.8 nm, equipped with a Zeeman background correction system, in a certified atomic absorption laboratory at the University Hospital in Wroclaw, Poland. Values were measured in micrograms per deciliter (mg/dL).

For the analysis, the Stoeppler and Brandt method was used [20]. For trace metal analysis, the samples were deproteinized with 65% nitric acid (Suprapur; Merck KGaA, Darmstadt, Germany). Using ClinCal Whole Blood Calibrators (Cat.) and comparing the absorbance of the sample to a standard curve, the concentration of cadmium in the sample was determined. No. 9943) and control tests were performed (ClinChek Entire Blood Controls, level I, II, III; Cat. No. 8840–8843; Recipe Chemicals + Instruments GmbH, Munich, Germany). Within the framework of the German External Quality Assessment Scheme (G-EQUAS), external laboratory control was carried out with the assistance of the Intercomparison Program for Toxicological Analyses in Biological Materials (Institute and Out-Patient Clinic for Occupational, Social and Environmental Medicine of the Friedrich-

Alexander University, Erlangen, Germany). The described method had a detection limit of 0.082 g/L.

2.4. Statistics

Statistical analysis was carried out based on the statistical software "Dell Statistica 13" (Dell Inc., Tulsa, OK, USA). The distribution of variables was examined with the Lilliefors and W-Shapiro–Wilk tests. In comparative analyses, subgroups were compared based on the median, first quartile or third quartile of the grouping variable. In the case of quantitative independent variables with a normal distribution, the t-test was used for further statistical analysis. In the case of variables with a distribution other than normal, the Mann–Whitney U test was used for quantitative independent variables. For qualitative independent variables, the maximum likelihood chi-square test was utilized. To determine the relationship between the studied variables, correlation and regression analysis was performed. In the case of quantitative variables with a normal distribution, Pearson's r correlation coefficients were marked. For quantitative variables with a non-normal distribution, on the other hand, Spearman's r coefficients were used. The parameters of the model obtained in the multivariable stepwise regression analysis were estimated using the least squares method. Results at the level of $p < 0.05$ were considered to be statistically significant.

3. Results

The data that were obtained from the study group and subsequently evaluated are demonstrated in Table 1. Overall, 44 patients were included in this study. The minimum sample group size required to conduct this study was estimated using a sample size calculator. The following estimation input conditions were used: population size: 3,000,000 (population size of the Lower Silesian Voivodeship); fraction size: 0.1 (assumed OSA prevalence in the Polish population); confidence level: 95% (default value); and maximum error: 10% (one of the typical values). The minimum required sample group size of 35 people was achieved.

Table 1. Polysomnographic parameters in the study group.

Parameter	Average	Median	Minimum	Maximum
AHI (*n*/h)	24.22 ± 25.34	14.85	0.50	86.20
ODI (*n*/h)	23.45 ± 24.11	13.65	0.00	86.70
Snore (% of TST)	25.79 ± 22.29	26.75	0.00	75.40
Average SpO_2 (%)	91.57 ± 4.50	92.55	74.60	95.80
Minimal SpO_2 (%)	79.82 ± 10.46	83.00	51.00	93.00
SpO_2 duration <90% (%)	16.01 ± 25.02	4.10	0.00	86.60
SL (min)	19.97 ± 15.79	13.65	1.00	64.60
WASO (min)	59.03 ± 44.11	44.50	7.50	186.10
SE (%)	82.80 ± 12.24	85.25	36.50	97.40
N1 (% of TST)	7.14 ± 7.74	3.40	0.30	32.70
N2 (% of TST)	52.03 ± 21.45	50.30	28.60	181.00
N3 (% of TST)	25.37 ± 20.55	23.00	6.40	146.50
REM (% of TST)	21.31 ± 6.53	21.70	0.00	34.40
ArI (*n*/h)	7.96 ± 13.57	3.75	0.10	88.30
BEI (*n*/h)	4.17 ± 3.29	3.30	0.00	13.60
Phasic bruxism episode index (*n*/h)	1.79 ± 2.18	1.40	0.00	10.70
Tonic bruxism episode index (*n*/h)	1.60 ± 1.39	1.10	0.00	5.50
Mixed bruxism episode index (*n*/h)	0.81 ± 0.80	0.60	0.00	3.40
AI (*n*/h)	11.96 ± 17.80	3.05	0.00	69.20
OA (*n*/h)	9.89 ± 15.60	2.00	0.00	62.40

Table 1. *Cont.*

Parameter	Average	Median	Minimum	Maximum
MA (n/h)	0.88 ± 2.39	0.00	0.00	14.20
CA (n/h)	1.19 ± 2.77	0.35	0.00	16.80
HI (n/h)	12.26 ± 12.15	8.35	0.10	50.60
Average pulse (bpm)	62.47 ± 8.83	61.35	48.70	94.40
Maximal pulse (bpm)	94.95 ± 14.28	96.50	64.00	140.00
Minimal pulse (bpm)	46.29 ± 11.37	48.00	4.60	71.0

AHI: apnea–hypopnea index; ODI: oxygen desaturation index; SL: sleep latency; WASO: wake after sleep onset; SE: sleep efficiency; REM: rapid eye movement; TST: total sleep time; ArI: arousal index; BEI: bruxism episode index; AI: apnea index; OA: obstructive apneas; MA: mixed apneas; CA: central apneas; HI: hypopneas index.

The average age of the study group was 47.45 ± 13.69 years old. In total, 38.63% (n = 17) of the participants were female, while 61.36% (n = 27) were male; 86.36% (n = 38) of patients were current smokers; and 29 (67.44%) of the 44 the patients were diagnosed as sleep bruxers. Obstructive sleep apnea (OSA) was present in 70.45% (n = 31) patients in the study group. The degree of OSA was determined in each subject: 20.45% (n = 9) of cases were mild, 22.72% (n = 10) moderate and 27.27% (n = 12) of subjects had severe OSA. The mean blood and urine cadmium concentration in the study group was 0.37 ± 0.39 µg/L and 0.78 ± 0.63 µg/g of creatinine, respectively.

Patients were divided into two groups in accordance with their median cadmium blood concentration, namely, a low cadmium concentration group (<0.25) and a high cadmium concentration group (>0.25). In the low cadmium group, the average cadmium concentration was 0.14 ± 0.07, while in the high cadmium group it was 0.57 ± 0.46. The average SpO_2% and minimal SpO_2% were decreased in both of these groups. Statistical significance was present in SpO_2 < 90% duration, minimal SpO_2, average SpO_2, REM sleep stage, N2 sleep stage, WASO, bruxism episode index and phasic bruxism (Table 2).

Table 2. Blood cadmium concentration (micrograms/g) regarding median (Me), lower (Q1) and upper quartile (Q3).

Paramerer	Average ≥ Me	Average < Me	p	Average ≥ Q1	Average < Q1	p	Average <Q3	Average ≥Q3	p
Cadmium blood concentration (µg/L)	**0.57 ± 0.46**	**0.14 ± 0.07**	**0.000**	**0.46 ± 0.42**	**0.09 ± 0.03**	**0.006**	**0.20 ± 0.10**	**0.85 ± 0.54**	**0.000**
AHI (n/h)	30.49 ± 26.72	17.35 ± 22.38	0.086	27.92 ± 26.70	13.14 ± 17.35	0.094	20.13 ± 21.99	36.50 ± 31.52	0.063
ODI (n/h)	29.34 ± 25.69	17.00 ± 20.97	0.090	27.24 ± 25.59	12.09 ± 14.63	0.071	19.74 ± 20.49	34.59 ± 31.19	0.076
Snore (%)	27.00 ± 24.58	24.46 ± 20.01	0.710	27.48 ± 22.89	20.73 ± 20.56	0.391	22.15 ± 19.04	36.72 ± 28.31	0.060
Average SpO_2 (%)	**90.29 ± 5.58**	**92.97 ± 2.33**	**0.048**	90.88 ± 4.94	93.62 ± 1.72	0.081	**92.58 ± 2.81**	**88.52 ± 6.94**	**0.008**
Minimal SpO_2 (%)	**76.04 ± 12.13**	**83.95 ± 6.24**	**0.010**	**77.76 ± 11.03**	**86.00 ± 4.96**	**0.022**	**82.94 ± 6.62**	**70.45 ± 14.19**	**0.000**
SpO_2 duration <90% (min)	20.03 ± 29.24	11.60 ± 19.15	0.270	19.30 ± 27.48	6.12 ± 11.47	0.132	**10.22 ± 16.15**	**33.38 ± 37.61**	**0.006**
SL (min)	21.76 ± 18.74	18.01 ± 11.91	0.438	20.34 ± 16.84	18.85 ± 12.74	0.789	19.18 ± 13.12	22.33 ± 22.64	0.573
WASO (min)	64.73 ± 41.07	52.79 ± 47.42	0.376	**67.04 ± 46.18**	**35.01 ± 26.38**	**0.035**	56.71 ± 43.45	65.99 ± 47.47	0.552
SE (%)	82.17 ± 9.90	83.49 ± 14.61	0.726	82.29 ± 10.57	84.32 ± 16.84	0.640	83.21 ± 12.77	81.55 ± 10.96	0.702
N1 (% of TST)	6.77 ± 6.79	7.55 ± 8.82	0.743	7.06 ± 7.83	7.38 ± 7.82	0.907	7.45 ± 8.45	6.20 ± 5.29	0.647
N2 (% of TST)	49.49 ± 9.09	54.80 ± 29.72	0.419	**48.07 ± 8.84**	**63.88 ± 39.02**	**0.033**	51.91 ± 24.38	52.37 ± 8.75	0.951
N3 (% of TST)	23.30 ± 10.39	27.62 ± 27.91	0.493	23.30 ± 9.30	31.55 ± 38.51	0.253	25.97 ± 23.10	23.55 ± 10.16	0.740

Table 2. *Cont.*

Paramerer	Average ≥ Me	Average < Me	*p*	Average ≥ Q1	Average < Q1	*p*	Average <Q3	Average ≥Q3	*p*
REM (% of TST)	20.41 ± 7.16	22.29 ± 5.77	0.348	21.54 ± 7.04	20.61 ± 4.87	0.687	**22.46 ± 5.25**	**17.85 ± 8.79**	**0.041**
Bruxism episodes index (*n*/h)	4.20 ± 3.25	4.14 ± 3.41	0.955	4.64 ± 3.23	2.80 ± 3.20	0.111	**3.60 ± 2.93**	**6.03 ± 3.87**	**0.039**
Phasic bruxism	2.06 ± 2.38	1.50 ± 1.96	0.407	2.02 ± 2.23	1.14 ± 1.96	0.253	**1.34 ± 1.65**	**3.27 ± 3.05**	**0.012**
Tonic bruxism	1.48 ± 1.04	1.73 ± 1.69	0.559	1.74 ± 1.28	1.19 ± 1.66	0.261	1.55 ± 1.47	1.75 ± 1.13	0.701
Mixed bruxism	0.70 ± 0.63	0.94 ± 0.94	0.323	0.93 ± 0.84	0.49 ± 0.56	0.119	0.74 ± 0.83	1.05 ± 0.65	0.289
ArI (*n*/h)	9.53 ± 18.08	6.23 ± 5.53	0.427	8.30 ± 15.43	6.93 ± 5.32	0.775	6.38 ± 5.83	12.70 ± 25.50	0.184
AI (*n*/h)	14.81 ± 19.43	8.84 ± 15.70	0.272	13.77 ± 19.13	6.55 ± 12.19	0.249	9.85 ± 15.61	18.30 ± 22.91	0.176
OA (*n*/h)	11.72 ± 16.39	7.89 ± 14.82	0.422	11.26 ± 16.57	5.78 ± 11.97	0.319	7.62 ± 12.78	16.71 ± 21.34	0.094
MA (*n*/h)	1.22 ± 3.14	0.50 ± 1.09	0.330	1.02 ± 2.68	0.46 ± 1.22	0.515	0.84 ± 2.56	0.99 ± 1.92	0.858
CA (*n*/h)	1.88 ± 3.71	0.43 ± 0.51	0.083	1.49 ± 3.15	0.28 ± 0.24	0.216	1.38 ± 3.16	0.62 ± 0.78	0.439
HI (*n*/h)	**15.68 ± 14.26**	**8.51 ± 8.09**	**0.049**	14.15 ± 12.97	6.58 ± 7.01	0.073	10.28 ± 10.32	18.21 ± 15.56	0.060

Me: median; Q: quartile; AHI: apnea–hypopnea index; ODI: oxygen desaturation index; SL: sleep latency; WASO: wake after sleep onset; SE: sleep efficiency; REM: rapid eye movement; TST: total sleep time; ArI: arousal index; BEI: bruxism episode index; AI: apnea index; OA: obstructive apneas; MA: mixed apneas; CA: central apneas; HI: hypopneas index; statistically significant values are shown in bold ($p < 0.05$).

The results for cadmium concentration in the urine were compared as shown in Table 3. Correlation analysis was also performed and is shown in Table 4.

Table 3. Urine cadmium concentration (micrograms/g creatinine) regarding median, lower (Q1) and upper quartile (Q3).

Parameter	Average < Me	Average ≥ Me	*p*	Average < Q1	Average ≥ Q1	*p*	Average < Q3	Average ≥ Q3	*p*
Cadmium urine concentration (µg/g of creatinine)	**0.34 ± 0.11**	**1.22 ± 0.62**	**0.000**	**0.24 ± 0.05**	**0.94 ± 0.63**	**0.001**	**0.47 ± 0.23**	**1.70 ± 0.54**	**0.000**
AHI (*n*/h)	16.85 ± 20.31	31.59 ± 28.09	0.053	13.94 ± 18.00	27.24 ± 26.59	0.147	20.02 ± 21.25	36.81 ± 32.92	0.056
ODI (*n*/h)	**15.76 ± 18.82**	**31.14 ± 26.68**	**0.033**	13.13 ± 15.00	26.49 ± 25.57	0.125	19.49 ± 19.77	35.34 ± 32.26	0.058
Snore (%)	25.50 ± 21.83	26.08 ± 23.25	0.933	16.74 ± 22.37	28.45 ± 21.89	0.146	26.30 ± 21.26	24.25 ± 26.20	0.794
Average SpO_2 (%)	**93.13 ± 2.20**	**90.00 ± 5.61**	**0.019**	93.57 ± 1.88	90.98 ± 4.88	0.110	**92.58 ± 2.75**	**88.53 ± 7.02**	**0.008**
Minimal SpO_2 (%)	**83.64 ± 7.13**	**76.00 ± 11.94**	**0.014**	84.80 ± 5.35	78.35 ± 11.18	0.087	**82.42 ± 7.15**	**72.00 ± 14.72**	**0.003**
SpO_2 duration <90% (% of TST)	9.09 ± 17.30	22.93 ± 29.70	0.066	9.26 ± 11.33	17.99 ± 27.62	0.338	**9.70 ± 15.55**	**34.94 ± 37.32**	**0.003**
SL (min)	18.64 ± 14.18	21.30 ± 17.48	0.582	26.03 ± 16.90	18.19 ± 15.24	0.170	19.42 ± 14.16	21.62 ± 20.63	0.694
WASO (min)	51.02 ± 41.30	67.05 ± 46.30	0.232	52.01 ± 41.65	61.10 ± 45.20	0.573	54.00 ± 42.31	74.14 ± 48.00	0.193
SE (%)	84.00 ± 14.26	81.59 ± 10.01	0.519	79.21 ± 18.12	83.85 ± 10.03	0.297	83.76 ± 12.99	79.91 ± 9.58	0.372
N1 (% of TST)	8.13 ± 9.03	6.15 ± 6.25	0.402	7.73 ± 7.61	6.97 ± 7.88	0.788	7.10 ± 8.06	7.27 ± 7.04	0.949
N2 (% of TST)	54.99 ± 28.66	49.06 ± 10.12	0.366	62.24 ± 42.09	49.02 ± 8.69	0.087	52.56 ± 23.83	50.42 ± 12.58	0.778
N3 (% of TST)	26.85 ± 27.73	23.88 ± 9.54	0.637	33.69 ± 40.26	22.92 ± 9.00	0.147	26.11 ± 22.80	23.15 ± 12.06	0.684
REM (% of TST)	21.74 ± 5.09	20.87 ± 7.80	0.664	22.09 ± 6.54	21.08 ± 6.60	0.671	22.03 ± 4.80	19.15 ± 10.10	0.208

Table 3. *Cont.*

Parameter	Average < Me	Average ≥ Me	*p*	Average < Q1	Average ≥ Q1	*p*	Average < Q3	Average ≥ Q3	*p*
Bruxism episode index (*n*/h)	4.11 ± 3.92	4.22 ± 2.56	0.914	3.65 ± 3.41	4.32 ± 3.29	0.576	3.98 ± 3.41	4.79 ± 2.92	0.501
Phasic bruxism episode index (*n*/h)	1.81 ± 2.74	1.77 ± 1.43	0.945	1.44 ± 1.99	1.90 ± 22.25	0.567	1.62 ± 2.32	2.35 ± 1.61	0.360
Tonic bruxism episode index (*n*/h)	1.55 ± 1.62	1.65 ± 1.12	0.812	1.55 ± 1.87	1.62 ± 1.24	0.898	1.61 ± 1.47	1.58 ± 1.12	0.959
Mixed bruxism episode index (*n*/h)	0.77 ± 0.83	0.86 ± 0.77	0.704	0.68 ± 0.66	0.85 ± 0.84	0.549	0.78 ± 0.84	0.94 ± 0.66	0.573
ArI (*n*/h)	6.99 ± 5.50	8.93 ± 18.57	0.640	6.51 ± 5.68	8.39 ± 15.18	0.706	6.29 ± 5.01	12.97 ± 25.98	0.160
AI(*n*/h)	8.26 ± 14.03	15.66 ± 20.58	0.171	7.09 ± 12.71	13.39 ± 18.97	0.331	9.95 ± 15.73	17.99 ± 22.75	0.198
OAI (*n*/h)	7.19 ± 13.21	12.60 ± 17.57	0.255	6.07 ± 12.59	11.01 ± 16.38	0.385	7.94 ± 12.91	15.75 ± 21.52	0.153
MAI (*n*/h)	0.52 ± 1.08	1.23 ± 3.21	0.332	0.53 ± 1.26	0.98 ± 2.64	0.608	0.89 ± 2.58	0.85 ± 1.82	0.960
CAI (*n*/h)	0.55 ± 0.60	1.83 ± 3.81	0.127	0.50 ± 0.47	1.39 ± 3.13	0.380	1.12 ± 2.94	1.39 ± 2.31	0.781
HI (*n*/h)	**8.60 ± 7.95**	**15.91 ± 14.53**	**0.045**	6.86 ± 7.28	13.85 ± 12.90	0.111	**10.08 ± 8.40**	**18.81 ± 18.60**	**0.037**
Average pulse (bpm)	**59.56 ± 9.30**	**65.37 ± 7.45**	**0.027**	59.58 ± 13.22	63.31 ± 7.12	0.244	61.00 ± 9.15	66.86 ± 6.28	0.055
Maximal pulse (bpm)	94.64 ± 11.09	47.95 ± 11.64	0.085	91.70 ± 20.09	95.91 ± 12.30	0.419	94.88 ± 15.51	45.36 ± 12.06	0.952
Minimal pulse (bpm)	44.62 ± 11.09	47.95 ± 11.64	0.336	41.16 ± 13.23	47.79 ± 10.50	0.105	46.59 ± 11.30	45.36 ± 12.06	0.760

Me: median; Q: quartile; AHI: apnea–hypopnea index; ODI: oxygen desaturation index; SL: sleep latency; WASO: wake after sleep onset; SE: sleep efficiency; REM: rapid eye movement; TST: total sleep time; ArI: arousal index; BEI: bruxism episode index; AI: apnea index; OAI: obstructive apneas index; MAI: mixed apneas index; CAI: central apneas index; HI: hypopneas index; statistically significant values are shown in bold ($p < 0.05$).

Table 4. Correlation analysis.

Variable	Cadmium Blood Concentration (µg/L)	*p*	Cadmium Urine Concentration [µg/g of Creatinine]	*p*
AHI (*n*/h)	**0.44**	**<0.05**	**0.36**	**<0.05**
ODI (*n*/h)	**0.44**	**<0.05**	**0.38**	**<0.05**
Snore (%)	**0.33**	**<0.05**	−0.02	>0.05
Average SpO_2 (%)	**−0.57**	**<0.05**	**−0.56**	**<0.05**
SpO_2 duration <90% (% of TST)	**0.47**	**<0.05**	**0.50**	**<0.05**
Average desaturation	**0.45**	**<0.05**	**0.52**	**<0.05**
Minimal SpO_2 (%)	**−0.54**	**<0.05**	**−0.53**	**<0.05**
Minimal pulse	**−0.46**	**<0.05**	0.07	>0.05
REM (% of TST)	**−0.44**	**<0.05**	−0.08	>0.05
ArI (*n*/h)	**0.60**	**<0.05**	**0.42**	**<0.05**
AI (*n*/h)	0.29	>0.05	**0.32**	**<0.05**
OAI (*n*/h)	**0.33**	**<0.05**	**0.35**	**<0.05**
HI (*n*/h)	**0.48**	**<0.05**	0.29	>0.05

AHI: apnea–hypopnea index; ODI: oxygen desaturation index; REM: rapid eye movement; ArI: arousal index; AI: apnea index; OAI: obstructive apneas index; HI: hypopneas index; statistically significant values are shown in bold ($p < 0.05$).

The result of the regression analysis is presented in Table 5. Age, high urine cadmium concentration, male gender and smoking are independent risk factors for increased AHI values (Table 5). Cadmium has not been found to be an independent risk factor for sleep bruxism.

Table 5. The regression model of obstructive sleep apnea predictors in the study population.

Parameter	RC	SEM of RC	*p*
Intercept	**−37.024**	**15.156**	**0.0193**
Age	**0.480**	**0.234**	**0.0438**
Cadmium urine concentration (µg/g of creatinine)	**15.795**	**5.921**	**0. 0111**
Male	**22.955**	**7.106**	**0.0025**
Smoking	**11.765**	**3.226**	**0.0257**

RC—regression coefficient; SEM of RC—standard error mean of RC; statistically significant values are shown in bold ($p < 0.05$).

4. Discussion

4.1. Evidence for Role of Cadmium in OSA

To the best of our knowledge, this is the first study investigating the role of cadmium on sleep parameters. In this study, cadmium was found to be a risk factor for an increased apnea/hypopnea index (AHI). As a result, our study shows that environmental exposure to cadmium may increase the risk of developing OSA.

We also determined that blood and urine cadmium concentration was correlated with blood oxygen saturation parameters. This suggests that cadmium exposure may affect the level of oxygen saturation in subjects with sleep disorders. As far as we know, no previous studies have ever investigated this specific relationship. However, it is known that cigarette smoking itself, which is the main source of cadmium exposure, has a negative influence on respiratory parameters [21].

Past studies evaluating the serum levels of heavy metals in patients with obstructive sleep apnea (OSA) revealed that, among others, the serum level of cadmium was increased in the study group (compared to controls), possibly due to oxidative stress and inflammation [22]. One such study, conducted by Asker et al., was based on recorded polygraphic measurements. No sleep architecture parameters were obtained in this study. However, despite this, the results are in agreement with the outcomes of the present study. Cadmium is known for its oxidative stress and inflammatory properties [7]. There is also a strong correlation between inflammation, oxidative stress and OSA, which has been proven in previous studies [23].

Cadmium may increase inflammation in the tissues of the respiratory tract, favoring the narrowing of the upper airway during sleep and affecting respiratory control stability/loop gain, the respiratory arousal threshold and upper airway muscle function via neurotoxic activity. On the other hand, hypoxia in OSA may affect the absorption of cadmium, thus the cadmium–OSA relationship may be bidirectional. However, these hypotheses require further research.

The influence of cigarette smoking on OSA development has recently been a subject of interest, with varying results in numerous studies [24]. Still, other proven risk factors for OSA include male gender, older age, obesity and craniofacial deformities [25]. No past studies have investigated the potential mechanisms (arising from cadmium exposure) that lead to the development of sleep apnea. To this day, the mechanisms underlying cadmium-induced airway pathologies have not yet been fully understood due to the complex relationship between biochemical and clinical outcomes. However, to the best of our knowledge, our study is the first to demonstrate that cadmium exposure is an independent OSA risk factor.

4.2. The Influence of Cadmium on Sleep Bruxism (SB) Intensity

No studies thus far have investigated the influence of cadmium exposure on SB intensity. In one of our previous studies, our team demonstrated that smoking, which is the main source of cadmium in humans, is a risk factor for SB development [26]. Our current study shows that cadmium itself is not a risk factor for the development of SB. However, we did find that the intensity of SB was increased in patients with a higher cadmium serum concentration, compared to subjects with a lower cadmium concentration. This result is not standalone though, and it is important to remember that many factors can influence the intensity of bruxism in patients with cadmium exposure, such as insomnia, psychological status or caffeine consumption. Sleep bruxism and obstructive sleep apnea are also two strongly connected disorders that can even co-occur [27]. Besides its nicotine content, various toxic components are present in a single cigarette, each of which may affect the intensity of bruxism. A host of reactive oxygen and nitrogen species (ROS and RNS) may alter the intensity of bruxism and endothelial function. The endothelium regulates the inflammatory state in a human's body and cigarette smoking is known to lead to endothelial dysfunction [28]. Thus, many proinflammatory and toxic compounds can affect the development of sleep bruxism but, as explained above, not cadmium.

In general, cigarettes act on the sympathetic nervous system by activating it [29]. On the contrary, though, in sleep bruxism the trigemino-cardiac reflex (TCR) plays an important role in the regulation of the autonomic nervous system. The activation of the TCR results in the suppression of sympathetic nervous activity, while parasympathetic activity is activated as a sort of defense mechanism [30]. As a result, the intensity of sleep bruxism is increased in smokers, however not due to the cadmium content, but rather due to other factors.

4.3. Evidence for the Role of Cadmium in Sleep Architecture Alterations

No research thus far has investigated the influence of cadmium on sleep architecture in humans. Only one study has explored the relationship between sleep and cadmium exposure in rats. However, this study only made use of an EEG investigation, which revealed that a high concentration of cadmium in drinking water led to an increase in non-REM sleep and a decrease in rhythms of locomotor activity [31]. Animal-based studies found that cadmium can influence sleep architecture and sleep duration, while acute cadmium exposure seemed to have an impact on the circadian rhythm [32–35]. Our results are consistent with previous investigations.

Past studies investigating the neurotoxic consequences of cadmium determined that cadmium exposure induces memory impairment and results in a decreased attention span in humans [36]. Interestingly, our present study demonstrates that cadmium exposure impacts the REM sleep stage by decreasing the duration of this phase of sleep. The REM stage of sleep participates in memory consolidation [37] and emotional processing [38]. These mechanisms can potentially be affected in patients exposed to cadmium. Further investigations are needed to explain this correlation.

We also found a positive correlation between cadmium content in blood/urine and the frequency of arousals during sleep. Higher concentrations of cadmium in the blood and urine were found among subjects with an increased arousal index. It is known that arousals favor sleep fragmentation and sleep architecture alterations [39]. It is worth noting that fragmented sleep is a known cardiovascular risk factor [40].

Our study group had environmental exposure to cadmium. The mean blood cadmium concentration was 0.37 ± 0.39 µg/g, while the concentration in the urine was 0.78 ± 0.63 µg/g of creatinine. In the general population, geometric cadmium levels in blood have been estimated to be around 0.315 ng/L, while in urine these levels are approximately 0.193 ng/g of creatinine [41]. In our study, these biomarkers were higher, and this result confirms environmental cadmium exposure in our patients.

In conclusion, the complexity of cadmium-dependent sleep architecture outcomes remains to be clarified and further studies on the various mechanisms that result in sleep

pattern changes are needed. It may help to develop new methods of OSA treatments. However, in conclusion of our study, patients with OSA should avoid environmental and occupational cadmium exposure.

4.4. Study Strengths

Full-night audio–video polysomnography, which is the gold standard in sleep examination, was performed in the whole study group. In addition, both blood and urine samples were obtained and measured to determine cadmium concentration. Blood and urine are known to be exposure biomarkers [3]. However, blood cadmium is more likely to indicate recent cadmium exposure, while cadmium found in the urine has been linked to chronic or past exposure and may indicate the total cadmium body burden [42].

4.5. Study Limitations

The relatively small study group (n = 44) was the major limitation of this study. In addition, there was no adaptive night prior to conducting the PSG examination due to a limited capacity in the sleep laboratory, and due to restrictions associated with the organization of the hospital. This study was not intended to show an influence of cigarette smoking on sleep parameters, but to investigate blood and urine cadmium influence on sleep architecture. However, smoking may explain some changes in sleep architecture and further research is needed to determine this relation.

5. Conclusions

1. Cadmium is an independent factor for increased AHI, similarly to age, gender and smoking status.
2. Cadmium is not a risk factor for sleep bruxism.
3. Cadmium favors sleep disturbances, including sleep fragmentation, and results in the limitation of the duration of the REM sleep stage.

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5. Streszczenie w języku polskim

Na rozprawę doktorską składa się cykl 3 artykułów opublikowanych w międzynarodowych czasopismach naukowych indeksowanych w bazie MEDLINE i uwzględnionych na liście Journal Citations Reports by Web of Science oraz znajdujących się w wykazie czasopism naukowych Ministerstwa Edukacji i Nauki (MEiN). Łączny współczynnik wpływu (IF) artykułów wchodzących w skład rozprawy doktorskiej wynosi 11,8, a punktacja MEiN wynosi 320 punktów. We wszystkich artykułach jestem pierwszą autorką.

Dwa pierwsze artykuły skupiają się na zbadaniu wpływu używek takich jak kawa, herbata, alkohol i papierosy na nasilenie bruksizmu sennego i architekturę snu. Trzeci artykuł skupia się na poznaniu wpływu kadmu, metalu, którego głównym źródłem jest palenie papierosów, na nasilenie bruksizmu sennego i architekturę snu. We wszystkich badaniach, zgodnie z międzynarodowym konsensusem, przeprowadzono całonocne badanie polisomnograficzne w celu ustalenia diagnozy bruksizmu sennego i oceny struktury snu.

Tematyka pierwszego artykułu dotyczy wpływu palenia papierosów i picia alkoholu na nasilenie bruksizmu sennego i architekturę snu. U 133 pacjentów przeprowadzono badanie polisomnograficzne i pobrano krew żylną w celu dalszych analiz. Dodatkowo pacjenci wypełnili ankiety dotyczące ich nawyków dotyczących spożywania kawy i herbaty. Po raz pierwszy zbadano elektromiograficzne fenotypy bruksizmu sennego oraz wpływ wzbudzeń i pozycji ciała na występowanie bruksizmu podczas snu u osób deklarujących palenie papierosów i spożywanie alkoholu. Udowodniono, że palacze papierosów intensywniej zgrzytają zębami i częściej wybudzają się ze snu w związku ze zgrzytaniem zębami, co może mieć związek z fragmentacją snu u tej grupy pacjentów. Dodatkowo ustalono, że palacze, którzy mają choroby współistniejące wykazują tendencję do zaburzeń elektrolitowych i lipidowych. Natomiast spożywanie alkoholu według tego badania nie wpływa na parametry bruksizmu sennego.

Druga praca jest oryginalną pracą badawczą, w której ustalono wpływ spożywania kawy i czarnej herbaty na intensywność bruksizmu sennego i zaburzeń struktury snu. Spożywanie kawy i czarnej herbaty jest szeroko rozpowszechnione w społeczeństwie i związane z uwarunkowaniami kulturowymi. Analiza badania polisomnograficznego u 106 pacjentów wykazała, że intensywność bruksizmu jest wyższa u pacjentów spożywających kawę, natomiast picie czarnej herbaty nie wpływa na parametry bruksizmu sennego. Ustalono, że zarówno kawa

jak i czarna herbata spożywana regularnie nie powoduje zaburzeń architektury snu. Ponadto, od pacjentów pobrano krew żylną w celu dalszych analiz, które wykazały, że regularne spożywanie kawy i czarnej herbaty nie wpływa na poziom białka C-reaktywnego (CRP), kwasu moczowego we krwi, jonogramu i lipidogramu u pacjentów ze zdiagnozowanymi zaburzeniami snu.

Ostatnia praca porusza temat wpływu środowiskowego narażenia na kadm na parametry bruksizmu sennego i architekturę snu oceniane w badaniu polisomnograficznym w grupie 44 pacjentów. Po raz pierwszy wykazano, że narażenie na kadm nie jest czynnikiem ryzyka bruksizmu sennego. Dowiedziono, że kadm zaburza architekturę snu i wpływa negatywnie na parametry oddechowe, co może zwiększać ryzyko rozwoju obturacyjnego bezdechu sennego (OSA).

Podsumowując, patogeneza bruksizmu sennego jest złożona i nie do końca poznana. Dzięki przeprowadzonym badaniom poszerzono wiedzę na temat patofizjologii bruksizmu sennego i wpływu używek na architekturę snu. Wyniki prac wchodzących w skład tej rozprawy doktorskiej wskazują na istotny wpływ kawy i palenia papierosów na nasilenie bruksizmu oraz kadmu na nasilenie obturacyjnego bezdechu sennego co niewątpliwie przyczyni się w przyszłości do opracowania nowych zaleceń dla pacjentów z zaburzeniami snu. Ponadto, wyniki dysertacji wskazują dalsze kierunki badań nad wpływem używek na architekturę i zaburzenia snu.

6. Streszczenie w języku angielskim

The doctoral dissertation consists of a series of 3 articles published in international scientific journals indexed in the MEDLINE database and included in the Journal Citation Reports by Web of Science list, as well as in the list of scientific journals of the Ministry of Education and Science (MEiN). The total impact factor (IF) of the articles included in the doctoral dissertation is 11,8, and the MEiN score is 320 points. In all articles, I am the first and lead author.

The first two articles focus on the evaluation of the influence of stimulants such as coffee, tea, alcohol, and cigarettes on the severity of sleep bruxism and sleep architecture. The third article focuses on the impact of cadmium, a metal whose main source is cigarette smoking, on sleep bruxism severity and sleep architecture. In all studies, according to the international consensus, overnight polysomnography was performed to establish a diagnosis of sleep bruxism and to assess sleep architecture.

The first article concerns the influence of smoking and drinking alcohol on sleep bruxism intensity and sleep architecture. Polysomnography was performed on 133 patients, and venous blood was collected for further analysis. In addition, patients completed questionnaires about their coffee and tea consumption habits. For the first time, the sleep bruxism electromyographic phenotypes and the influence of arousal and body position on sleep bruxism in people who declare smoking and alcohol consumption were examined. It has been proven that cigarette smokers grind their teeth more intensively and wake up more often due to teeth grinding, which may be related to sleep fragmentation in this patient group. In addition, it has been established that smokers who have comorbidities tend to have electrolyte and lipid disorders. In contrast, alcohol consumption, according to this study, does not affect sleep bruxism parameters.

The second paper is an original research paper in which the effect of coffee and black tea consumption on sleep bruxism intensity and sleep structure is established. Consumption of coffee and black tea is widespread in society and culturally related. The analysis of the polysomnography study in 106 patients showed that sleep bruxism intensity is higher in patients who drink coffee, while drinking black tea does not affect sleep bruxism parameters. It has been proven that both coffee and black tea consumed regularly do not cause sleep

architecture disturbances. In addition, venous blood was collected from the patients for further analysis, which showed that regular consumption of coffee and black tea did not affect the level of C-reactive protein (CRP), blood uric acid, ionogram, or lipidogram in patients diagnosed with sleep-related disorders.

The last paper discusses the influence of cadmium environmental exposure on sleep bruxism parameters and sleep architecture assessed in a polysomnographic study in a group of 44 patients. For the first time, cadmium exposure has been shown not to be a risk factor for sleep bruxism. It has been proven that cadmium disrupts sleep architecture and negatively affects respiratory parameters, which may increase the risk of developing obstructive sleep apnea (OSA).

In conclusion, sleep bruxism's pathogenesis is complex and not fully understood. On account of the conducted research, knowledge about the pathophysiology of sleep bruxism and the impact of stimulants on sleep architecture has been expanded. The results of the work included in this doctoral dissertation indicate a significant impact of coffee and cigarette smoking on sleep bruxism severity and cadmium on obstructive sleep apnea severity, which will undoubtedly contribute in the future to the development of new recommendations for patients with sleep disorders. In addition, the results of the dissertation indicate further directions for research on the impact of stimulants on sleep architecture and sleep disorders.

7. Etyka

Projekt pracy doktorskiej opartej na powyższych publikacjach został zatwierdzony przez Komisję Bioetyczną Uniwersytetu Medycznego we Wrocławiu – Nr KB 790/2022. Badania przeprowadzono przestrzegając zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej Światowego Stowarzyszenia Lekarzy przyjętą przez 18 Zgromadzenie Ogólne Światowego Stowarzyszenia Lekarzy (WMA), w Helsinkach w czerwcu 1964 r., a zmienionej przez 64 Zgromadzenie Ogólne WMA, w Brazylii w październiku 2013 r. Wszelkie badania zostały przeprowadzone z zachowaniem anonimowości uzyskanych danych.

8. Opinia komisji bioetycznej

KOMISJA BIOETYCZNA
przy
Uniwersytecie Medycznym
we Wrocławiu

OPINIA KOMISJI BIOETYCZNEJ Nr KB –790/2022

Komisja Bioetyczna przy Uniwersytecie Medycznym we Wrocławiu, powołana zarządzeniem Rektora Uniwersytetu Medycznego we Wrocławiu nr 278/XVI R/2020 z dnia 21 grudnia 2020 r. oraz działająca w trybie przewidzianym rozporządzeniem Ministra Zdrowia i Opieki Społecznej z dnia 11 maja 1999 r. (Dz.U. nr 47, poz. 480) na podstawie ustawy o zawodzie lekarza z dnia 5 grudnia 1996 r. (Dz.U. nr 514 z 2020 r.) w składzie:

dr Joanna Birecka (psychiatria)
dr Beata Freier (onkologia)
dr hab. Tomasz Fuchs (ginekologia, położnictwo)
prof. dr hab. Dariusz Janczak (chirurgia naczyniowa, transplantologia)
dr hab. Krzysztof Kaliszewski, prof. UMW (chirurgia endokrynologiczna)
dr prawa Andrzej Malicki (prawo)
dr hab. Marcin Mączyński, prof.UMW (farmacja)
Urszula Olechowska (pielęgniarstwo)
prof. dr hab. Leszek Szenborn (pediatria, choroby zakaźne)
prof. dr hab. Andrzej Szuba (choroby wewnętrzne, angiologia
ks. prof. Andrzej Tomko (duchowny)
prof. dr hab. Mieszko Więckiewicz (stomatologia)
dr hab. Andrzej Wojnar, prof. nadzw. (histopatologia, dermatologia) przedstawiciel Dolnośląskiej Izby Lekarskiej)
dr hab. Jacek Zieliński (filozofia)

pod przewodnictwem
prof. dr hab. Jerzego Rudnickiego (chirurgia, proktologia)

Przestrzegając w działalności zasad Good Clinical Practice oraz zasad Deklaracji Helsińskiej, po zapoznaniu się z projektem badawczym pt.

„Ocena wpływu palenia papierosów i picia alkoholu na architekturę snu i intensywność bruksizmu sennego"

zgłoszonym przez **dr hab. Helenę Martynowicz, prof. UMW** zatrudnioną w Katedrze i Klinice Chorób Wewnętrznych, Nadciśnienia Tętniczego i Onkologii Klinicznej Uniwersytetu Medycznego we Wrocławiu oraz złożonymi wraz z wnioskiem dokumentami, w tajnym

głosowaniu postanowiła **wyrazić zgodę** na przeprowadzenie badań w Katedrze i Klinice Chorób Wewnętrznych, Nadciśnienia Tętniczego i Onkologii Klinicznej Uniwersytetu Medycznego we Wrocławiu pod warunkiem zachowania anonimowości uzyskanych danych.

UWAGA: Jeśli projekt/badanie wymaga ubezpieczenia na podstawie Rozporządzenia Ministra Finansów, Funduszy i Polityki Regionalnej z dnia 2.12.2020r. w sprawie obowiązkowego ubezpieczenia odpowiedzialności cywilnej podmiotu przeprowadzającego eksperyment medyczny , Wnioskodawca zobowiązany jest do zawarcia umowy ubezpieczenia odpowiedzialności cywilnej. W takim przypadku pozytywna opinia Komisji Bioetycznej ma charakter warunkowy i będzie uprawniała do prowadzenia Badania pod warunkiem zawarcia przez Wnioskodawcę umowy ubezpieczenia OC zgodnie z Rozporządzeniem wskazanym w zdaniu poprzednim

Pouczenie: W ciągu 14 dni od otrzymania decyzji wnioskodawcy przysługuje prawo odwołania do Komisji Odwoławczej za pośrednictwem Komisji Bioetycznej UM we Wrocławiu.

Opinia powyższa dotyczy projektu badawczego realizowanego w ramach działalności statutowej Uczelni

Przewodniczący Komisji Bioetycznej
przy Uniwersytecie Medycznym

prof. dr hab. Jerzy Rudnicki

Wrocław, dnia 27 10 [illegible]2

9. Curriculum Vitae

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PROFIL

Absolwentka Wydziału Lekarskiego. W trakcie studiów uzyskałam stypendium Rektora za wyróżniające wyniki w nauce i osiągnięcia naukowe.

DOŚWIADCZENIE

Koordynator działań prozdrowotnych, Fundacja Kolorowe Dni — 2021-obecnie

Wolontariuszka w fundacji „Kolorowe Dni" prowadzącej działalność edukacyjną i wspierającą seniorów.

Wyróżnienie, Międzynarodowa Konferencja „Program służby wobec Człowieka w medycynie paliatywnej i opiece hospicyjnej. Aspekt medyczny, filozoficzny, etyczny, prawny i kulturowy". — grudzień 2018

Wyróżnienie za prezentację ustną podczas sesji studenckiej.

WYKSZTAŁCENIE

Uniwersytet medyczny im. Piastów Śląskich we Wrocławiu — Wydział Lekarski wrzesień 2017 — czerwiec 2023

UMIEJĘTNOŚCI

Biegła znajomość języka angielskiego (potwierdzona certyfikatem FCE na poziomie B2).

Biegła znajomość języka niemieckiego.

Ukończone liczne kursy z zakresu medycyny estetycznej.

10. Dorobek naukowy (z wyłączeniem prac stanowiących cykl publikacji do Rozprawy Doktorskiej)

1. Kanclerska Justyna, Więckiewicz Mieszko, Poręba Rafał, Szymańska-Chabowska Anna, Gać Paweł, Wojakowska Anna, Frosztęga Weronika, Michałek-Zrąbkowska Monika, Mazur Grzegorz, Martynowicz Helena:

   Polysomnographic evaluation of sleep bruxism intensity and sleep architecture in nonapneic hypertensives: a prospective, observational study, Journal of Clinical Medicine, 2022, vol. 11, nr 11, art.3113 [10 s.], DOI:10.3390/jcm11113113, 140 punktów, IF (3.9)

2. Michałek-Zrąbkowska Monika, Poręba Rafał, Gać Paweł, Frosztęga Weronika, Wojakowska Anna, Więckiewicz Mieszko, Kanclerska Justyna, Macek Piotr, Więckiewicz Włodzimierz, Mazur Grzegorz:

   Telemetric assessment of continuous positive airways pressure (CPAP) effectiveness and adherence in obstructive sleep apnea during COVID-19 pandemic, Biomedicines, 2022, vol. 10, nr 5, art.1011 [13 s.], DOI:10.3390/biomedicines10051011, 100 punktów, IF (4.7)

3. Stojanowski Jakub, Konieczny Andrzej, Lis Łukasz, Frosztęga Weronika, Brzozowska Patrycja, Ciszewska Anna, Rydzyńska Klaudia, Sroka Michał, Krakowska Kornelia, Gołębiowski Tomasz, Hruby Zbigniew, Kusztal Mariusz, Krajewska Magdalena:

   The Artificial Neural Network as a Diagnostic Tool of the Risk of *Clostridioides difficile* Infection among Patients with Chronic Kidney Disease, Journal of Clinical Medicine, 2023, vol. 12, nr 14, art.4751 [10 s.], DOI:10.3390/jcm12144751, 140 punktów, IF (3.9)

4. Michałek-Zrąbkowska Monika, Więckiewicz Mieszko, Wichniak Adam, Jenca Jr Andrej, Jencova Janka, Frosztęga Weronika, Wieczorek Tomasz, Justyna Chojdak-Łukasiewicz, Służewska-Niedźwiedź Monika, Wojakowska Anna, Poręba Rafał, Mazur Grzegorz:

   Sleep-related rhythmic movement disorder in adults - A systematic review with a case report, Journal of Sleep Research, 2023, doi: 10.1111/jsr.13985, online ahead of print, 100 punktów, IF (4.4)

11. Oświadczenia współautorów

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Polysomnographic Assessment of Effects of Tobacco Smoking and Alcohol Consumption on Sleep Bruxism Intensity
Weronika Frosztega, Mieszko Wieckiewicz, Dorian Nowacki, Monika Michalek-Zrabkowska, Rafal Poreba, Anna Wojakowska, Justyna Kanclerska, Grzegorz Mazur, Helena Martynowicz

The effect of coffee and black tea consumption on sleep bruxism intensity based on polysomnographic examination
Weronika Frosztega, Mieszko Wieckiewicz, Dorian Nowacki, Rafal Poreba, Gabriella Lachowicz, Grzegorz Mazur, Helena Martynowicz

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