Drugs and Bruxism: A Critical Review

Ephraim Winocur, DMD
Lecturer and Coordinator

Anat Gavish, DMD
Lecturer in Pharmacology

Michal Voikovitch, MSc

Alona Emodi-Perlman, DMD
Clinical Instructor

Ilana Eli, DMD
Associate Professor and Head

Department of Occlusion and Behavioral Sciences
The Maurice and Gabriela Goldschleger School of Dental Medicine
Tel Aviv University
Tel Aviv, Israel

Correspondence to:
Dr Ephraim Winocur
Department of Occlusion and Behavioral Sciences
The Maurice and Gabriela Goldschleger School of Dental Medicine
Tel Aviv University
Tel Aviv, Israel
Fax: +972-3-6409250
E-mail: winocur@post.tau.ac.il

Aims: *Bruxism associated with drugs can be destructive, resulting in severe consequences to health that include destruction of tooth structure, irreversible harm to the temporomandibular joint, severe myofascial pain, and muscle contraction headache. However, reports concerning a possible association between bruxism and various pharmacologic drugs are scarce and mostly anecdotal. The purpose of this article was to review the existing literature concerning the exacerbating or ameliorating effect of drugs on bruxism in humans.* ***Methods:*** *A search of the MEDLINE, EMBASE, and PsicINFO databases from 1982 to 2001 was conducted, and the term bruxism and one of the following terms were used: drugs, medicine(s), pharmaceutical, movement disorders, akathisia, dyskinesia, dystonia, central or autonomic nervous system, dopamine, serotonin, and GABA. Furthermore, a search using the term bruxism was carried out on the weekly journal* Reactions, *which deals with side effects of drugs. Several chemical terms were searched separately (eg, caffeine, nicotine). Relevant information was also derived from reference lists of the retrieved publications.* ***Results:*** *The search yielded complex information referring to the association between bruxism and dopamine-related drugs, antidepressant drugs, sedative and anxiolytic drugs, and drugs of abuse.* ***Conclusion:*** *There is insufficient evidence-based data to draw definite conclusions concerning the effects of various drugs on bruxism. Although certain substances related to the dopaminergic, serotonergic, and adrenergic systems suppress or exacerbate bruxist activity in humans and animals, the literature is still controversial, and based mostly on anecdotal case reports. More controlled, evidence-based research on this under-explored subject is needed.*

J OROFAC PAIN 2003;17:99–111.

Key words: bruxism, medication(s), drug(s), dopamine, serotonin, GABA, SSRI

Various movement disorders exist in neurology (eg, Parkinson's disease and Meige's syndrome), in psychiatry (eg, akathisia, tardive dyskinesia),[1] and in sleep disorders (eg, restless-leg syndrome).[2] Some develop spontaneously while others are iatrogenic in nature due to medications affecting the central nervous system (CNS).

Bruxism, a known dysfunction of the orofacial musculature, is defined by the American Academy of Orofacial Pain as "a diurnal or nocturnal parafunctional activity including clenching, bracing, gnashing, and grinding of the teeth."[3] "Bracing" refers to a static, prolonged position of the mandible maintained by masticatory

and tongue muscle activity, not necessarily involving tooth contact. Idiopathic faciomandibular myoclonus activity, which has been reported to mimic sleep bruxism,[4,5] confuses the diagnosis. Facial movements and masticatory muscle activity during sleep, unrelated to bruxist activity, have been described in both bruxing and nonbruxing individuals.[6] Therefore, orofacial movement, including bruxism, may be considered as a normal phenomenon in some instances until some factor turns this activity into a detrimental one.[7] The reported factors include stress and personality,[8–10] disease,[7] alcohol,[11] and drugs of abuse.[12] Severe consequences to health, including destruction of tooth structure, irreversible harm to the temporomandibular joint, severe myofascial pain, muscle contraction headache, etc, are attributed to bruxism.[13] Long-term bruxist activity may cause the transition of pain from an acute to a chronic phase, causing disability and psychologic distress.[14] Thus, bruxism induced or exacerbated by drugs can be destructive, impeding daily life.[15–18]

The purpose of this article was to review the existing literature concerning the exacerbating and ameliorating effect of drugs on bruxism in humans.

Methods

The MEDLINE, EMBASE, and PsicINFO databases were searched from 1982 to 2001, and the term bruxism and one of the following terms were used: drugs, medicine(s), pharmaceutical, movement disorders, akathisia, dyskinesia, dystonia, central or autonomic nervous system, dopamine, serotonin, and GABA. A further search using the term bruxism was carried out on the weekly journal *Reactions*, which deals with side effects of drugs (including The Adverse Newsletter from the Uppsala Monitoring Center). Several chemical terms were also searched separately (eg, caffeine, nicotine). Relevant information was also derived from the reference lists of the retrieved publications.

Since the existing literature regarding the association between drugs and bruxism was confusing, tables were used to summarize the reports according to the pharmacologic use of each drug group. The effect of each drug on bruxism was specified for each report in the relevant table according to its reported activity (exacerbation, ameliorating, or no effect) as well as to the design of the relevant study, number of patients, etc. The most representative or illustrative studies were analyzed in more detail in the text.

Results

Dopamine-Related Agents

The effect of dopamine-related drugs (agonists and antagonists) on rhythmic jaw movement in animals has been described.[19–25] Spooren et al[20] found that dopamine D_1 receptors within the ventral pallidal area are involved in mediating orofacial dyskinesia in cats. Animal models of drinking-like jaw movements have also been described for apomorphine in ketamine-anesthetized guinea pigs.[23] Naidu and Kulkarni[25] succeeded in reducing haloperidol-induced empty chewing movements in rats with the administration of a serotonin (5-HT) agonist of 5-HT_{1A} receptors or 3 different 5-$HT_{2A/2C}$ receptor antagonists. Their findings indicate that the serotonergic system could be involved in haloperidol-induced orofacial dyskinesia.

However, these results should be interpreted judiciously, since tooth contacts or grinding observed in animals after administering either dopamine agonists or antagonists may be more closely related to oral tardive dyskinesia than to human bruxism.[7]

Lobbezoo et al[26] studied the possible existence of functional abnormalities of the central dopaminergic system in humans with sleep bruxism. This was assessed by functional neuroimaging of dopamine D2 receptors with single-photon-emission computed tomography. The study included 10 polysomnographically confirmed sleep bruxing individuals (bruxers) and 10 controls. Striatal D2 receptor binding potential did not differ significantly between bruxers and controls, but side-to-side differences between unilateral values of the striatal D2 binding potential were significantly larger for the bruxers. It was suggested that an abnormal side imbalance in striatal D2 receptors expression could be associated with sleep bruxism, which reinforces the possibility that the central dopaminergic system plays a role in the pathophysiology of sleep bruxism.

Dopamine Agonists. Levodopa and dopamine agonist play an important role as an initial treatment for Parkinson's disease. Long-term use of levodopa has been found to cause dose-related dyskinesia.[27]

Reports regarding a possible association between dopamine-related products and bruxism are scarce. The existing literature refers to 26 subjects: 24 participated in double-blind, crossover studies[28–31] and 2 are described as clinical case reports[32,33] (Table 1). Most of these studies showed an ameliorating or no effect on bruxism. In the study of Magee,[32] levodopa exacerbated bruxism

Table 1 Effects on Bruxism of Dopamine Agonists

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Magee[32]	Case report	1	0	Levodopa	(+)	
Harris et al[33]	Case report	1	0	Carbidopa, Levodopa	(–)	Relieved haloperidol-induced bruxism
Nishioka et al[28]	Double-blind, crossover	5	5	Bromocriptine vs placebo	(0)	Polysomnographic study
Lobbezoo et al[29]	Double-blind, crossover	10	10	Levodopa vs placebo	(–)	
Lobbezoo et al[30]	Double-blind, crossover	2	2	Bromocriptine vs placebo	(–)	4 out of 6 patients dropped out
Lavigne et al[31]	Double-blind, crossover	7	7	Bromocriptine vs placebo	(0)	Domperidone added to reduce side effects
Total		26	24		(+) 1 (–) 13 (0) 12	

* (+) Exacerbate; (–) ameliorate; (0) no effect.

in humans; however, there have been no other reports to support this.

Several studies have been conducted based on the assumption that the central dopaminergic system may be involved in the modulation of sleep bruxism.[29–31] Lobbezoo et al[29] found a significant decrease in the average number of bruxism episodes, as well as a significant reduction of the level of electromyographic (EMG) activity per bruxism burst, in bruxing patients who received low doses of short-term levodopa combined with benserazide (a peripheral decarboxylase inhibitor Prolopa), compared to a placebo. In a further study,[30] short-term administration of bromocriptine, a preferential dopamine D2 receptor agonist was used in a double-blind, placebo-controlled, polysomnographic and neuroimaging study with a single crossover design. Of the 6 patients (bruxers searching for treatment), 4 discontinued because of intensive side effects and 2 completed the trial. Both of these patients showed a decrease in the number of bruxism episodes per hour of sleep (20% to 30%) compared to a placebo following a 2-week administration of bromocriptine. Recently this same group[31] repeated the study and found that a nightly dose of bromocriptine did not have an effect on (exacerbate or reduce) sleep bruxism activity. One explanation for this deviant finding may be that the authors combined bromocriptine with domperidone, a peripheral D2 receptor antagonist, to suppress adverse side effects.[8] Nishioka et al[28] also did not find any significant effect of bromocriptine on nocturnal masseter EMG activity and sleep parameters.

Dopamine Antagonists. Antipsychotic drugs are pharmacologically characterized as dopamine receptor antagonists although many also act on other targets, particularly serotonin. These drugs are primarily used to treat schizophrenia and other behavioral or psychotic disorders.[34]

The existing literature regarding the effect of dopamine antagonists on bruxism in humans refers to 15 patients: 5 participated in double-blind, crossover studies and 10 were described as case reports (Table 2). The reports are inconsistent. While some reports show an exacerbating effect on bruxism (9 patients using haloperidol[33,35] or other dopamine antagonists[36]), one report[16] shows an ameliorating effect (1 patient using risperidone) and another no effect whatsoever (5 patients using haloperidol).[28]

The case reports presented by Micheli et al[36] suggest that long-term treatment with dopamine antagonist medicines causes diurnal bruxism, which is alleviated by sleep. They attribute the finding to a tardive dystonic reaction to treatment.

Amir et al[35] presented 2 cases of acute bruxism and akathisia, occurring as an early side effect of antipsychotic drug treatment, which were relieved by the addition of propranolol, a beta-adrenergic blocker. A clinical case has been described by Shiwach and Woods[16] in which a dopamine antagonist, risperidone, helped to alleviate a quite severe bruxism in an elderly man with dementia that emerged as part of an antipsychotic withdrawal dyskinesia. The apparent conflict between these 2 studies can be explained by the existence of the different mechanism involved. Akathisia is considered to be related to receptor blockade, while withdrawal dyskinesia is usually similar to tardive drug use that worsens with antipsychotic withdrawal, but improves with second and third generation atypical antipsychotic drugs.[37,38]

Table 2 Effects on Bruxism of Dopamine Antagonists

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Harris et al[33]	Case report	1	0	Haloperidol	(+)	Successfully treated with carbidopa and levodopa
Nishioka et al[28]	Double-blind, crossover	5	5	Haloperidol vs placebo	(0)	Polysomnographic study
Micheli et al[36]	Case report	6	0	Variety of drugs	(+)	Diurnal bruxism alleviated by sleep
Amir et al[35]	Case report	2	0	Haloperidol	(+)	Successfully treated with propranolol
Shiwach and Woods[16]	Case report	1	0	Risperidone	(–)	Successfully treated drug-withdrawal bruxism
Total		15	5		(+) 9 (–) 1 (0) 5	

* (+) Exacerbate; (–) ameliorate; (0) no effect.

Table 3 Effects on Bruxism of Cyclic Antidepressants

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Mohamed et al[41]	Double-blind, crossover	10	10	Amitriptyline vs placebo	(0)	Bruxers seeking treatment
Raigrodski et al[42,43]	Double-blind, crossover	10	10	Amitriptyline vs placebo	(0)	Bruxers seeking treatment
Brown and Hong[44]	Case report	1	0	Venlafaxine	(+)	Successfully treated with gabapentin
Jafee and Bostwick[18]	Case report	2	0	Venlafaxine	(+)	Successfully treated with buspirone
Total		23	20		(+) 3 (0) 20	

* (+) Exacerbate; (0) no effect.

Thus, the effect of dopamine-related drugs (agonists and antagonists) on bruxism in humans remains unclear.

Antidepressant Agents

Some of the most commonly used medications in modern society are antidepressant agents. These include a variety of drugs, such as cyclic (tricyclic or heterocyclic) antidepressants and selective serotonin reuptake inhibitors.[39]

Cyclic Antidepressants. Tricyclic antidepressants were proposed as a treatment for "destructive" bruxism occurring in rapid eye movement (REM) sleep.[40] The opinion was that since antidepressants suppress the physiologic REM sleep state, they should be administered to those patients diagnosed as destructive (REM) bruxers. However, no sufficient evidence-based data exist in the literature to support this assumption. The existing literature regarding the possible effect of amitriptyline, a tricyclic antidepressant, on bruxism refers to 3 double-blind crossover studies,[41–43] were apparently conducted on the same patients, Therefore, the total number of subjects in these 3 studies is only 20. Two other clinical case reports[18,45] refer to 3 patients treated with venlafaxine, a hetrocyclic antidepressant (Table 3).

The rationale for the administration of amitriptyline in alleviating bruxism in these studies[41,42] was not related to sleep architecture, but to the possible relation between the state of mental depression and the bruxist phenomenon. However, no association between the intake of this drug and bruxism was found in either study, possibly due to the low and insufficient dose (25 mg/night) and/or short-term treatment (7 nights).

Raigrodski et al[42] examined the effect of amitryptiline on pain intensity and perception of stress in 10 female bruxers in a randomized double-blind, crossover study. Amitryptiline administered over a 4-week period did not significantly reduce pain intensity associated with bruxist activity, but significantly reduced the level of stress perception. In another study, this same group[43] reported the effect of amitryptiline on nocturnal masseteric EMG activity and duration in 10 female patients (possibly the same patients). Amitryptiline did not significantly decrease the mean EMG activity and did not significantly increase the duration of sleep. Thus, the results do not support the administration of 25 mg of amitryptiline per night over a 4-week period for the management of sleep bruxism. According to Melis,[45] who analyzed these results, a greater decrease of EMG activity with the administration of amitryptiline is found in some subjects. He concluded that clinicians should learn to distinguish which patients will benefit from treatment with amitryptiline from those who will not, rather than not utilize treatment that could be beneficial to many patients.

Venlafaxine has been found to exacerbate bruxism in 2 studies.[18,44] Jaffee and Bostwick[18] proposed a pathophysiologic model for antidepressant-induced bruxism as an akathisia-like phenomenon resulting from disrupted serotonergic modulation of dopamine neurons in the mesocortical tract. Since venlafaxine acts as a serotonin reuptake inhibitor at low doses, Jaffee and Bostwick[18] were of the opinion that it is reasonable that venlafaxine could induce bruxism according to this model.

Selective serotonin reuptake inhibitors (SSRI). Lavigne and Montplaisir[7] have suggested a possible relationship between SSRI and bruxism, claiming that substances known to increase serotonin transmission in the CNS could affect bruxism. Although there seems to be a general agreement that SSRI exacerbate bruxism, the information regarding a possible association between SSRI and bruxism comes mainly from sporadic clinical case reports in which 23 patients are described[15,17,46–53]; however, there has been no controlled study (Table 4).

Christensen and Byerly[50] reported a clinical case in which the co-administration of sertraline and metoclepramide, a dopamine antagonist, resulted in mandibular dystonia. One theory expressed by the authors was that the additive pharmacodynamic action of both drugs was responsible for the adverse side effect. Another study[53] collected data from 166 family physicians in Amsterdam concerning side effects of various prescriptions. Only 5 (3.2%) reported the occurrence of SSRI-induced bruxism among their patients. The authors concluded that the use of SSRI could be associated with the occurrence of bruxism and presented 1 case report to corroborate this suggestion.

In a comprehensive review, Gerber and Lynd[54] reported that SSRI are positively associated with the development of various movement disorders, including bruxism. However, due to the inconsistent definition of bruxism, it was excluded from their database and separately discussed. Thus, out of 127 reviewed reports regarding SSRI and movement disorders, they reported only 10 cases of SSRI-induced bruxism occurring as a single disorder and another 6 cases occurring concurrently with other movement disorders. Although manufacturers of SSRI provided 60 cases of drug-induced bruxism, they were excluded from the database due to lack of specific patient information. The authors concluded that SSRI are associated with the development of movement disorders, either as a direct result of the drug or as an exacerbation of an underlying condition.

In conclusion, the association of SSRI and bruxism is based more on anecdotal rather than on evidence-based information. Nevertheless, the number of case reports justifies further investigation.

Sedative and Anxiolytic Drugs

As stress has been implicated in the exacerbation of bruxism in humans and animals,[13,55–58] anxiolytic or sedative hypnotic drugs are often suggested as effective in the treatment of bruxism. For example, Cocchi[59] is of the opinion that benzodiazepines, carbamazepine, and pyridoxine (vitamin B6) can be used successfully for bruxism in adults, due to their sedative action. However, data concerning this issue are insufficient and confusing. Clonazepam has been found effective in the treatment of temporomandibular disorders, but its action on bruxist activity was not reported.[60]

The effect of sedatives on bruxism refers to 1 crossover, placebo-controlled study (9 children),[61] 1 open trial study (11 subjects),[62] and several case reports describing the effect of buspirone in the treatment of bruxism induced or exacerbated by drugs (Table 5).

Reimao and Lefevre[61] reported the clinically observed effects of flurazepam in 40 children (1 to 15 years of age) presenting with sleep disturbances. Of these, 15 were diagnosed as bruxers. Among the 15 bruxers, 9 (60%) presented statistically significant improvement with flurazepam compared to a placebo. However, the authors did not report

Table 4 Effects on Bruxism of Selective Serotonin Reuptake Inhibitors

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Ellison and Stanziani[46]	Case report	3	0	Fluoxetine	(+)	Successfully treated with buspirone or by dose reduction
	Case report	1	0	Sertraline	(+)	Successfully treated with buspirone
Fitzgerald and Healy[15]	Case report No. 1	1	0	Sertraline	(+)	Ameliorated with propranolol and paroxetine. No effect with buspirone
	Case reports Nos. 2, 4, 5, 6	4	0	Fluoxetine	(+)	No effect with propranolol (2); ameliorated with buspirone (2); stopped by changing drug (4, 5); no effect with buspirone (6)
	Case report No. 3	1	0	Paroxetine	(+)	No effect with buspirone
Romanelli et al[47]	Case report	1	0	Paroxetine	(+)	Successfully treated with buspirone
Por et al[48]	Case report	1	0	Sertraline	(+)	Symptoms of bruxism diminished after discontinuation
Ellison[49]	Case report	1	0	Fluoxetine	(+)	Successfully treated by dose reduction
Christensen and Byerly[50]	Case report	1	0	Sertraline	(+)	Possible additive effect with metoclopramide
Stein et al[51]	Case report No. 1	1	0	Paroxetine	(–)	Incidental finding†
	Case report No. 2	1	0	Citalopram	(–)	Incidental finding†
Bostwick and Jaffee[17]	Case report	4	0	Sertraline	(+)	Successfully treated with buspirone
Wise[52]	Case report	2	0	Citalopram	(+)	Successfully treated with buspirone
Lobbezoo et al[53]	Case report	1	0	Paroxetine	(+)	Symptoms of bruxism diminish after discontinuation
Total		23	0		(+) 21 (–) 2	

* (+) Exacerbate; (–) ameliorate.
†An incidental observation, encountered during treatment of patients with the above drugs.

how bruxism was diagnosed or how clinical improvement was evaluated. Since the study was conducted on children, one should remain cautious when referring the results to adults.

Montgomery et al[62] found that short-term use of diazepam reduced bruxism in 11 patients. No raw data were presented, but the authors reported that nocturnal masseter EMG activity was significantly reduced following the ingestion of diazepam at bedtime in patients suffering from clinical symptoms of masticatory hyperactivity.

More recently, buspirone, a new medication believed to diminish anxiety by means of a partial agonist effect at postsynaptic 5-HT receptors and interaction with dopamine receptors, was introduced into treatment. Anxiety has been reported to be relieved without causing sedative or euphoric effects, and it has no hypnotic, anticonvulsant, or muscle relaxant properties.[63] However, there are conflicting reports. Buspirone has been reported to relieve bruxism induced or exacerbated by drugs in 13 patients,[17,18,46,47,52] to have no such effect in 3 patients,[15] and to cause bruxism in 1 case.[64]

Drugs of Abuse

Drugs of abuse are a heterogeneous pharmacologic group linked by their hedonic effect. Drugs

Table 5 Effects on Bruxism of Sedative and Anxiolytic Drugs

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Reimao and Lefevre[61]	Crossover	9 6	9 6	Flurazepam vs placebo	(–) (0)	Conducted on children
Montgomery et al[62]	Open trial	11	0	Diazepam	(–)	Conducted on portable EMG equipment
Ellison and Stanziani[46]	Case report	3	0	Buspirone	(–)	Relieved sertraline and fluxetine-induced bruxism
LeWitt et al[64]	Case report	1	0	Buspirone	(+)	Persisted after discontinued use of drug
Fitzgerald and Healy[15]	Case report Nos. 1, 3, 6	3	0	Buspirone	(0)	No effect on sertraline, fluxetine, and paroxetine-induced bruxism
	Case report No. 2	1	0	Buspirone	(–)	Relieved fluxetine-induced bruxism
Romanelli et al[47]	Case report	1	0	Buspirone	(–)	Relieved paroxetine-induced bruxism
Bostwick and Jaffee[17]	Case report	4	0	Buspirone	(–)	Relieved sertraline-induced bruxism
Jaffee and Bostwick[18]	Case report	2	0	Buspirone	(–)	Relieved venlafaxine-induced bruxism
Wise[52]	Case report	2	0	Buspirone	(–)	Relieved citalopram-induced bruxism
Total		43	15		(+) 1 (–) 33 (0) 9	

* (+) Exacerbate; (–) ameliorate; (0) no effect.

capable of producing addiction have a positive reinforcing action ("reward") associated with the influence of the mesolimbic dopaminergic pathway. All addiction-producing drugs tested so far (opioids, nicotine, amphetamines, alcohol, and cocaine) increase the release of dopamine in the nucleus accumbens. Other mediators, particularly serotonin, glutamate, and GABA, influence the mesolimbic dopaminergic pathway and possibly other reward pathways.[34] Drug addicts have been reported to suffer from a significantly higher prevalence of temporomandibular disorders and oral motor parafunctional activity compared to controls.[12]

Ethical issues complicate controlled clinical trials on abusive drugs. Population surveys are the most common method used to obtain this information and are an important scientific tool. However, their results should be interpreted with caution, since they could be biased by the subjective opinion, thoughts, or feelings of the participant. This is especially true when dealing with illicit drugs or with addicted persons who may have been inclined to suppress or alter their reports.[65]

Alcohol. Alcohol consumption, in the form of ethanol, far exceeds that of any other drug, and is the most commonly abused drug in the world. Like other sedative-hypnotic drugs, alcohol is a CNS depressant that relieves anxiety in low-to-moderate doses and fosters a feeling of well-being or euphoria. Alcohol causes an acute increase in the local concentration of serotonin, opioids, and dopamine (neurotransmitters involved in brain reward circuits), whereas its chronic use lowers the basal level of these chemicals. Thus, a strong desire for alcohol may represent the brain's effort to return these neurotransmitters to normal levels. It also appears that GABA plays a central role in the development of tolerance and withdrawal associated with chronic alcohol consumption.[66]

Although it is usually accepted that alcohol intake increases bruxism,[67] the evidence-based data are rather scarce. Hartman[68] initially suggested that alcohol aggravated bruxism, which was based on 4 patients observed over a 4- to 12-month period. However, in a later crossover, placebo-controlled, sleep-laboratory study,[69] no statistically significant effect of alcohol on bruxism was found

Table 6 Effects on Bruxism of Alcohol

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Hartman[68]	Crossover	1	1	Alcohol vs no alcohol	(+)	Nocturnal polygraphic recording
	Case report	3	0	Alcohol	(+)	Bruxism based on bed partner's report
Hartman et al[69]	Double-blind, crossover	16	16	Alcohol vs placebo	(0)	
Total		20	17		(+) 4 (0) 16	

* (+) Exacerbate; (0) no effect.

with 1 or 2 drinks and only a slight, not statistically significant, increase with 4 drinks (Table 6).

Recently, a large cross-sectional telephone survey was conducted in the United Kingdom, Germany, and Italy, which included 13,057 adults. The epidemiology of bruxism and its risk factor in the general adult population were examined. Bruxism was evaluated with the help of the self-report, Sleep-EVAL system.[70] Bruxers reported drinking alcohol at bedtime more often than a nonbruxing group.[11] However, as previously mentioned, results should be interpreted with caution. Additional studies are necessary to conclude the possible effect of alcohol on bruxist activity in humans.

Nicotine. Nicotine is one of the most widely used licit drugs and one of the most insidiously addicting substances, because of the rapidly developed tolerance and persistent craving for it when the user is trying to quit.[71]

To date, the only information concerning a possible effect of nicotine on bruxism is based on self-reported surveys. A nationwide survey conducted in Canada (2,019 adults) showed that cigarette smoking may be considered as a risk factor or an exacerbating factor for restless leg syndrome and sleep bruxism.[72] Although almost twice as many smokers (12%) as nonsmokers (7%) who participated in the study were aware of sleep bruxing, the estimated risk of a smoker to grind the teeth was moderate. In a telephone survey conducted by Ohayon et al,[11] smoking was reported to be a risk factor for bruxism. Another study based on a questionnaire regarding smoking status and bruxism[73] reported that smokers are about 3 times more likely to experience symptoms of bruxism than nonsmokers. However, as the study included 165 nonsmokers and only 18 smokers, these results should be interpreted with caution.

Caffeine. Caffeine, a widely used social drug, is not considered by most people to be a drug of abuse. However, withdrawal syndromes, characterized by lethargy and headache, have been recognized in people who drink about 6 cups of coffee a day (600 mg/d).[71]

In the telephone survey by Ohayon et al,[11] it was suggested that caffeine drinkers were at higher risk of reporting sleep bruxism (with quantity consumed being significant only for caffeine, and not for the daily use of alcohol and tobacco). The only controlled study on caffeine and bruxism found no significant differences between caffeine or placebo intake in masseteric activity associated with bruxism in 14 volunteers.[74]

Opioids. The source of opium and morphine is the opium poppy, *Papaver somniferum*. Its properties have been known for thousands of years and its use can be found in ancient Egyptian, Greek, and Roman documents. The principal effects of opioids are on the CNS, which include nausea and vomiting, analgesia, euphoria, sedation, respiratory depression, myoclonus, and rigidity of the large trunk muscles. With repeated use, there is a high degree of tolerance to all of these effects.[75]

Opioids, known as motor suppressants, are an effective treatment for various sleep movement disorders.[76] No clinical case reports or trials have been found for opioid or morphine effects on bruxism.

Cocaine. Natives of the South American Andes have used cocaine for at least 1,200 years by chewing the coca leaves. Cocaine binds to the dopamine reuptake transporter in the CNS, effectively inhibiting dopamine and norepinephrine reuptake. It is classified as a stimulant drug.[71]

Friedlander and Gorelick[77] have claimed that subjects addicted to cocaine tend to have severe bruxism, and those who abuse both cocaine and

alcohol tend to have the most severe bruxism complications due to the additive adverse effects of alcohol. Another adverse side effect of cocaine intake is tooth grinding.[78]

No research or clinical reports have been found to support these assumptions in humans. However, Gomez et al[79] found that repeated stimulation of the dopaminergic systems with apomorphine and cocaine enhances nonfunctional masticatory movements and increases the attrition rate of the mandibular incisors in rats.

Amphetamines. Amphetamines were first synthesized in the late 1920s. Dextroamphetamine is a closely related compound with similar actions to amphetamines. Others in this class are methedrine ("speed"), phenmetrazine (Preludin), methylphenidate (Ritalin), and methylenedioxymethamphetamine ([MDMA], "ecstasy"), which act centrally mainly by increasing the release of catecholaminergic neurotransmitters, including dopamine.[75]

In the 1960s, Ashcroft et al[80] suggested that amphetamine addicts perform typical, continuous chewing or tooth-grinding movements, and rubbing the tongue along the inside of the lower lip. It was later reported that bruxism is an adverse side effect of amphetamines.[81–83]

Liester et al[65] conducted an open trial on the subjective experience and psychologic and behavior sequel of the intake of MDMA. Using a semi-structured interview, 20 psychiatrists who had previously taken MDMA were evaluated. Of these, 6 (30%) reported the appearance of bruxism as an adverse side effect of the drug.

Miscellaneous Drugs

The effects on bruxism of several other drugs are outlined in Table 7.

Propranolol. This antihypertensive drug, which acts as a beta-adrenoreceptor blocking agent, has been used effectively in the treatment of drug-induced bruxism in 5 patients.[15,35,84] According to Amir et al,[35] the response of iatrogenic bruxism to propranolol suggests the involvement of the adrenergic and the serotonergic pathways in the CNS in the pathogenesis of bruxism. As well, Sjoholm et al[83] found an association between the autonomic regulation of circulation and the rhythmic activation of the masticatory muscles.

Flecainide. An anti-arrythymic drug, flecainide, has been reported to induce severe bruxism that persists even after cessation of the drug.[85]

Fenfluramine. Fenfluramine, an anorexigenic drug closely related to amphetamine, may cause changes in sleep architecture and produce bruxism.[86]

Gamma-hydroxybutyrate (GHB). Derived from GABA, GHB functions as an inhibitory chemical transmitter in the CNS. Lavigne and Montplaisir[87] reported a severe case of bruxism successfully treated with GHB. In pharmacologic doses, GHB is a powerful CNS depressant and has been used as a general anesthetic and for certain sleep disorders. Recreational use is popular due to its ability to induce euphoria.[88]

Methylphenidate. Methylphenidate was used for 2 children (aged 4 and 6) for attention-deficit hyperactivity disorder (ADHD) and concomitant valproic acid for seizure prophylaxis.[89] They developed dyskinesia and bruxism. The authors commented that the potential for interaction between these 2 drugs exists since they compete for the same metabolic pathway via the cytochrome P450 2D6. Valproate has been associated with chorea after long-term use,[90] but it is also effective in the treatment of choreiform movements in Syndenham's chorea.[91]

Flunarizine/Cinnarizine. These drugs are calcium antagonists, and their effects were described in a series of 101 patients who developed abnormal movement disorders after 1 to 20 months of use.[92] One patient who received flunarizine developed bruxism. In a later study, flunarizine caused diurnal bruxism in 2 additional patients.[36]

Lithium/Thorazine. Lithium and later thioridazine were used in a patient suffering from manic-depressive psychosis who then developed severe choreoathetoid movements, akathisia, orofacial dyskinesia, and bruxism. Symptoms subsided after 6 days of administration of procyclidine, a drug with anti-muscarinic properties used in parkinsonism. According to Standish-Barry and Shelly,[93] the choreoathetoid movements observed in this case were not associated with typical lithium neuroleptic neurotoxicity. However, no plausible alternative explanation is presented.

L-tryptophan. A precursor of serotonin, L-tryptophan was studied in a randomized, double-blind, crossover experiment on nocturnal bruxism.[94] No significant treatment differences in bruxing levels were found, which suggests that L-tryptophan supplementation in the absence of dietary manipulation is ineffective in the treatment of nocturnal bruxism.

Gabapentin. An antiseizure drug. A patient suffering from venlafaxine-induced bruxism reported that the bruxism completely resolved after 1 to 2 days of starting gabapentin.[44]

Table 7 Effects on Bruxism of Miscellaneous Drugs

Author	Study design	No. of patients	No. of controls	Generic name of drug	Influence on bruxism*	Remarks
Fitzgerald and Healy[15]	Case report	1	0	Propranolol	(–)	Ameliorated sertraline-induced bruxism
	Case report	1	0	Propranolol	(0)	No effect on fluoxetine-induced bruxism
Amir et al[35]	Case report	2	0	Propranolol	(–)	Relieved haloperidol-induced bruxism
Sjoholm et al[84]	Single-blind, crossover	1	1	Propranolol vs no medication	(–)	Polysomnographic study
Miller and Jankovic[85]	Case report	1	0	Flecainide	(+)	Relieved by botulinum toxin
Lewis et al[86]	Single-blind, crossover	6	6	Fenfluramine vs placebo	(+)	Polysomnographic study
Lavigne and Montplaisir[87]	Case report	1	0	Gamma-hydroxybutyrate	(–)	
Gara and Roberts[89]	Case report	2	0	Methylphenidate and valporic acid	(+)	Children (aged 4 and 6)
Micheli et al[92]	Case report	1	0	Flunarizine	(+)	Out of a series of 101 patients
Micheli et al[36]	Case report	2	0	Flunarizine	(+)	Diurnal bruxism alleviated by sleep
Standish-Barry and Shelly[93]	Case report	1	0	Lithium and thioridazine	(+)	Relieved by procyclidine
Etzel et al[94]	Double-blind, crossover	8	8	L-tryptophan vs placebo	(0)	Nocturnal EMG recording
Brown and Hong[44]	Case report	1	0	Gabapentin	(–)	Relieved by venlafaxine-induced bruxism
Total		28	15		(+) 13 (–) 6 (0) 9	

* (+) Exacerbate; (–) ameliorate; (0) no effect.

Discussion

The CNS is one of the most complex and least understood systems of the human body. The etiology of many central disorders is still an enigma. Substances that act in the CNS are not only of special clinical and therapeutic significance to mankind, but are also the most commonly used, often with no immediate medical need (eg, alcohol, tea and coffee, nicotine, cannabis, opiates, amphetamines, etc). Due to the complexity of the CNS, the mechanisms by which centrally acting drugs interact with each other are not always clear, and CNS pharmacology is mostly descriptive. Although dramatic advances in knowledge have been made,[95] much of the drug-interacting mechanisms are still unclear.

Controlled clinical experiments on the effects of drugs on the CNS in humans are extremely difficult to conduct due to their possible effect on the subjects' mental and physical health. As well, drawing conclusions from animal experiments regarding the possible effect of these drugs on humans is problematic.

Since the available information is contradictory, no clear-cut answer can be presented to the many questions concerning bruxism: Are iatrogenic drug-induced bruxism and sleep-related idiopathic bruxism 2 distinct disorders?[29] Is bruxism a functional disturbance of the CNS,[96] or is it part of other movement disorders?[97] Can bruxism be classified as dystonia or dyskinesia?[15] Is it an extrapyramidal disorder?[56] Is sleep bruxism a motor disorder,[98] or is it an oromotor activity secondary to micro-arousal?[99] Unfortunately, definite answers to these questions remain, as yet, enigmatic. A better understanding of the central mechanism of drugs on bruxism may answer some of these complex phenomena.

Appropriate research of the association between different drugs and bruxism clinically is important. Treatment modes of bruxism are closely related to its major etiology. Behavioral modification techniques or occlusal treatment should be used if bruxism is a local, oral phenomenon. A centrally acting

medication, experimentally proven to ameliorate the problem, should be used if it is a neurologic disorder. However, drugs that may have an alleviating effect on bruxism pose severe adverse side effects, sometimes worse than the damage of the bruxism itself. Thus, the risk/benefit ratio of these drugs should be considered with utmost caution.

It was not the intention of this study to determine links between bruxism, tardive dyskinesias, and other movement disorders since they may occur by different mechanisms. A more detailed and profound examination of these issues is beyond the limitations of this review, and the reader is referred to the studies reviewed in this article for further information. Nonetheless, it is clear from this review that there is insufficient evidence-based data to draw definite conclusions concerning the association between drugs and bruxism. Although certain substances related to the dopaminergic, serotonergic, and adrenergic systems ameliorate or exacerbate bruxist activity in humans and animals,[7,23,100] the literature is still controversial and based mostly on anecdotal case reports. Furthermore, there may be differential effects mediated by different dopamine, serotonergic, and adrenergic receptor subtypes. Needless to say, more controlled, evidence-based research on this under-explored subject is essential.

Acknowledgments

The authors wish to thank Mrs Ruth Kritchman of the Computerized Information Unit, The Gitter-Smolarz Library of Life Sciences and Medicine, Tel-Aviv University, Israel, and to Ms Rita Lazar for editorial assistance.

References

1. Wirshing WC. Movement disorders associated with neuroleptic treatment. J Clin Psychiatry 2001;62(22, suppl):15–18.
2. Allen RP, Earley CJ. Restless legs syndrome: A review of clinical and pathophysiologic features. J Clin Neurophysiol 2001;18:128–147.
3. McNeill C (ed). Temporomandibular Disorders: Guidelines for Classification, Assessment, and Management. The American Academy of Orofacial Pain. Chicago: Quintessence, 1993.
4. Kato T, Montplaisir JY, Blanchet PJ, Lund JP, Lavigne GL. Idiopathic myoclonus in the oromandibular region during sleep: A possible source of confusion in sleep bruxism diagnosis. Mov Disord 1999;14:865–871.
5. Vertrugo R, Provini F, Plazzi G, et al. Familial nocturnal facio-mandibular myoclonus mimicking sleep bruxism. Neurology 2002;58:644–647.
6. Velly-Miguel AM, Montplaisir JY, Rompre PH, Lund JP, Lavigne GL. Bruxism and other orofacial movements during sleep. J Craniomandib Disord 1992;6:71–81.
7. Lavigne GJ, Montplaisir JV. Bruxism: Epidemiology, diagnosis, pathophysiology, and pharmacology. In: Fricton JR, Dubner R (eds). Orofacial and Temporomandibular Disorders. New York: Raven Press, 1995:387–404.
8. Lobbezoo F, Naeije M. Bruxism is mainly regulated centrally not peripherally. J Oral Rehabil 2001;28: 1085–1091.
9. Pierce CJ, Chrisman K, Bennett ME, Close JM. Stress, anticipatory stress, and psychologic measures related to bruxism. J Orofac Pain 1995;9:51–56.
10. Pingitore G, Chrobac V, Petrie J. The social and psychological factors of bruxism. J Prosthet Dent 1991;65: 443–446.
11. Ohayon MM, Li KK, Guilleminault C. Risk factors for sleep bruxism in the general population. Chest 2001;119: 53–61.
12. Winocur E, Gavish A, Volfin G, Halachmi M, Gazit E. Oral motor parafunctions among heavy drug addicts and their effects on signs and symptoms of temporomandibular disorders. J Orofac Pain 2001;15:56–63.
13. Rugh JD, Harlan J. Nocturnal bruxism and temporomandibular disorders. In: Jankovic J, Tolosa E (eds). Advances in Neurology, Vol 49: Facial Dyskinesias. New York: Raven Press, 1988:329–341.
14. Gatchel RJ. Psychological disorders and chronic pain: Cause-and-effect relationships. In: Gatchel RJ, Turk DC (eds). Psychological Approaches to Pain Management: A Practitioner's Handbook. New York, London: The Guilford Press, 1996:33–54.
15. Fitzgerald K, Healy D. Dystonias and dyskinesias of the jaw associated with the use of SSRIs. Hum Psychopharmacology 1995;10:215–219.
16. Shiwach RS, Woods S. Risperidol and withdrawal bruxism in Lewy body dementia. Int J Geriatr Psychiatry 1998;13:64–67.
17. Bostwick JM, Jaffee MS. Buspirone as an antidote to SSRI-induced bruxism. J Clin Psychiatry 1999;60: 857–860.
18. Jaffee MS, Bostwick JM. Buspirone as an antidote to venlafaxine-induced bruxism. Psychosomatics 2000;41: 535–536.
19. Koshikawa N, Koshikawa F, Tomiyana T, Kikuchi de Beltran K, Kamimura F, Kobayashi M. Effects of dopamine D1 and D2 agonists and antagonists injected into the nucleus accumbens and globus pallidus on jaw movements on rats. Eur J Pharmacol 1990;182:375–380.
20. Spooren WPJM, Petra A, Cools AR. Dopamine D1 receptors in the sub-commissural part of the globus pallidus and their role in oro-facial dyskinesia in cats. Eur J Pharmacol 1991;204:217–222.
21. Andreassen OA, Meshuk CK, Moore C, Jorgensen HA. Oral dyskinesias and morphological changes in rat striatum during long-term haloperidol administration. Psychopharmacology 2001;157:11–19.
22. Waddington JL. Spontaneous orofacial movements induced in rodents by very long-term neuroleptic drug administration: Phenomenology, pathophysiology and putative relationship to tardive dyskinesia. Psychopharmacology 1990;101:431–447.

23. Lambert RW, Goldberg LJ, Chandler SH. Comparison of mandibular movements trajectories and associated patterns of oral muscle electromyography. Activity during spontaneous and apomorphine-induced rhythmic jaw movements in the guinea pig. J Neurophysiol 1986;55: 301–319.
24. Naidu PS, Singh A, Kulkarni SK. Carveditol attenuates neuroleptic-induced orofacial dyskinesias: Possible antioxidant mechanisms. Br J Pharmacol 2002;136:193–200.
25. Naidu PS, Kulkarni SK. Effect of 5HT1A and 5HT2A/2C receptor modulation on neuroleptic-induced vacuous chewing movements. Eur J Pharmacol 2001;428:81–86.
26. Lobbezoo F, Soucy JP, Montplaisir JY, Lavigne GJ. Striatal D2 receptor binding in sleep bruxism: A controlled study with iodine-123-iodobenzamide and single-photon-emission computed tomography. J Dent Res 1996;75:1804–1810.
27. Aminoff MJ. Pharmacologic management of Parkinson's and other movement disorders. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, Medical Publishing Division, 2001:463–477.
28. Nishioka GJ, Montgomery M, Boutros N, Haslam S. Dopaminergic modulation of nocturnal masticatory muscle EMG activity and sleep [abstract 1679]. J Dent Res 1989;68:391.
29. Lobbezoo F, Lavigne GJ, Tanguay R, Montplaisir JY. The effect of the catecholamine precursor L-Dopa on sleep bruxism: A controlled clinical trial. Mov Disord 1997; 12:73–78.
30. Lobbezoo F, Soucy JP, Hartman NG, Montplaisir JV, Lavigne GJ. Effects of the D2 receptor agonist bromocriptine on sleep bruxism: Report of two single-patient clinical trials. J Dent Res 1997;76:1610–1615.
31. Lavigne GJ, Soucy JP, Lobbezoo F, Manzini C, Blanchet PJ, Montplaisir JV. Double-blind, crossover, placebo-controlled trial of bromocriptine in patients with sleep bruxism. Clin Neuropharmacol 2001;24:145–149.
32. Magee KR. Bruxism related to levodopa therapy [letter]. J Am Med Assoc 1970;214:147.
33. Harris M, Nora L, Tanner CM. Neuroleptic malignant syndrome responsive to cardidopa/levodopa. Clin Neuropharmacol 1988;10:186–189.
34. Rang HP, Dale MM, Ritter JM (eds). Pharmacology, ed 4. Edinburgh: Churchill Livingstone, 1999:464–644.
35. Amir I, Hermesh H, Gavish A. Bruxism secondary to antipsychotic drug exposure: A positive response to propranolol. Clin Neuropharmacol 1997;20:86–89.
36. Micheli FE, Pardal MF, Gatto M, Asconape J, Giannaula R, Parera IC. Bruxism secondary to chronic antidopaminergic drug exposure. Clin Neuropharmacol 1993;16: 315–323.
37. Poyurovsky M, Hermesh H, Weizman A. Severe withdrawal akathisia following neuroleptic discontinuation successfully controlled by clonazapine. Int Clin Psychopharmacol 1996;11:283–286.
38. Glazer WM. Expected incidence of tardive dyskinesia associated with atypical antipsychotics. J Clin Psychiatry 2000;61(4, suppl):21–26.
39. Potter WZ, Hollister LE. Antidepressant agents. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001:498–511.
40. Ware JC, Rugh JD. Destructive bruxism: Sleep stage relationship. Sleep 1988;11:172–181.
41. Mohamed SE, Christensen LV, Penchas J. A randomized double blind clinical trial of the effect of amitriptyline on nocturnal masseteric motor activity (sleep bruxism). J Craniomandib Pract 1997;15:326–332.
42. Raigrodski AJ, Christensen LV, Mohamed SE, Gardiner DM. The effect of four-week administration of amitryptiline on sleep bruxism. A double blind crossover clinical study. J Craniomandib Pract 2001;19:21–25.
43. Raigrodski AJ, Mohamed SE, Gardiner DM. The effect of amitryptiline on pain intensity and perception of stress in bruxers. J Prosthodont 2001;10:73–77.
44. Brown ES, Hong SC. Antidepressant-induced bruxism successfully treated with gabapentin. J Am Dent Assoc 1999; 130:1467–1469.
45. Melis M. Comments [Letter to the Editor - Raigrodski et al]. J Craniomandib Pract 2001;19:149.
46. Ellison JM, Stanziani P. SSRI-associated nocturnal bruxism in four patients. J Clin Psychiatry 1993;54:432–434.
47. Romanelli F, Adler DA, Bungay KM. Possible paroxetine-induced bruxism. Ann Pharmacother 1996;30:1247–1248.
48. Por CP, Watson L, Doucette D, Dolovich L. Sertraline associated bruxism. Can J Clin Pharmacol 1996;3: 123–125.
49. Ellison JM. Exercise-induced orgasms associated with fluoxetine treatment of depression. J Clin Psychiatry 1996; 57:596–597.
50. Christensen RC, Byerly MJ. Mandibular dystonia associated with the combination of sertraline and metoclopramide. J Clin Psychiatry 1996;57:596.
51. Stein DJ, Van Greunen G, Niehaus D. Can bruxism respond to serotonin reuptake inhibitors? J Clin Psychiatry 1998;59:133.
52. Wise M. Citalopram-induced bruxism. Br J Psychiatry 2001;178:182.
53. Lobbezoo F, Van Denderen RJA, Verheij JGC, Naeije M. Reports of SSRI-associated bruxism in the family physician's office. J Orofac Pain 2001;15:340–346.
54. Gerber PE, Lynd LD. Selective serotonin-reuptake inhibitor-induced movement disorders. Ann Pharmacother 1998;32:692–698.
55. Scharer P, Kasahara Y, Kawamura Y. Tooth contact patterns during stimulation of the rabbit brain. Arch Oral Biol 1967;12:1041–1051.
56. Nishioka GJ, Montgomery MT. Masticatory muscle hyperactivity in temporomandibular disorders: Is it an extrapyramidally expressed disorder? J Am Dent Assoc 1988;116:514–520.
57. Takeuchi Y, Satoda T, Tashiro T, Matsushima R, Uemura-Sumi M. Amygdaloid pathway to the trigeminal motor nucleus via the pontine reticular formation in the rat. Brain Res Bull 1988;21:829–833.
58. Gomez FM, Giralt MT, Sainz B, Arrue A, Prieto M, Garcia-Vallejo P. A possible attenuation of stress-induced increases in dopamine metabolism by the expression of non-functional masticatory activity in the rat. Eur J Oral Sci 1999;107:461–467.
59. Cocchi R. Drug therapy of bruxism as modulation of stress answers. Ital J Intellective Impairment 1999;12: 3–12.
60. Harkins S, Linford J, Cohen J, Kramer T, Cueva L. Administration of clonazepam in the treatment of TMD and associated myofascial pain: A double-blind pilot study. J Cranimandib Disord 1991;5:179–186.
61. Reimao R, Lefevre AB. Evaluation of flurazepam and placebo on sleep disorders in childhood. Arq Neuropsiquiatr 1982;40:1–13.

62. Montgomery MT, Nishioka G, Rugh JD, Thrash WJ. Effect of diazepam on nocturnal masticatory muscle activity [abstract 96]. J Dent Res 1986;65:180.
63. Trevor JT, Way WL. Sedative-hypnotic drugs. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001: 364–381.
64. LeWitt PA, Walters A, Hening W, McHale D. Persistent movements disorders induced by buspirone. Mov Disord 1993;8:331–334.
65. Liester MB, Grob ChS, Bravo GL, Walsh RG. Phenomenology and sequelae of 3,4-methylenedioxymethamphetamine use. Nerv Mental Dis 1992;180:345–352.
66. Masters SB. The alcohols. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001:382–394.
67. Hartman E. Bruxism. In: Kryger MH, Roth T, Dement WC (eds). Principles and Practice of Sleep Medicine, ed 2. Philadelphia: WB Saunders, 1994:598–601.
68. Hartman E. Alcohol and bruxism. N Engl J Med 1979;301:333–334.
69. Hartman E, Mehta N, Forgione A, Brune P, LaBrie R. Bruxism: Effects of alcohol [abstract]. Sleep Res 1987;16:351.
70. Ohayon MM. Sleep-EVAL knowledge-based system for the diagnosis of sleep and mental disorders. Registration No. 437699, copyright office, Canadian Intellectual Property Office. Ottawa, Canada: Industry Canada, 1994.
71. Kosten TR, Hollister LE. Drugs of abuse. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001: 533–547.
72. Lavigne GJ, Lobbezoo F, Rompre PH, Nielsen TA, Montplaisir J. Cigarette smoking as a risk or an exacerbating factor for restless leg syndrome and sleep bruxism. Sleep 1997;20:290–293.
73. Madrid G, Madrid S, Vanesh JG, Hicks RA. Cigarette smoking and bruxism. Percept Mot Skills 1998;87:898.
74. Bastien R, Gale EN, Mohl ND. An exploratory study on increases in masseteric activity induced by caffeine. J Can Dent Assoc 1990;56:943-947.
75. Way WL, Fields HL, Schumacher MA. Opioids, analgesics and antagonists. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001:512–531.
76. Hening WA, Walter A, Kavey N, Gidro-Frank S, Cote L, Fahn S. Dyskinesias while awake and periodic movements in sleep in restless legs syndrome: Treatment with opioids. Neurol 1986;36:1363–1366.
77. Friedlander AH, Gorelick A. Dental management of the cocaine addicts. Oral Surg Oral Med Oral Pathol 1988; 65:45–48.
78. Bates CK. Medical risks of cocaine use. West J Med 1988;148:440–444.
79. Gomez FM, Areso MP, Giralt MT, Sainz B, Garcia-Vallejo P. Effects of dopaminergic drugs, occlusal disharmonies, and chronic stress on non-functional masticatory activity in the rat, assessed by incisal attrition. J Dent Res 1998;77:1454–1464.
80. Ashcroft GW, Eccleston D, Waddell JL. Recognition of amphetamine addicts [letter]. Br Med J 1965;1:57.
81. Peroutka SJ, Newman H, Harris H. Subjective effects of 3,4-methylene-dioxy-methamphetamine in recreational users. Neuropsychopharmacol 1988;1:273–277.
82. Cohen RS. Subjective reports on the effects of the MDMA ("Ectasy") experience in humans. Prog Neuropsychopharmacol Biol Psychiatry 1995;19:1137–1145.
83. Murray JB. Ecstacy is a dangerous drug. Psychol Rep 2001;88:895–902.
84. Sjoholm TT, Lehtinen I, Piha SJ. The effect of propranolol on sleep bruxism: Hypothetical considerations based on a case report. Clin Auton Res 1996;6:37–40.
85. Miller LG, Jankovic J. Persistent dystonia possibly induced by flecainide. Mov Disord 1992;7:62–63.
86. Lewis SA, Oswald I, Dunleavy DLF. Chronic fenfluramine administration: Some cerebral effects. Br Med J 1971;3: 67–70.
87. Lavigne GJ, Montplaisir JV. Effect of gamma-hydroxybutyrate on sleep bruxism: A case report [abstract]. Sleep Res 1992;21:36.
88. Tunnicliff G. Sites of action of gamma-hydroxybutyrate: A neuroactive drug with abuse potential. J Toxicol Clin Toxicol 1997;35:581–590.
89. Gara L, Roberts W. Adverse response to methylphenidate in combination with valproic acid. J Child Adolesc Psychopharmacol 2000;10:39–43.
90. Lancman ME, Asconape JJ, Penry JK. Choreiform movements associated with the use of valproate. Arch Neurol 1994;51:702–704.
91. Genel F, Arslanoglu S, Ura N, Saylan B. Syndenham's chorea: Clinical findings and comparison of the efficacies of sodium valproate and carbamazepine regimens. Brain Dev 2002;24:73–76.
92. Micheli FE, Fernandez-Pardal MM, Giannaula R, et al. Movements disorders and depression due to flunarizine and cinnarizine. Mov Disord 1989;4:139–146.
93. Standish-Barry HM, Shelly MA. Toxic neurological reaction to Lithium/ Thioridazine. Lancet 1983;1:771.
94. Etzel KR, Stockstill JW, Rugh JD, Fisher JG. Tryptophan supplementation for nocturnal bruxism: Report of negative results. J Craniomandib Disord 1991;5:115–119.
95. Nicoll RA. Drugs that act in the central nervous system. In: Katzung BG (ed). Basic & Clinical Pharmacology, ed 8 (Int Ed). New York: Lange Medical Books/McGraw-Hill, 2001:351–363.
96. Lohr JB, Wisniewski AA (eds). Movement Disorders: A Neuro-Psychiatric Approach. New York: Guilford, 1987:251–274.
97. Bader G, Kampe T, Tagdae T. Body movement during sleep in subjects with long-standing bruxing behavior. Int J Prosthodont 2000;13:327–333.
98. De Laat A, Macaluso GM. Sleep bruxism as a motor disorder. Mov Disord 2002;17:67–69.
99. Kato T, Rompre P, Monplaisir JY, Sessle BJ, Lavigne GJ. Sleep bruxism: An oromotor activity secondary to microarousal. J Dent Res 2001;80:1940–1944.
100. Gerstner E, Goldberg J, De Bruyne K. Angiotensin II-induced rhythmic jaw movements in the ketamine-anesthetized guinea pig. Brain Res 1989;478:233–240.