European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2017

Review

BRUXISM: REPORTS ON CENTRAL DOPAMINERGIC PATHOGENESIS

C. Lorenzi[1], A.M. Pujia[2], P. Carosi[2]

[1]Department of Chemical Science and Technologies, University of Rome "Tor Vergata", Rome, Italy
[2]Department of Clinical Sciences and Translational Medicine, University of Rome "Tor Vergata", Rome, Italy

Correspondence to:
Dr Claudia Lorenzi
Department of Chemical Science and Technologies,
University of Rome "Tor Vergata",
Rome, Italy
e-mail: claudialorenzimartinez@gmail.com

ABSTRACT

Bruxism is a parafunctional activity which causes the clenching and grinding of teeth. It is divided into two types: bruxism during sleep and bruxism during wakefulness. Bruxism has a multifactorial aetiology. The purpose of this study is to review the literature and summarize the current evidence regarding the association between these central neuronal pathways, especially dopaminergic pathways, and the onset of bruxism episodes.

KEYWORDS: *bruxism, abrasion, erosion, dopamine, central nervous system*

INTRODUCTION

Bruxism is an oral condition of great interest to researchers and clinicians in the dental, neurological and sleep medicine domains (1). Bruxism can be defined as "a repetitive jaw-muscle activity characterized by clenching or grinding of teeth and/or by bracing or thrusting of mandible". Bruxism has two distinct circadian manifestations: it can occur during sleep (i.e., sleep bruxism - SB) or during wakefulness (i.e., awake bruxism - AB) (1). Although bruxism represents a common clinical phenomenon (2), the prevalence of "generic bruxism" (i.e., without any distinction between AB and SB) is between 8% to 31,4% in the examined population. A prevalence of 22-31% for the AB and 13-23% for the SB in the adult population.

Beyond the different circadian manifestations of bruxism, there is consensus that it has a multifactorial aetiology and expresses a centrally mediated rather than peripherally mediated phenomenon (3).

Several studies focused on factors associated with its pathogenesis which included: alcohol smoking, drugs (4, 5),

Received: 19 January 2017
Accepted: 04 March 2017

ISSN: 2038-4106

psychotropic substances (6), anxiety (7), stress (8-11), psychiatric diseases (5), malocclusions (12, 13), obstructive sleep apnea syndrome (OSAS) (14).

It is believed that these biological, environmental, and psychosocial factors may represent a motor stimulus at the central nervous system (CNS) level, triggering an altered response to transmission channels of the dopaminergic system, which will correspond to the clenching or grinding of the teeth (15-17). However, the exact molecular mechanism that regulates these neuronal circuits and allows them to play a primary role in the pathogenesis of bruxism is still unclear.

The aim of this review is to analyze the association between central neuronal pathways (dopaminergic pathways) and the onset of bruxism, including both AB and SB.

MATERIALS AND METHODS

The research was performed with MEDLINE / PubMed database, using the term "bruxism" associated with appropriate word combinations, such as dopamine; dopamine antagonists; neurochemicals; dopamine receptor; amphetamines; antipsychotic agents; psychostimulants; attention deficit disorder with hyperactivity; ecstasy.

The original works published in English were thus selected. Additional sources were selected through the previously published articles by searching their references. Since the works concerning the association between dopaminergic transmission and the pathogenesis of bruxism are entirely incongruent and confusing, tables have been created to summarize the data of selected papers.

Inclusion criteria include:

1) clinical studies showing an association between a single molecule and bruxism;
2) experimental studies that demonstrate a cause-effect relationship between a specific molecule (drugs, psychotropic substances) and bruxism;
3) studies based on diagnostic methods such as anamnestic questionnaires, clinical examination, recording by polysomnography (PSG) and/or electromyography of masticatory muscles (EMG);
4) studies whose samples represent an adult and/or adolescent-pediatric population.

Exclusion criteria include:

1) studies in which participants are affected by genetic or neuromuscular diseases;
2) studies in which patients present with temporomandibular disorders (TMJ) and/or obstructive sleep apnea syndrome;
3) studies in which the diagnosis of bruxism does not meet the diagnostic criteria approved by the scientific community;
4) animal studies;
5) studies whose subjects are under pharmacological treatment for psychiatric pathologies.

The study selection process was performed in three phases. In the first phase, titles and abstracts were analyzed to identify papers focusing on the research topic. In the second phase, the complete text was read. Finally, in the third phase, studies that met the inclusion criteria were selected and included in this review.

RESULTS

A total of 140 articles were identified from the MEDLINE / PubMed database. Ninety-two studies were selected from the analysis of the titles, of which 10 were then excluded as animal studies; after evaluation of the abstract of each work, 31 works were selected for full-text reading and analysis of the inclusion criteria.

Finally, 15 articles met the inclusion criteria and were therefore included in this review (Table I). Each study evaluated the relationship between dopaminergic neuronal pathways and the genesis of bruxism in different modalities.

Table I. *Inclusion criteria.*

Bruxism and Dopaminergic Agonists	10 studies
Bruxism and Dopaminergic Antagonists	2 studies
Bruxism and D2 Receptors	2 studies
Bruxism and ADHD	1 study

Most studies reveal a prominent role of dopaminergic transmission in tooth clenching and grinding pathophysiology, as it represents the major neurotransmitter involved in motor control. However, it was demonstrated that dopamine does not always act similarly.

The final effect dopamine can exert in triggering the hyperactivity of the chewing muscles is strongly dependent on its quantity (excess/defect) and pharmacokinetics. The studies showed a great complexity of dopaminergic transmission due to many circuits and receptors. The heterogeneity of bruxism patterns presents among the population (sleep bruxism, awake bruxism or both) and the relationship existing with hyper- and hypo-dopaminergic states derive from the involvement of different brain regions and from the complex pharmacology of different receptor subtypes to which dopamine binds. The interactions between dopamine and bruxism are summarized below in Table II and III, showing each study's specificity.

DISCUSSION

Selected studies confirm the hypothesis that an altered dopaminergic transmission at the nigrostriatal and mesocortical pathways level is involved in the onset of bruxism. Conversely, depletion of dopaminergic transmission at the level of the meso-cortical pathway and the nigro-striatal pathway can result in an imbalance of the basal ganglia circuit, which determines muscle hyperactivity (3, 18, 19).

These neuronal pathways, therefore, represent the two main dopaminergic pathways involved in the pathophysiology

Table II. *The interactions between dopamine and bruxism.*

	Study design	*Population (n° of partecipants)*	*Group A*	*Group B*	*Effect on Bruxism*
Magee, 1970	Case Study	1	L-Dopa (short term)		↑
Lobbezoo F et al. 1996	Controlled clinical trial	20	SB	Control Group	↓
Lobbezoo F et al, 1997	Controlled clinical trial	10(5M and 5W)	L-Dopa 100mg + bensarazide 25mg	Placebo	↓30%
Lobbezoo F, 1997	Clinical Trial	2	Bromocriptin 7,5mg	Placebo	↓
J.Van Der Zaag et al, 2007	Open trial	1(SB)	Pergolide (o.o5-0.5mg)+domperidone		↓
Lavigne et al, 2001	Double blind trial	7	Bromocriptine 7.5mg + domperidone	Plcebo + Domperidone	No Effects
Cahlin B et al, 2017	Randomized open trial	13(SB)	Pramipexole (o.9-0.54mg)	Placebo	No effects
Chen et al, 2005	Case Study	3 (AB + SB)	Metaclopramide 15mg o.s		↓
Ho Sung Yi et al. 2013	Case Study	2(AB)	Metaclopramide 15 mg o.s	Metaclopramide 9mg o.s	↓

Table III: ***AB****= awake bruxism;* ***SB****= sleep bruxism;* ***t****= bruxism enhancement.*

	Study design	***Population (n° of participants)***	***Drugs***	***Mean Age***	***Effect on bruxism***
See S-J e Tan E-K 2003	Case Report	1 (AB + SB)	Amphetamine (chronic use)	37	**t**
Ricardo Jorge Dinis-Oliveira 2010	Case Reports	3 (AB + SB)	3,4-Methylenedioxymethamphetamine (ecstasy)	35.33	**t**
Mendhekar. et al. 2008	Case Report	1	Methylphenidate 10 mg per die	9	**t**
Mendhekar D. &., 2009	Case Report	1	Atomoxetine 10 mg/ dia	12	**t**
Micheli et al. 2003	Case Reports	8 (5 men e 3 women)	Haloperidol 8mg	68.5	**t**
Mendhekar D. &., 2009	Case Report	1 (AB + SB	Trifluoperazine 15 mg Triesiphenidyl 4 mg	56	**t**

of bruxism. Suppression of the nigro-striatal pathway, following the administration of typical antipsychotic drugs, determines the establishment of "iatrogenic" bruxism due to loss of motor control.

"Idiopathic" bruxism, on the other hand, could be alleviated with short-term administration of L-DOPA and dopaminergic agonists. They stimulate dopaminergic receptors in basal ganglia, thus increasing dopamine control over motor functions by the nigrostriatal pathways.

An imbalance of the dopaminergic pathway in the meso-cortical tract may represent a key to the genesis and pathophysiology of wakefulness and/or sleep bruxism (20-22). This feature is even more evident in patients with frontal lobe cerebral hypo-perfusion. In fact, in these patients, there is a hypersensitivity of the presynaptic receptors.

One study suggests that bruxism can also be induced by the action of other neurotransmitters, such as serotonin (5-HT) and noradrenaline (23). Thus, we assume the existence of an "alternative" pathway between bruxism and the neuronal circuits of the central nervous system, demonstrating the complexity of these interactions in our brain. Indeed, it is known that nicotine addiction is closely associated with bruxism (24, 25). Nicotine represents a powerful stimulus for the transmission and release of dopamine in the brain, which could explain the evidence that the prevalence of SB in smokers is two times higher than in non-smokers (26, 27).

CONCLUSIONS

Bruxism can be considered a parafunction of the central nervous system, a fact that implies a multifactorial aetiology. The reported data suggest that bruxism is an expression of disorders of the dopaminergic central system, and these alterations can be of two types: direct or indirect.

Direct alterations are mainly related to the effect of substances (such as dopaminergic agonists or antagonists) which act directly on the dopaminergic pathways by exerting an up or down-regulation of the nigro-striatal pathway. Indirect alterations are mainly due to molecules (re-uptake inhibitors or 5-HT antagonists) that interfere with these central neuronal circuits, inhibiting or enhancing the meso-cortical pathway.

Finally, it should be remembered that the dentist is usually the first specialist to diagnose bruxism. Deep knowledge of bruxism origin is essential to counterbalance or eliminate the factors responsible for the phenomenon where possible.

REFERENCES

1. Lobbezoo F, Ahlberg J, Glaros AG, et al. Bruxism defined and graded: an international consensus. *Journal of Oral Rehabilitation*. 2013;40(1):2-4. doi:https://doi.org/10.1111/joor.12011
2. Manfredini D. *Il Bruxismo Nella Clinica Odontoiatrica*. Quintessenza Edizioni; 2015.
3. Lobbezoo F, Rompré PH, Soucy JP, et al. Lack of associations between occlusal and cephalometric measures, side imbalance in striatal D2 receptor binding, and sleep-related oromotor activities. *Journal of Orofacial Pain*. 2001;15(1):64-71.
4. Rintakoski K, Ahlberg J, Hublin C, et al. Bruxism Is Associated With Nicotine Dependence: A Nationwide Finnish Twin Cohort Study. *Nicotine & Tobacco Research*. 2010;12(12):1254-1260. doi:https://doi.org/10.1093/ntr/ntq190
5. Ohayon MM, Li KK, Guilleminault C. Risk Factors for Sleep Bruxism in the General Population. *Chest*. 2001;119(1):53-61. doi:https://doi.org/10.1378/chest.119.1.53
6. Falisi G, Rastelli C, Panti F, Maglione H, Quezada Arcega R. Psychotropic drugs and bruxism. *Expert Opinion on Drug Safety*. 2014;13(10):1319-1326. doi:https://doi.org/10.1517/14740338.2014.947262
7. MANFREDINI D, LANDI N, FANTONI F, SEGU M, BOSCO M. Anxiety symptoms in clinically diagnosed bruxers. *Journal of Oral Rehabilitation*. 2005;32(8):584-588. doi:https://doi.org/10.1111/j.1365-2842.2005.01462.x
8. Kulis A, Türp JC. Bruxism--confirmed and potential risk factors. A systematic review of the literature]. *Schweizer Monatsschrift Fur Zahnmedizin = Revue Mensuelle Suisse D'odonto-Stomatologie = Rivista Mensile Svizzera Di Odontologia E Stomatologia*. 2008;118(2):100-107.
9. Tsai CM ., Chou SL ., Gale EN, Mccall WD. Human masticatory muscle activity and jaw position under experimental stress. *Journal of Oral Rehabilitation*. 2002;29(1):44-51. doi:https://doi.org/10.1046/j.1365-2842.2002.00810.x
10. Giraki M, Schneider C, Schäfer R, et al. Correlation between stress, stress-coping and current sleep bruxism. *Head & Face Medicine*. 2010;6(1). doi:https://doi.org/10.1186/1746-160x-6-2
11. Abekura H, Tsuboi M, Okura T, Kagawa K, Sadamori S, Akagawa Y. Association between sleep bruxism and stress sensitivity in an experimental psychological stress task. *Biomedical Research*. 2011;32(6):395-399. doi:https://doi.org/10.2220/biomedres.32.395
12. Demir A, Uysal T, Guray E, Basciftci FA. The relationship between bruxism and occlusal factors among seven- to 19-year-old Turkish children. *The Angle Orthodontist*. 2004;74(5):672-676. doi:https://doi.org/10.1043/0003-3219(2004)074%3C0672:TRBBAO%3E2.0.CO;2
13. Sari S, Sonmez H. The relationhip between occlusal factors and bruxism in permanent and mixed dentition in Turkish children. *Journal of Clinical Pediatric Dentistry*. 2001;25(3):191-194. doi:https://doi.org/10.17796/jcpd.25.3.84m695q650622568
14. Lavigne G, Palla S. Transient Morning Headache. *The Journal of the American Dental Association*. 2010;141(3):297-299. doi:https://doi.org/10.14219/jada.archive.2010.0163
15. Wieckiewicz M, Paradowska-Stolarz A, Wieckiewicz W. Psychosocial aspects of bruxism: the most paramount factor influencing teeth grinding. *BioMed Research International*. 2014;2014:469187. doi:https://doi.org/10.1155/2014/469187
16. 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. *Journal of Dental Research*. 1996;75(10):1804-1810. doi:https://doi.org/10.1177/00220345960750101401
17. Seraidarian P, Seraidarian PI, das Neves Cavalcanti B, Marchini L, Claro Neves AC. Urinary levels of catecholamines among individuals with and without sleep bruxism. *Sleep & Breathing = Schlaf & Atmung*. 2009;13(1):85-88. doi:https://doi.org/10.1007/

s11325-008-0193-7

18. Lobbezoo F, Lavigne GJ, Tanguay R, Montplaisir JY. The effect of the catecholamine precursorL-Dopa on sleep bruxism: A controlled clinical trial. *Movement Disorders*. 1997;12(1):73-78. doi:https://doi.org/10.1002/mds.870120113
19. Lobbezoo F, Soucy JP ., Hartman NG, Montplaisir JY, Lavigne GJ. Effects of the D2 Receptor Agonist Bromocriptine on Sleep Bruxism: Report of Two Single-patient Clinical Trials. *Journal of Dental Research*. 1997;76(9):1610-1614. doi:https://doi.org/10.1177/00220345970760091401
20. Yi HS, Kim HS, Seo MR. Trial of Oral Metoclopramide on Diurnal Bruxism of Brain Injury. *Annals of Rehabilitation Medicine*. 2013;37(6):871. doi:https://doi.org/10.5535/arm.2013.37.6.871
21. Chen WH, Lu YC, Lui CC, Liu JS. A proposed mechanism for diurnal/nocturnal bruxism: hypersensitivity of presynaptic dopamine receptors in the frontal lobe. *Journal of Clinical Neuroscience*. 2005;12(2):161-163. doi:https://doi.org/10.1016/j.jocn.2004.07.007
22. Zervogiannis FH, Bester G, Wiechers E. The "E" in Rave: A Profile of Young Ecstasy (MDMA) Users. *South African Journal of Psychology*. 2003;33(3):162-169. doi:https://doi.org/10.1177/008124630303300304
23. Mendhekar DN, Andrade C. Antipsychotic Induced Bruxism Treated with Clozapine. *The Journal of Neuropsychiatry and Clinical Neurosciences*. 2009;21(1):105-106. doi:https://doi.org/10.1176/jnp.2009.21.1.105
24. Rintakoski K, Hublin C, Lobbezoo F, Rose RJ, Kaprio J. Genetic Factors Account for Half of the Phenotypic Variance in Liability to Sleep-Related Bruxism in Young Adults: A Nationwide Finnish Twin Cohort Study. *Twin Research and Human Genetics*. 2012;15(6):714-719. doi:https://doi.org/10.1017/thg.2012.54
25. Ahlberg J, Savolainen A, Rantala M, Lindholm H, Kononen M. Reported bruxism and biopsychosocial symptoms: a longitudinal study. *Community Dentistry and Oral Epidemiology*. 2004;32(4):307-311. doi:https://doi.org/10.1111/j.1600-0528.2004.00163.x
26. Ashcroft GW, Eccleston D, Waddell JL. Recognition of Amphetamine Addicts. *BMJ*. 1965;1(5426):57-57. doi:https://doi.org/10.1136/bmj.1.5426.57-b
27. Madrid G, Madrid S, Vranesh JG, Hicks RA. Cigarette Smoking and Bruxism. *Perceptual and Motor Skills*. 1998;87(3):898-898. doi:https://doi.org/10.2466/pms.1998.87.3.898