

## The Effect of Selective Serotonin Reuptake Inhibitor Antidepressants on Bruxism: A Systematic Review

Oliveira F P S L<sup>1\*</sup>, Jansen W C<sup>2</sup>, Côrtes M I S<sup>3</sup>, Seraidarian P I<sup>4</sup>

<sup>1</sup>PhD in Dentistry with emphasis on Public Health - Professor at the Department of Dentistry of the Fipmoc University Center, Montes Claros, Minas Gerais, Brazil.

<sup>2</sup>PhD in Dental Materials - Professor at the Department of Dentistry of Pontifical Catholic University in Minas Gerais, Belo Horizonte, Brazil. (in memory).

<sup>3</sup>PhD in Epidemiology Professor at the Department of Dentistry of Pontifical Catholic University in Minas Gerais, Belo Horizonte, Brazil.

<sup>4</sup>PhD in Restorative Dentistry - Professor at the Department of Dentistry of Pontifical Catholic University in Minas Gerais, Belo Horizonte, Brazil.

### ABSTRACT

The aim of this research was to perform a systematic review of the literature using the Cochrane Library criteria to establish whether there is a relationship between the use of selective serotonin reuptake inhibitor (SSRI) antidepressants and bruxism. We performed a review of randomised clinical trials studies that compared individuals treated with SSRI antidepressants to those treated with a placebo to detect an association between treatments with SSRIs the clinical and/or polysomnographic diagnosis of sleep bruxism. Studies were excluded from the review if the methods used were unclear or if they presented results that were inconsistent with their stated aims. In addition, descriptive and observational studies, literature reviews, case reports, and case series were not included. In the selection process, there were no requirements with regard to the language of the study or the source of the information. The MEDLINE, LILACS, CENTRAL, Embase and PsycINFO databases were examined using pre-established electronic search strategies. None of the 48 selected articles met the criteria for the present review. Thus, we were not able to perform a systematic review using the Cochrane Library criteria. There are no studies that have been conducted using consistent, validated methods that elucidate the relationship between sleep bruxism and the use of SSRIs. Studies should be conducted using appropriate methods to validate this relationship.

### KEYWORDS

Bruxism, sleep bruxism, bruxomania, antidepressants, selective serotonin reuptake inhibitors, paroxetine, fluoxetine, sertraline, citalopram, escitalopram.

### Corresponding Author Information

Fernanda Piana Santos Lima de Oliveira

Av. Profa. Aida Mainartina Paraiso, 80 Ibituruna, Montes Claros – Minas Gerais, Brazil, CEP: 39408-007; Telephone: +5531984497715.

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## Introduction

Science requires the continual pursuit of new knowledge and improvement of current practices. In the field of dentistry, for example, new evidence-based medicine has revealed various philosophical issues that have affected clinical practise for years. Professionals have a duty to choose appropriate procedures for their patients. Any uncertainty regarding the effects of an intervention and any lack of knowledge about an intervention can significantly interfere with patient comprehension or patient care.

Countless articles in the literature suggest that selective serotonin reuptake inhibitor (SSRI) antidepressants may cause sleep bruxism. When choosing a pharmacological agent, one must weigh the benefits and side effects of the drug. As medication use increases, dentists must become increasingly alert to the potential side effects of different drugs.

Systematic reviews, when conducted using established methods and criteria, virtually eliminate incorrect information; thus, the reliability of systematic reviews is unquestionable. Unfortunately, many articles in the literature are conducted using such heterogeneous methodological criteria that they cannot be combined into a systematic review using the Cochrane criteria.

The present study sought to establish whether there is an association between the use of SSRI antidepressants and sleep bruxism.

## Methods

The present review is based on the principles formulated by HIGGINS, J.P.T. and GREEN, S. (editors) in the Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 [updated March 2011] [1].

We aimed to perform a systematic review of randomised controlled clinical trials that would indicate the relationship between SSRI uses and sleep bruxism.

Search strategies defined by The Cochrane Library were used to identify the studies in question, and those that met the eligibility criteria were included. In addition, we included studies that examined the effects of drugs such as sedatives, muscular relaxants, dopaminergic agents and botulinum toxins on sleep bruxism.

The participants included individuals of various ages and both genders who had been given a clinical and/or polysomnographic diagnosis of sleep bruxism. The clinical diagnosis is defined by the International Classification of Sleep Disorders – Second Edition (ICSD-2) [2].

Patients meet the clinical diagnostic criteria if they complain of grinding or clenching the teeth during sleep and present with one or more of the following: abnormal tooth wear, muscular discomfort, fatigue or pain upon waking or evident hypertrophy of the masseter muscle. The ICSD-2 polysomnographic diagnostic criteria include the following: muscular activity of the mandible

during sleep in the absence of associated epileptic activity; more than four episodes of bruxism per hour; more than six bursts of bruxism per episode and/or 25 bursts of bruxism per hour of sleep and at least two episodes in which a grinding noise is produced.

The investigated intervention was the use of SSRI antidepressants, and primary and secondary outcomes were evaluated. The primary outcomes were an index of motor activity using electromyography (EMG) of the masseter muscle, the frequency of episodes of bruxism per hour of sleep and the number of episodes in which a grinding noise was produced. Secondary outcomes included tooth wear, fracture of restorations, alterations in quality of life, grinding of teeth, pain in the temporomandibular joint, limitation of mandibular movement, myofascial pain, headache and effects on sleep.

Studies that did not describe reproducible methods were excluded. Likewise, studies that included individuals with neurological and psychiatric diseases or that did not indicate their stated aims were not included. Only randomised controlled clinical trials studies were included. Descriptive and observational studies, literature reviews, case reports and case series were excluded.

The inclusion of a particular study was not determined based on the language of the study or source of information. An electronic search strategy was employed for each database based on the search strategy developed for MEDLINE/PubMed.

This strategy allows differences in controlled vocabulary by using the Medical Subject Headings (MeSH), the Health Sciences Descriptors (Descritores em Ciências da Saúde - DeCS) and syntax rules. The search included phase 1 (which considered the clinical situation), phase 2 (which considered the intervention) and phase 3 (which considered the study design). Controlled vocabulary and free-text terms were employed together using the Boolean operators “AND” and “OR”.

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*MEDLINE via PubMed and PsycINFO®*

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#1 – (“bruxism” OR “sleep bruxism” OR “bruxism nocturnal” OR “sleep bruxers” OR “bruxist” OR “bruxe” OR “teeth grind” OR “teeth clench” OR “tooth grind” OR “tooth clench”)  
AND  
#2 – (“selective serotonin reuptake inhibitor” OR “sertraline” OR “fluvoxamine” OR “fluoxetine” OR “paroxetine” OR “citalopram” OR “escitalopram”)  
AND  
#3 – (“randomised controlled trial [pt]” OR “controlled clinical trial [pt]” OR “randomised [tiab]” OR “placebo [tiab]” OR “drug therapy [sh]” OR “randomly [tiab]” OR “trial [tiab]” OR “groups [tiab]”).

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**Table 1:** Search strategy used in the MEDLINE and PsycINFO® databases.

### LILACS via PubMed

#1 – (“bruxism” OR “sleep bruxism” OR “bruxism nocturnal” OR “sleep bruxers” OR “bruxist” OR “bruxe” OR “teeth grind” OR “teeth clench” OR “tooth grind” OR “tooth clench”).  
 #2 – (“selective serotonin reuptake inhibitor” OR “sertraline” OR “fluvoxamine” OR “fluoxetine” OR “paroxetine” OR “citalopram” OR “escitalopram”).  
 #3 – (PT: “randomised controlled trial” or PT: “controlled clinical trial” or MH: “randomised controlled trials” or MH: “random allocation” or MH: “double-blind method” or MH: “single-blind method” or MH: “placebos” or TW: “placebo\$” or TW: “random\$” or TW: “randon\$” or TW: “casual\$” or TW: “acaso\$” or TW: “azar” or TW: “aleator\$”).  
 (#1) (#2) (#3) –The Boolean operator “AND” is not required.

**Table 2:** Search strategy used in the LILACS database

### CENTRAL/ The Cochrane Library

#1 – (“bruxism” OR “sleep bruxism” OR “bruxism nocturnal” OR “sleep bruxers” OR “bruxist” OR “bruxe” OR “teeth grind” OR “teeth clench” OR “tooth grind” OR “tooth clench”).  
 AND  
 #2 – (“selective serotonin reuptake inhibitor” OR “sertraline” OR “fluvoxamine” OR “fluoxetine” OR “paroxetine” OR “citalopram” OR “escitalopram”).  
 AND  
 #3 –Filters are not required because there is a specific directory for randomised studies.

**Table 3:** Search strategy used in the CENTRAL database

### Embase

#1 – (“bruxism” OR “sleep bruxism” OR “bruxism nocturnal” OR “sleep bruxers” OR “bruxist” OR “bruxe” OR “teeth grind” OR “teeth clench” OR “tooth grind” OR “tooth clench”).  
 AND  
 #2 – (“selective serotonin reuptake inhibitor” OR “sertraline” OR “fluvoxamine” OR “fluoxetine” OR “paroxetine” OR “citalopram” OR “escitalopram”).  
 AND  
 #3 – (“random\$” OR “factorial\$” OR “crossover\$” OR “cross over\$” OR “cross-over\$” OR “volunteer\$” OR “cross-over procedure” OR “double-blind procedure” OR “randomised controlled trial” OR “placebo\$” OR “double\$ adj blind\$” OR “singl\$ adj blind\$” OR “assign\$” OR “allocate\$” OR “single-blind procedure”).

**Table 4:** Search strategy used in the Embase database

The references listed in the studies generated by the searches were examined so that additional studies might also be identified. Two independent reviewers applied the inclusion criteria to the studies, and when a disagreement occurred, a third reviewer intervened. The participants, interventions and types of studies were considered. The authors of this study recorded the date of

publication and authors of each study identified, the methods used, the participant data (including data on age, gender and diagnosis), the interventions (including their duration) and the outcomes.

This type of review must be conducted annually. If no new significant randomised clinical trials are discovered, updates and corrections are not necessary. However, the date must be updated.

## Results

The present review confirmed that there have been no randomised controlled clinical trials studies on the investigated subject. The search strategies did not retrieve any articles when filters were used. The only near exception was The Cochrane Library; one article was identified but was ultimately excluded. The search was then repeated without filters.

Initially, 195 studies were identified, of which 29 were duplicates and 2 could not be obtained from any library linked to the Regional Library of Medicine (Biblioteca Regional de Medicina – BIREME). Of the 164 remaining studies, 116 were excluded because they did not address the subject being investigated. Then, 47 of the 48 remaining studies were excluded because other drugs were investigated or because the studies were not randomised controlled trials or case-control studies. A single study remained that was excluded because it described a protocol for a systematic review. Because no relevant articles were identified, we did not assess the methodological quality of the studies. Table 5 summarises the types of studies and their authors and dates of publication.

Author	Date	Type of study
Albayak and Ekinci [3]	2011	Case report
de la Hoz-Aizpurua et al. [4]	2011	Literature review
Macedo et al. [5]	2011	Protocol for systematic review
Chang et al. [6]	2011	Case report
Kuloglu et al. [7]	2010	Case report
Poggio et al. [8]	2010	Protocol for systematic review
Saletu et al. [9]	2010	Clinical trial (other antidepressant)
Celik and Balci [10]	2010	Case report
Shuster [11]	2010	Case series
Kwak et al. [12]	2009	Cross-sectional
Mehmet et al. [13]	2009	Protocol for systematic review
Osman Sabuncuoglu et al. [14]	2009	Case report
Navarro et al. [15]	2009	Case report
Kuoglu and Ekinci [16]	2009	Literature review
Ak et al. [17]	2009	Case report
Mayer [18]	2009	Literature review

Bilen et al. [19]	2008	Case report
Kishi [20]	2007	Case report
Beers and van Grootheest [21]	2007	Case report
Inagaki et al. [22]	2007	Protocol for systematic review
Ranjan et al. [23]	2006	Protocol for systematic review
Chen and Swope [24]	2005	Case report
Saletu et al. [25]	2005	Clinical trial (other antidepressant)
Wilson and Argyropoulos [26]	2005	Literature review
Plavovic [27]	2004	Case report
Sokolski et al. [28]	2004	Case series
Winocur et al. [29]	2003	Critical literature review
Miyaoka et al. [30]	2003	Case report
Jaffee and Bostwick [31]	2000	Case series
Journal of the American Dental Association – Section NEWS [32]	2000	Case series
Kato et al. [33]	2001	Literature review
Wise [34]	2001	Case report
Lobbezoo et al. [35]	2001	Cross-sectional and case report
Lobbezoo and M. Naeije [36]	2001	Literature review
Bostwick and Jaffee [37]	1999	Case series
Brown and Hong [38]	1999	Case report
Spigset [39]	1999	Observational and retrospective study
Gerber and Lynd [40]	1998	Literature review
Stein et al. [41]	1998	Case series
Possidente et al. [42]	1997	Case series
Por et al. [43]	1996	Case report
Romanelli et al. [44]	1996	Case report
Christensen and Byerly [45]	1996	Case report
Leo [46]	1996	Literature review
Fitzgerald and Healy [47]	1995	Case series
Chong [48]	1995	Case report
Ellison and Stanzani [49]	1993	Case series
Micheli et al. [50]	1993	Descriptive study (other antidepressants)

**Table 5:** Excluded studies, dates of publication and reasons for exclusion

## Discussion and Conclusions

The 48 selected studies could not be included in the present review. These papers could not be reviewed systematically because of the heterogeneity of the methods, inclusion and exclusion criteria and other variables used across the studies (different behavioural disorders treated with the same drug, drug interactions and the education level and socioeconomic status of the participants). These factors would surely have influenced the primary and secondary outcomes.

We were frustrated at our inability to perform a systematic review of the literature on the relationship between the use of SSRIs and sleep bruxism. Perhaps the criteria used by the journals to assess and accept these articles were responsible for the lack of acceptable sources. There may be differences of opinion between the reviewers who conduct the assessments of articles for these journals and the reviewers at The Cochrane Library.

Using the rigorous criteria chosen for the present study, a relationship between sleep bruxism and SSRIs or other drugs could not be established. Moreover, this relationship may not be confirmable in the future due to the variables listed above, which may interfere with central dopamine levels. In essence, we question the possibility of performing two different homogenous studies that can assess the relationship between sleep bruxism and SSRIs in samples of individuals who are subjected to countless factors that alter their levels of neurotransmitters. When a number of individuals present with a particular behavioural disorder, we must search for a relationship between the intensity of the disorder and the drug regimen. However, the studies identified during our literature search also did not indicate whether each patient had been formally diagnosed with bruxism.

Venlafaxine acts as an SSRI at doses of 75-150 mg/kg and as a selective inhibitor of noradrenalin and (to a lesser degree) dopamine reuptake at higher doses [7,15,21,23,31]. These effects were also associated with duloxetine [3]. However, the literature does not identify the levels of serotonin or dopamine associated with motor control, so it is not yet possible to establish the appropriate dose for each individual patient.

SSRI-induced bruxism is dose dependent, but the dose that induces this effect varies from one individual to another and even within a same individual over time [21,23].

For these reasons, professionals must use their common sense. Because the research results are unclear, researchers should more closely examine the relationship between SSRI uses and sleep bruxism.

The present review did not accomplish its stated goal because there is no scientific evidence that treatment with SSRIs may induce sleep bruxism. Our understanding of this association is grounded in the available studies and the experience of providers.

The present study highlights the need for further studies to use validated methods to establish the relationship between sleep bruxism and the use of SSRIs. An update of this systematic review must be carried out.

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