

## Morning Awakening With Pain in Sleep Bruxers with Craniomandibular Disorders and Concomitant Use of Selective Serotonin Reuptake Inhibitors (SsrIs): A Intra-Group Comparison Study

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### Abstract:

**Introduction:** Subjects with sleep bruxing behavior may present with morning awakening with pain in multiple anatomic areas. Awakening with pain may be influenced to a certain extent by previous or current use of Selective serotonin reuptake inhibitors.

**Aim:** Evaluate frequency of selective serotonin reuptake inhibitors in sleep bruxers with craniomandibular disorders, assess frequency of anatomic areas reported with pain on awakening in the morning.

**Methods:** Clinical examination, palpation of masticatory muscles and temporomandibular joints, use of questionnaires and self-report to gather data in 53 subjects currently using selective serotonin reuptake inhibitors, 31 subjects with history of past SSRIs use, 21 subjects who reported that used or were using another antidepressant type and 39 who never used antidepressants. Data from all these subjects were reviewed retrospectively.

**Results:** The frequency of current use of selective serotonin reuptake inhibitors was about 53=36,8% and 31=21,5% of bruxers and craniomandibular disorders subjects reported past SSRIs use. 21=14,5% of all bruxers reported past or current use of another antidepressant type and 39=27% of the sample reported that never used antidepressants. In those subjects reporting current Selective serotonin reuptake inhibitors use, the most common sites with morning awakening with pain were the head (54,7%), cervical area (50,9%), temporomandibular joints (43,4%), face (35,8%), and teeth (32,1%). The frequency of morning awakening with pain in these anatomic areas was higher in the "current use of SSRIs" subgroup as compared with the control group that never used any antidepressant. The mean frequency of anatomic areas with pain on awakening in the morning was higher in the "have used SSRIs" subgroup as compared with the "never used AD" subgroup and the difference was statistically significant (Kruskal-Wallis statistics  $p < 0.05$ ). Mean painful areas on awakening in the morning were about 2,9 (subgroup using SSRIs); 2,6 (Have used SSRIs subgroup); 2,1 (used/using another antidepressant subgroup) and 1,6 (never used antidepressant subgroup). The difference was statistically significant only when the subgroups "Have used SSRIs and "Never used antidepressant", were contrasted (Kruskal-Wallis statistics  $p < 0.05$ ).

**Conclusions:** Because higher frequencies of awakening with headache, facial pain, and dental pain were reported by subjects who had used or were using SSRIs as compared with the subgroup that never used SSRIs, such antidepressants may play a role increasing loading on the masticatory structures. However, further studies are needing to substantiate findings in the current investigation.

**Keywords:** Sleep Bruxism. Craniomandibular Disorders. Selective Serotonin Reuptake Inhibitors. Pain on awakening.

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## I. Introduction

Craniomandibular Disorders (CMDs) is a set of disorders affecting the masticatory muscles and temporomandibular joints (TMJs) characterized by specific signs and symptoms of jaw movements and dysfunction<sup>[1]</sup> including a complaint of pain, joint noises, impaired jaw movements, tenderness to palpation of the masticatory muscles and headache<sup>[2]</sup> affecting 20-30% of the general population between the ages of 20 and 40 years old. Sleep bruxism (SB) is characterized the involuntary clenching or grinding of the teeth during sleep and can cause severe masticatory disorders including the destruction of tooth surface, TMJ pain and dysfunction, myofascial pain and severe sleep disturbances<sup>[3]</sup>.

There is a group of antidepressants known as selective serotonin reuptake inhibitors (SSRIs) that were introduced in the clinical practice in the late 1980 usually associated with motor disorders including dystonia, dyskinesias and restlessness<sup>[4]</sup>. Such antidepressants include paroxetine, fluoxetine, sertraline, citalopran,<sup>[5]</sup> duloxetine, venlafaxine, and fluvoxamine<sup>[6]</sup>. SSSRIs are drugs which prevent the reuptake of 5-HT by the presynaptic neuron and are usually prescribed to treat mood, depression, anxiety and obsessive-compulsive disorders<sup>[7]</sup>.

Intense occlusal loads may occur in patients with nocturnal bruxing behavior (BB) in response to any of the group of SSRIs. Such sustained or intermittent intense loads are not properly dissipated by the supporting structures of the masticatory system, thus resulting in pain, discomfort and abnormal jaw movements, more specifically on awakening in the morning. Thus, patients may complaint of painful TMJs<sup>[8]</sup>, facial pain and tooth destruction<sup>[3]</sup>, headache<sup>[9]</sup> cervical pain, sore gums<sup>[4]</sup> and severe tooth pain<sup>[10]</sup>. Currently, there are no clinical studies correlating the use of SSRIs with pain in some anatomic areas of the masticatory system in large samples of individuals presenting with sleep and mixed BB. Thus, this study was designed to:

1. Evaluate the frequency of SSRIs use in individuals presenting with sleep bruxing behavior with concomitant CMDs;
2. Evaluate the frequency of anatomic areas of the masticatory system more frequently reported with pain on awakening in the morning in the experimental and control subgroups.

## II. Material and Methods

### Sample

All those records having complete information about signs and symptoms of CMDs, BB and anatomic sites with pain in the masticatory system on awakening in the morning and no use, past and current use of antidepressants including SSRIs were retrieved, evaluated retrospectively and compared. Following a comprehensive retrospective examination of such charts, subjects were allocated to four different subgroups: Those that were currently using SSRIs, those that have used SSRIs before clinical evaluation, those that have used and/or were using another type (non-SSRIs) of antidepressant, and those CMDs and BB individuals who never used and were not currently using antidepressants. We evaluated data from four different subgroups: 53 subjects in "currently using SSRIs subgroup; 31 individuals in the "had used SSRIs" subgroup, 21 subjects in the subgroup "had used or were using" another antidepressant type, and 39 subjects in the "never used" any antidepressant type (control subgroup). Thus, the records of 144 subjects were retrospectively evaluated. Inclusion criteria for CMDs: Presence of three of the following signs and symptoms: A complaint of pain in the masticatory system, tenderness to palpation, difficulties to perform normal jaw movements, presence of joint noises and headache with origin in the TMJ and/or masticatory muscles.

Inclusion criteria for sleep BB: Sleep bruxism was diagnosed as such if at least three of the following characteristics or signs and symptoms were reported: Awakening with pain in the TMJs and/or masticatory muscles, awakening with dental pain or soreness in the morning, grinding noises at night based on sleep partner or others' report, patient's report of catching herself/himself grinding the teeth at night, difficulties to open the jaw on awakening in the morning including jaw locking.

Inclusion criteria for SSRIs or other antidepressant use: Patients report of past or current used of antidepressants including those of the SSRIs type: Citalopran (celexa), Escitalopran (Lexapro), Fluoxetine (prozac), Paroxetine (paxil), Sertraline (Zoloft), Fluvoxamine (Luvox), Duloxetine (Cymbalta), Venlafaxine (effexor), Desvenlafaxine (Pristiq).

Criteria for morning awakening with pain: Any headache, pain in the face, TMJs, the lower jaw, maxilla, teeth, cervical area, ear, behind the lower jaw, frontal area, behind the hard palate and vertex, was recorded if present based on patient information..

Exclusion criteria: Subjects were not included in the comprehensive evaluation and consequently in the current study if they demonstrated severe psychiatric disorders and cognitive impairment, and unwillingness to respond to the questionnaire and participate in the comprehensive clinical evaluation.

### III. Statistical Analysis

Data were analyzed using Tukey's analysis of variance (age) and Kruskal-Wallis test (anatomic areas with pain, pain duration).

### IV. Results

A total of 144 clinical records were evaluated retrospectively in the current study. Fifty-three subjects (53/144=36.8%) demonstrated signs and symptoms of CMDs, sleep BB and reported current use of SSRIs (**Current SSRIs use subgroup**); thirty-one (31) subjects demonstrated signs and symptoms of CMDs, sleep BB and reported previous use of SSRIs or other antidepressant before initial interview (**Previous SSRIs/other AD use subgroup**); twenty-one individuals (n=21) reported signs and symptoms of CMDs, BB and had used and/or were currently using a non SSRIs antidepressant (**Had used/were using other AD subgroup**), and thirty-nine subjects (n=39) had signs and symptoms of CMDs, BB and reported no previous use of any antidepressant (**never used subgroup**). There were 52 females and 1 male (mean age 32.2, SD= 12.2, range 18-72) in the "current SSRIs subgroup", 30 females and 1 male in the "previous SSRIs use" (mean age 37,9, SD=9,7, range 19-55 years); 20 females and one male in the "had used/were using other AD" (mean age 37, SD=13, range 18-57; there were 36 females and 3 males in the "never used AD" (mean age= 32.8 years, SD= 124, range= 17-66). One way analysis of variance (Tukey's test) demonstrated that there was no difference in age in the four subgroups evaluated, p=0.15. See Table 1 for further analysis.

Regarding anatomic sites painful on awakening in the morning, the "Current SSRIs use"; "Previous SSRIs/Other AD use"; "Had used/were using other AD"; " Never used any AD" subgroups, demonstrated the following means, SD and ranges: 2,54 (SD=1.6, range=0-7); 2,8 (SD=1,3, range=1-5); 2,09 (SD=1.2, range=0-4); and 1.7 (SD=1.3, range=0-4), respectively. Kruskal-Wallis statistics p<0.01: "Previous SSRIs use/Other AD use" versus "Never used AD", p<0.05. See Table 2 for additional informations. Regarding duration of pain complaint evaluated on initial interview and considering the same subgroups in the same order, we found the pain durations as follows: 75.4 months (SD=85.7, range=1-360); 132.5 months (SD=132, range 24-540); 65.4 months (SD=56.5, range=6-240); 62 months (SD=54.8, range 1-180). Kruskal-Wallis' statistics p<0.02: "Current SSRIs use" versus " previous SSRIs/Other AD use", p<0.05; "Had used SSRI/and/or other" versus "Never used AD", p<0.05.

### V. Discussion

#### Frequency of SSRIs use in sleep bruxers with craniomandibular disorders

Data in the current research demonstrate that 36,8% and 21,5% of a large sample of 144 subjects presenting with sleep BB and CMDs, reported current and past use of SSRIs, respectively. Because such percentages are considered very high, findings in the current investigation are endorsed by another study<sup>[11]</sup> asserting that the recent widespread use of SSRIs is based on the perception that these drugs are effective to treat depression and have a lower side effect profile than do other categories of antidepressant medications, for instance, monoamine oxidase inhibitors.

Noteworthy to mention is that such medication was not prescribed for the treatment of such disorders, but for the management of **depression** and probably **headache**. The interpretation of such data in this population of CMDs and BB subjects in this investigation is that they did not seek previous treatment for their TMJ and facial pain, but for other disorders including headache and depression, thus, SSRIs were prescribed relatively frequently in such subjects. A high percentage of CMDs patients may seek treatment for depression and anxiety initially neglecting their facial, cervical and head pains. Such patients may be prescribed with both SSRIs or TCA antidepressants. However, there may be other subgroup of patients with pain that because of their unsatisfactory treatment of their chronic facial, cervical and head pain, become depressed and seek medical advice for their depression. The final outcome is a high prevalence of CMDs and BB patients with pain in multiple sites more frequently headache and with a history of past or present use of antidepressants.

SSRIs is a group of medications used to treat depression and many other mental illnesses. However, these drugs produce the side effect of increased sustained nonspecific activation of the jaw and tongue musculature, thus resulting in more intense headache, tightness in the jaw, tongue and other masticatory structures<sup>[12]</sup>. SSRIs, are the most widely prescribed psychopharmacological agents for depression, worldwide and are indicated for the treatment of depression, obsessive compulsive disorders, posttraumatic stress disorder and social phobia<sup>[13]</sup>. Some adverse effects of these drugs include insomnia and sleep bruxism, vivid dreams and restless legs

The frequency of SSRIs and other antidepressants use was very high in this selected sample of 144 subjects with both BB and CMDs. In general, CMDs are characterized by a complaint of pain, joint noises, headache and impaired jaw movements. Spasm and muscle hyperactivity do constitute some of the mechanism of both TMJ internal derangements and myofascial pain. Chronic pains, muscular spasm in CMDs patients

may be treated using a combination of clonazepam, and SSRIs including fluoxetine which is more recommended in patients with depression, chronic pain, fibromyalgia and headache.

There are many roads to explain why patients that have used/ are using SSRIs are still in pain: patients are usually treated regarding their pain without considering the whole range of diagnosis that can be present in such patients, for instance, facial pain, cervical disorders, BB, internal derangements of the TMJ, tension - type headache and so on; the various mechanisms involved in pain disorders are not being treated, for instant, longer duration of pain, stressful events, depression, multiple pain disorders, and finally, only one mode of therapy is used (antidepressants and or analgesics). Further, the side effects of medications are not considered in the treatment. Reinforcing at least in part this point of view, data from one investigation<sup>[14]</sup> indicate that subjects taking the SSRI Celexa were more likely to report experiencing more TMD symptoms as compared to those prescribed an SSRI other than Celexa.

**Anatomic areas of the masticatory system more frequently reported with pain on awakening in the morning.** There was a very close similarity regarding frequency of reported painful anatomic areas in the subgroups with a history of "current use" and "past use" of SSRIs antidepressants. The most common anatomic areas in both groups were the head, cervical area, TMJ, face and teeth. All these anatomic areas are involved in motor function including chewing, swallowing, posture and motor activity. One investigation<sup>[11]</sup> asserts that when SB and sustained habitual forceful clenching (day or night) are very severe, these motor disorders may cause strong headaches, damage to the teeth and TMJs, and difficulties with motor control of the jaw.

During many years CMDs have been correlated in many studies with sustained muscle hyperactivity leading to sustained or intermittent muscle and joint pain. This point of view is in line with one research<sup>[11]</sup> indicating that similar to many neuroactive medications, antidepressants have widespread nonselective effects including potential repercussions on motor function and spasticity. Fluoxetine prescribed in a short period of time may increase skeletal muscle tone and such a disorder decreases following fluoxetine discontinuation<sup>[11]</sup>. In the current study, subjects with past and current use of antidepressants demonstrated higher frequency of headache, cervical, TMJ, facial and dental pain as compared to the group which never used antidepressants. Although the difference was not statistically significant, this outcome has some clinical utility. Increased muscle activity during the day may cause TMJ and facial pain<sup>[15]</sup>. Short - time use of paroxetine (SSRIs) antidepressant causes jaw pain and masticatory muscle stiffness on awakening in the morning<sup>[16]</sup>. One investigation<sup>[11]</sup> indicates that SSRIs medication causes increased and sustained non specific activation of the jaw and tongue musculature, more intense headache, tightness of the jaw, tongue and other structures of the masticatory system.

In the current study, the group that reported current use of SSRIs and the other one reporting past use of such medications, fulfilled the characteristics of nocturnal BB and CMDs. It is very likely that the higher prevalence of headache, cervical, facial, TMJ and dental pain in such groups may have been caused by exacerbation of nocturnal and perhaps diurnal BB. In this regard, one study<sup>[17]</sup> reports that sleep bruxism tends to increase in younger age groups making them more vulnerable to pain in such anatomic locations as a reaction induced by SSRIs. In the current investigation one way to detect sleep bruxism was to ask the patients about signs and symptoms that are perceived soon on awakening in the morning as patients<sup>[18]</sup> report that such signs and symptoms are worst in the morning but improve during the course of the day.

Dopamine is a neurotransmitter in the Central Nervous System which inhibits spontaneous movements whereas excessive serotonin inhibits dopaminergic transmission in the mesocortical tract associated with masticatory motor activity<sup>[19]</sup>. Thus, such "failed" dopamine inhibition results in facilitation of repetitive muscle contraction in nocturnal bruxism. Such prolonged contraction may lead to facial, head, TMJ, cervical and even dental pain in those who used or are currently taking SSRIs. BB has been observed during both Non-REM and REM sleep. Some antidepressants used in the treatment of depression, may also cause excessive muscle tone in the masticatory region causing excessive muscle activity, SB exacerbation<sup>[20]</sup>, thus leading to facial, TMJ, and cervical pain. There is some information indicating that antidepressants especially, SSRIs, and TCAs may increase REM sleep muscle tone in patients with or without RBD<sup>[21]</sup>. If the patient is a sleep bruxer characterized by masticatory muscle hyperactivity at least at night, thus, medications may further increase masticatory muscle activity, thus facilitating the development of headache, TMJ, facial and cervical pain. In part, this non statistically significant difference may be explained by the fact that although the group "never used" did not report use of any antidepressants, they were also bruxers and reported CMDs.

In one case report, researcher<sup>[11]</sup> indicated that fluoxetine used for the treatment of obsessive-compulsive disorders, causes severe dental pain and headache, thus that study is in line with the outcome reported in this investigation. Because in the current investigation most CMDs and BB subjects reported pain in the head, cervical area, teeth, face and TMJ, this outcome is endorsed by one investigation<sup>[22]</sup> carried out in nine patients using SSRIs and reporting bruxism and pain on awakening in the morning in the same anatomic structures.

When the frequency of headache in the "current SSRIs use" was compared with the "never used AD", subgroup, the difference was statistically significant  $p=0.05$ . This outcome is very interesting as headache may represent the sum of increased muscle activity and nociception from many adjacent anatomic orofacial structures, which may be influenced by SSRIs associated increased muscle activity. In the current study, we report a relatively high prevalence of dental pain in those who used, were using and never used SSRIs, but the prevalence of dental pain on awakening in the morning was higher in those who used/were using SSRIs and were using other AD types. Thus, this outcome is in line with some studies reporting that dental soreness or dental pain on awakening in the morning is a common complaint in those who report antidepressant use<sup>[19,20,22]</sup>.

Extreme masticatory and cervical muscle tension associated with SSRIs use, may result in dental damage, TMJ pain and inflammation, facial pain and tension-type headache or migraine<sup>[19]</sup>. Second-generation antidepressants have been the more cited drugs prone to cause and/or exacerbate bruxism<sup>[20]</sup>. A complaint of TMJ, facial and headache pain is reported very frequently by CMDs and sleep BB patients. Although patients in the "used/were using other type of antidepressant subgroup", had been in treatment using antidepressants, they still had a high prevalence of headache, cervical and TMJ pain and even dental pain on awakening in the morning. This may indicate that an adequate and comprehensive plan of treatment had not been established, that antidepressants had been the only mode of treatment instituted in these patients, or that their pain was very severe, chronic and frequent, rendering antidepressants ineffective or partially effective. Supporting in part this point of view, one investigation<sup>[21]</sup> indicates that tricyclic antidepressants are not totally effective in the alleviation of headache.

## VI. Conclusion

This investigation demonstrated that the frequency of past and current use of SSRIs in CMDs and BB subjects was very high. Anatomic areas awakening with pain in the morning were the head, cervical, TMJs, face and teeth. Such anatomic areas were very similar when subgroups were compared indicating that painful areas with pain in the morning are "stereotyped" in sleep bruxers with CMDs independent of the use of SSRIs. These anatomic areas painful on awakening in the morning were also the same in those that did not report previous or current use of SSRIs or other antidepressants. SSRIs may influence in some way, motor mechanisms including motor pathways as those who have used SSRIs antidepressants demonstrated a higher frequency of painful anatomic areas on awakening in the morning as compared with those who never used antidepressants and the difference was statistically significant.

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**Table 1:** Social and demographic data in different subgroups with BB and CMDs.

	SUBGROUPS							
	Using SSRIs		Previous SSRIs/ other use		Had used/using other		Never used	
	n=53		n=31		n=21		n=39	
GENRE	n	%	n	%	n	%	n	%
Females	52	98,1	30	96,8	20	95,3	36	92,3
Males	1	1,9	1	3,2	1	4,7	3	7,7
Total	53	100	31	100	21	100	39	100
AGE								
Mean	38,2		37,8		37		32,8*	
SD	12,2		9,7		13		12,4	
Range	18-72		19-55		18-57		17-66	

\*Tukey's test: p=0,15, No significant difference.

**Table 2:** Frequency of current use of SSRIs, past use of SSRIs or other antidepressants, past/current use of other antidepressants, and "never used" antidepressants N=144

ANTIDEPRESSANTS	n	%
Using SSRIs	53	36,8
Past use of SSRIs	31	21,5
Used or using other type of antidepressant	21	14,6
Never used antidepressant	39	27,1
Totals	144	100

**Table 3.** More frequently reported anatomic areas with pain on awakening in four groups.

SUBGROUPS Using SSRIs Have used Used/using other Never Used ANATOMIC antidepressant

AREAS	n=53		n=31		n=21		n=39	
	n	%	n	%	n	%	n	%
Headache	29	54,7	19	61,3	10	47,6	13	33,3*
Cervical Pain	27	50,9	16	51,6	12	57,1	17	43,6**
TMJs	23	43,4	13	41,9	6	28,6	16	41**
Face	19	35,8	13	41,9	5	23,8	8	21**
Teeth	17	32,1	14	45,2	9	42,8	8	21**
Ear	5	9,4	2	6,5	0	0	2	5,1**
Painful areas on awakening in the morning								
Mean	2,9		2,6		2,1		1,6***	
SD	4,2		1,2		1,2		1,3	
Range	1-5		1-5		0-4		0-4	

\*Chi-squared for independence p=0,09, for trends p<0,03

\*\* Chi-squared for independence and for trends p>0,05

\*\*\*Kruskal-Wallis's statistics, p<0.01, "Have used SSRIs" versus "Never used AD", p<0.05

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