The Excitability of the Trigeminal Motor System in Sleep Bruxism: A Transcranial Magnetic Stimulation and Brainstem Reflex Study

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Aims: *Since sleep bruxism (SB) is characterized by grinding and clenching of the teeth during sleep and could be an exaggerated manifestation of normal spontaneous rhythmic masticatory muscle activity, the aim of this study was to obtain a neurophysiological assessment of the excitability of the central jaw motor pathways in patients with signs and symptoms suggestive of SB.* ***Methods:*** *A total of 30 subjects diagnosed with SB on the basis of self-report of tooth grinding were studied using the "recovery cycle" of the masseter inhibitory reflex (MIR) elicited by electric and magnetic stimulation of the mental nerves and by recording the motor potentials evoked in masseter muscles by transcranial magnetic stimulation. Tests were done during daytime, when the subjects were awake. The data obtained were compared with data from a population of normal subjects.* ***Results:*** *In the putative SB patients and in normal subjects, the MIRs evoked by single electric and magnetic stimuli were similar. With paired stimuli, the degree of suppression of the late silent period was significantly lower (*$P < .01$*) in the patients compared to normal subjects, particularly for magnetic stimuli, at various interstimulus intervals. No significant differences were found between the 2 groups of subjects in the masseter motor potentials evoked by transcranial magnetic stimulation.* ***Conclusion:*** *Although the data were only obtained during wakefulness in patients self-reporting signs and symptoms suggestive of SB, the findings suggest that an abnormal excitability of the central jaw motor pathways may be present in SB subjects. This increased excitability could derive from an impaired modulation of brainstem inhibitory circuits and not from altered cortical mechanisms. These results support the view that bruxism is mainly centrally mediated and that it involves subcortical structures. The study also indicates that use of the MIR elicited by the double-shock technique could be valuable in the evaluation of bruxism.*
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Sleep bruxism (SB) has been defined as "a stereotyped movement disorder characterized by grinding or clenching of the teeth during sleep."[1] It is also classified among the parasomnias, and the following definition was recently proposed: "a parasomnia and an oral parafunction activity, that is characterized during sleep by either jaw clenching (tonic activity) and/or repetitive, phasic jaw muscle activity that produces tooth grinding."[2] SB can cause dysfunction of the jaw system, eg, wear, attrition, tooth

destruction, and periodontal problems. It might also sometimes be associated with temporomandibular disorders (TMD), as well as headaches or facial pain, but the functional relationship between bruxism and these painful conditions is not clear.[3]

SB is a very common condition, with a prevalence estimated around 8%.[4,5] It can occur in association with neurological and psychiatric disorders (eg, Parkinsonism, schizophrenia). It can also be caused by certain drugs (eg, antidepressants, cocaine). It also exists in normal healthy individuals (so-called primary SB). The etiology and pathophysiology of "primary" SB are not completely explained.[2,6,7] A 1961 electromyographic study[8] hypothesized that interferences in the dental occlusion represent an important etiologic factor. Although this study was carried out during daytime wakefulness and no assessment of sleep bruxism status nor any correlation was made, nevertheless this hypothesis has had a long-term influence on research and treatment of bruxism.[9]

More recently, SB has been associated with central factors involving brain neurotransmitters, basal ganglia, and the limbic system,[2,6,7,10] and currently SB is usually considered a multifactorial disorder, where peripheral factors (such as dental occlusion or other morphological features of the jaw system) have much less importance compared to central factors.[3,11] This view is supported by polysomnographic studies that suggest that SB is a transient motor activity that occurs in normal sleepers and may be related to normal fluctuations in sleep[10] but may be transformed into a pathophysiologic condition by several factors that increase jaw-muscle activity.[12] Current neurophysiologic methods offer approaches to study the excitability of the trigeminal motor system by recording the motor potentials evoked by transcranial magnetic stimulation (TMS) in the masseter muscles and the masseter inhibitory reflex (MIR) elicited by electrical and magnetic stimulation with single and double-shock techniques.[13,14] MIR recordings also allow the excitability of a reflex circuit to be assessed by studying its recovery curve.[15] Unfortunately, these tests are not possible to perform during sleep or during grinding or clenching of the teeth during sleep, because it is necessary to have voluntary contraction of the jaw-closing muscles and to repeat various stimuli that would trigger arousals and awake the subjects.[16–18] Despite this limitation, these neurophysiological approaches were used in the present study to test the excitability of the central jaw motor system in awake subjects with signs and symptoms suggestive of primary SB.

Materials and Methods

Thirty patients (mean age ± SD, 32.4 ± 12.9 years; median, 29 years; 16 male and 14 female) and 31 healthy subjects of comparable age (mean, 34.9 ± 13.8 years; median, 31 years; 18 male and 13 female) were enrolled in the study.

Inclusion criteria for the patients were based on the clinical criterion of moderate to severe chronic bruxism, based on the criteria of the American Sleep Disorders Association (ASDA). These subjects were defined as putative SB patients. They showed a positive history of tooth grinding for at least 3 nights per week for 6 months.[19] In the majority of patients, clinical features that were suggestive of a diagnosis of primary SB included the presence of sounds associated with bruxism during sleep, reported by a bed partner, roommate, or family member; awareness of current tooth-grinding, abnormal tooth wear due to abrasion; masseter and temporalis muscle hypertrophy on voluntary contraction; and tooth fracture/failure.[2,7] In 3 cases, the reports were incomplete and/or the clinical signs were not clear; in these cases, the diagnosis was confirmed by polysomnographic monitoring, based on the following criteria: *(1)* tooth grinding or clenching during sleep (more than 4 bruxism episodes or more than 25 bruxism bursts per hour of sleep), *(2)* abnormal tooth wear and/or sounds associated with bruxism, and *(3)* presence of jaw muscle activity during sleep and absence of associated epileptic activity.[20]

Subjects who revealed the presence of jaw muscle pain, stiffness, fatigue or craniofacial pain, or temporomandibular joint (TMJ) problems or headaches were excluded from the study in order to avoid any nociceptive afferent influence on the neurophysiologic results. Furthermore, subjects suffering from depression or anxiety and 2 subjects who demonstrated a specific anxious reaction to the neurophysiological evaluation were also excluded. No subject used drugs that could alter neuromuscular excitability or drugs associated with bruxism (in particular, substances related to the dopaminergic, serotoninergic, and adrenergic systems)[21] either during the evaluation or for 48 hours prior to it. Female subjects were not examined during the menstrual period because of the possible reduction of the masseteric late silent period (SP) elicited by electrical stimulation.[22] Neurological examinations excluded the presence of any cranial nerve pathology or any medical or psychiatric disorders that could produce abnormal movements, particularly during sleep, and other sleep disorders such as apnea, a rapid eye move-

ment (REM) behavioral disorder, insomnia, and periodic leg movements in sleep.

All of the examinations were carried out in the late afternoon. The tests, which were carried out in random order, began at 6 pm and lasted for 2 hours. The subjects sat in a dental chair, relaxed, with the head supported in a median position in order to avoid excessive contraction of the neck muscles. Instructions were given on how to bite in intercuspal position and maintain a constant muscle activity at approximately 80% of the electromyographic (EMG) maximum voluntary contraction for the inhibitory reflex studied and at approximately 30% for the motor-evoked potential studied, with audio-visual raw EMG feedback. The masticatory muscles were relaxed for at least 20 seconds between each recording, and the evaluation was suspended as long as necessary when tiredness or pain in the joints or muscles was reported.

The EMG activity was recorded from 2 masseter muscles by surface electrodes; each active electrode was placed on the belly of the muscle, and the reference electrode was placed 2 cm below the mandibular angle, with an interelectrode distance of approximately 4 cm. Skin impedance was lower than 5 kilo-ohm. The raw signals were amplified 2,000 to 4,000 times, filtered (20 to 5,000 Hz; –3 dB) by a standard EMG machine (Keypoint; Dantec Medical) with time constant, and then captured on a computer and converted by an analog-to-digital interface at a sampling rate of 5 kHz. EMG activity was stored on disk for off-line analysis. Magnetic stimulation was carried out with a Dantec magnetic stimulator (MagLite-r25 Twin Top; Dantec Medical) using single and paired pulses and a figure-8 coil, with a loop of 8 cm (external diameter), and a peak of magnetic fields around 2.5 tesla; the intensity of stimulation was expressed as a percentage of the maximum power output of the magnetic stimulator.

Masseter motor-evoked potentials (MEPs) were elicited by TMS. The stimuli were delivered on the scalp close to the face area of the motor cortex at the location known to produce the highest MEP in the contralateral active masseter muscle.[16,23] The coil was placed with an anterolateral orientation, approximately paralleling the central sulcus, as recommended for the study of masseter MEPs.[24] The lowest threshold to elicit MEPs of the contralateral masseter muscle was found in an area 4 to 10 cm lateral to the vertex and 0 to 4 cm anterior to the biauricular line. In this position, the TMS also simultaneously elicited an ipsilateral MEP that had a shorter latency and a higher amplitude. This likely represented the direct activation of the trigeminal root (r-MEP), given the peripheral conduction time,[16] whereas the contralateral MEP (c-MEP) reflected the activation of corticobulbar fibers projecting to the trigeminal motoneurons.

The following parameters were measured:

1. The active motor threshold for the c-MEP, defined as the minimum stimulus intensity needed to produce 5 discrete MEPs, with a peak-to-peak amplitude of at least 0.1 mV discernible visually on a video monitor in a series of 10 consecutive stimuli with at least 15 seconds between stimuli.[25]
2. The onset latency and peak-to-peak amplitude over 3 trials for the c-MEP, the onset latency of the r-MEP, and the central conduction time (CCT). The latency was measured from the start of the magnetic stimulus to the onset of the first part of the potential, and its mean value was derived from 3 single responses.[26] The CCT was therefore calculated by subtracting the latency of the r-MEP from the latency of the c-MEP. MEP onset was defined as the first negative deflection from baseline. The intensity of the magnetic stimulus was around 130% of the active motor threshold value.
3. MIR, which was obtained with single and paired electrical and magnetic peripheral stimuli, as previously described.[14] In brief, a stimulus that excites trigeminal afferents can evoke a reflex interruption of the voluntary activation of the jaw closer muscles. The reflex is composed of 2 separate SPs, an early one (SP1) and a later one (SP2). The MIR evoked by electrical stimuli was obtained by stimulation of the right and left mental nerves at an intensity of more than 30% of the excitability threshold of a complete SP (usually 15 to 30 mA). Single electrical shocks (0.1 ms) were delivered through a cathode placed at the mental foramen, while the anode was placed lateral to the mental foramen. The MIR evoked by magnetic stimuli was obtained at an intensity that was more than 130% of the excitability threshold of a complete SP by placing the figure-8 coil at mental level in the midline position. The coil of the magnetic stimulator was maintained in position by a fixed frame in order to reduce the possibility of position changes. The recovery curve of the MIR evoked by electrical and magnetic stimuli was obtained by delivering paired stimuli at interstimulus intervals (ISIs) of 100, 200, 300, 400, 500, and 600 ms. The stimulation parameters have been described, and the intensities of the first (conditioning) and second stimuli (test) were identical.

Table 1 MEPs Evoked by TMS

	Normal subjects (n = 31)	Patients (n = 30)
Active motor threshold (%)	64 ± 10.1	62.5 ± 10.2
Latency c-MEP (ms)	6.7 ± 0.3	6.6 ± 0.3
Amplitude c-MEP(mV)	0.86 ± 0.35	0.92 ± 0.27
Latency r-MEP (ms)	2.9 ± 0.3	2.9 ± 0.3
CCT (ms)	3.8 ± 0.3	3.7 ± 0.2

There were no statistical significances between the 2 groups. Means ± 1 SD shown.

For each time interval, a series of at least 6 trials was obtained. The EMG signals were full-wave rectified and averaged.[27] Onset and end of the SPs were taken at the intersection of the rectified and averaged signal and a line indicating 80% of the background pretrigger EMG level during voluntary contractions.[28,29]

The following parameters were evaluated: *(1)* Latency (in ms) was measured from the stimulus to the onset of SPs, with duration measured in ms from the onset to the end of the SPs, and amplitude of the late SP (SP2) measured as a percentage of the early SP elicited by the single electrical and magnetic stimulus. *(2)* For the MIR recovery curve, the area of the late SPs elicited by the second stimulus (test) was compared with the area of the late SPs of the first stimulus (unconditioned), with 100% considered as reference.[30] The area was calculated offline with Dantec software (Keypoint Medtronic), utilizing the integrated values of the rectified and averaged EMG signals between the onset and offset markers of the 2 SPs.

At the end of the assessment, each subject was asked to evaluate the level of pain of the 2 methods on a visual analog scale (VAS) in which 0 represented absence of discomfort; 5, presence of pain; and 10, nontolerability of the stimulation. The data are presented as means ± SD or as confidence limits around the respective means, ie, surrounded by standard error intervals, computed at 5% or 1%.

The study protocol was approved by the local ethics committee and, in accordance with the Declaration of Helsinki, written informed consent for the neurophysiological evaluation was obtained from each patient.

Statistics

The onset latency and amplitudes of the MEPs, the latency and duration of the SPs of the MIR obtained from both left and right masseter, and the recovery curve of the MIR evoked by electrical and magnetic stimulation were compared by means of an analysis of variance—repeated measures (ANOVA-RM) procedure, taking into account the multiple time intervals and employing the Bonferroni correction. The results of the TMS data were compared between the 2 groups of subjects by an ANOVA "between" factor analysis. The differences in SP2 (by single stimulus) presence between the 2 groups were calculated with the nonparametric Fisher exact test. Since the correlation between interstimulus interval (ISI) and size of the test SP2 is logarithmic to the base 10,[30] data obtained with magnetic stimulation were linearized by logarithmic transformation and compared between the 2 groups. The statistical significance threshold was set at an α-error level of 0.05 (2-tailed test), while the β-error was held within 0.1. For the magnetic stimulation data processing in particular, a power test of approximately 95% was performed. Statgraphics (STSC) and Systat packages were employed for statistical processing.

Results

The comparison between the data obtained from the right and left masseters did not show any statistical difference ($P > .05$) for either the MEP or the MIR for all subjects. Therefore, to simplify the results, only the data from the right masseter muscle were considered. In order to reduce the stimulus artifact in the MIR evoked by the electric stimulus, only the data obtained by stimulation of the left mental nerve were used. The prolonged jaw-closing muscle contraction necessary to perform the neurophysiologic tests gave only rare discomfort to patients and normal subjects, with no evident differences between the 2 groups in terms of frequency, intensity, or duration. Relatively high discomfort that necessitated a prolonged suspension of the evaluation was reported in 4 of 26 patients (1 for 35 minutes, 2 for 10 minutes, 1 for 5 minutes), and 3 of 31 control subjects (all for 10 minutes). In all other subjects, the masticatory muscles were relaxed for between 20 and 60 seconds between each recording.

The results of the TMS are shown in Table 1. There were no statistically significant differences between the patients and the normal subjects for any

Table 2 Unconditioned Early SP (SP1) and Late SP (SP2) of the MIR Evoked by Magnetic and Electrical Single Stimulation

	Normal subjects (n = 31)		Patients (n = 26)	
	M	E	M	E
SP1 latency (ms)	12.8 ± 2.5	12.2 ± 1.6	12.4 ± 3.1	12.1 ± 2.7
SP1 duration (ms)	18.7 ± 2.7	18.9 ± 2.9	19.1 ± 4.4	18.9 ± 4.2
SP2 latency (ms)	49.5 ± 7.2	47.3 ± 6.5	48.6 ± 5.9	50.2 ± 4.1
SP2 duration (ms)	39.0 ± 10.6	39.5 ± 11.5	36.6 ± 9.8	40.2 ± 9.5
SP2 amplitude (%)*	98.8 ± 6.2	99.2 ± 3.3	93.8 ± 11.7	99.0 ± 3.0

No statistical differences were found between the 2 groups. Means ± 1SD shown.
M = magnetic, E = electrical.
*SP1/SP2.

Table 3 Recovery Curve of the MIR: Means and Confidence Limits of the Percentage of the Test SP2 Evoked by Magnetic and Electrical Paired Stimuli

	Normal subjects (n = 31)		Patients (n = 26)	
ISI (ms)	M	E	M	E
100	13.9 ± 9.0	42.9 ± 9.2	8.7 ± 9.6	18.7 ± 8.2
200	54.9 ± 12.6	64.2 ± 11.0	28.3 ± 13.0	43.8 ± 10.2
300	78.3 ± 14.7	83.8 ± 8.8	39.0 ± 15.9	61.3 ± 9.3
400	90.3 ± 12.3	97.3 ± 6.4	48.7 ± 13.2	73.8 ± 6.6
500	96.8 ±12.9	98.6 ± 6.0	56.5 ± 13.8	84.8 ± 6.0
600	98.9 ± 12.2	100.9 ±6.4	72.7 ± 12.8	84.3 ± 6.4

of the parameters (active motor threshold, latency, or amplitude of the MEP, or CCT) of the MEP.

The intensities of the electrical and magnetic stimuli evoking the MIR were the following: mean 22.7 ± 7.8 mA for electrical stimuli and 35.9% ± 5.4% maximum output of the magnetic stimulator for the patients and 20.5 ± 5.3 mA and 36% ± 4.8%, respectively, for normal subjects. A definite inhibitory reflex composed of the 2 SPs was evoked in 26 of 30 patients. In 4 patients (13%), the SP2 was inconstant or incomplete; these data were excluded from the analysis. A late SP was observed in all normal subjects. This difference in the frequency of absence of the late SP between SB patients and normal subjects was not significant ($P = .053$, Fisher exact test). The differences in the electrical and magnetic stimulus intensities between the 2 groups also did not reach statistical significance ($P > .05$), and there were no significant differences for either type of stimulation between the 2 groups or between different sessions in the same subjects. The onset latencies, durations, and amplitudes of the SPs obtained by the 2 types of stimulation, both in patients and in normal subjects, are reported in Table 2.

The paired stimuli technique was used to determine the MIR recovery curve. The test late SP varied according to the ISIs and revealed a similar trend between the 2 methods of stimulation in normal subjects (Table 3, Figs 1 and 2), with a complete recovery by approximately the 400-ms ISI. In contrast, the late SP was significantly reduced in the patients ($P < .01$ at almost all ISIs for magnetic stimulation and $P < .05$ at all ISIs for electric stimulation). The patients did not show complete recovery of the test SP2, not even at long ISIs (600 ms) (Table 3, Figs 1 and 2), and the slope of the logarithmic-scale curves obtained with magnetic stimulation was significantly lower ($P < .01$) in the patient group (0.76) than in the control group (1.11) (Fig 3). In patients, the 2 types of stimulation also produced a different degree of suppression at ISIs between 100 and 500 ms ($P < .05$): the magnetic stimulus produced a greater degree of suppression at these ISIs, while at 600 ms the percentage area of the test SP2 was not significantly different between magnetic and electrical stimulation ($P > .5$) (Fig 3). In patients, the 2 types of stimulation produced a different degree of suppression at ISIs between 100 and 500 ms ($P < .05$): the magnetic stimulus produced a greater degree of suppression at these ISIs, while at 600 ms the percentage area of the test SP2 was not significantly different between magnetic and electrical stimulation ($P > .5$) (Table 3).

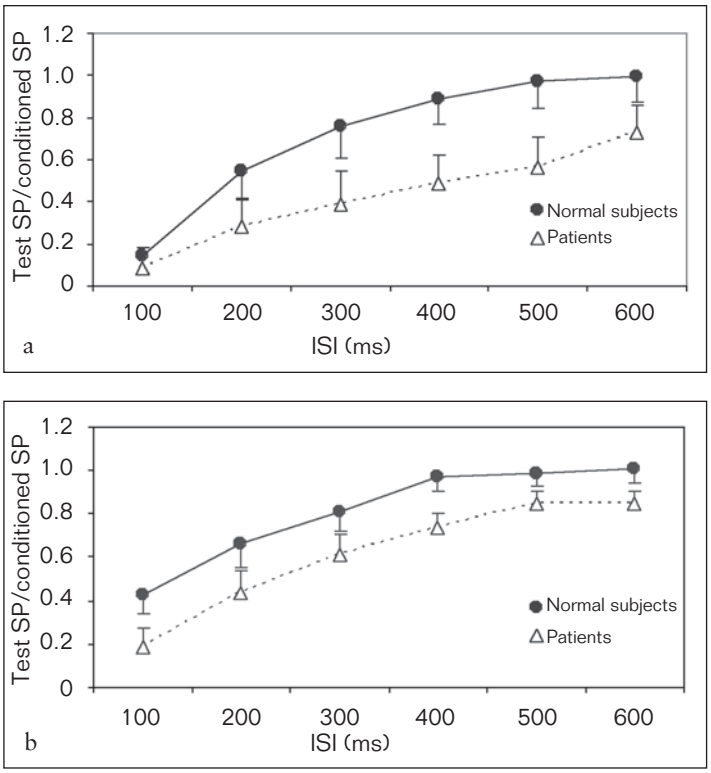

Fig 1 Graph of the recovery function of the MIR elicited by *(a)* magnetic (1% confidence interval) and *(b)* electrical stimulation (5% confidence interval) in patients and normal subjects. The y-axis is the area of the SP2 evoked by the second stimulus (stimulus test) expressed as percentage of the unconditioned response evoked by the first stimulus. Values obtained by magnetic stimulation showed a high statistical difference between the 2 groups at an ISI of 200 to 600 ms ($P < .01$). Values obtained by electrical stimulation differed significantly for the 2 groups at all ISIs ($P < .05$).

All normal subjects and patients expressed significantly greater subjective tolerability for magnetic as compared to electrical stimuli. Mean VAS scores for electrical and magnetic stimulations in normal subjects were 5.5 ± 1.2 and 3.3 ± 1.2, respectively. Mean VAS scores in the patients were 5.3 ± 2.2 and 2.9 ± 2, respectively ($P < .01$).

Discussion

This study employed the TMS-evoked MEPs and recordings of the MIR and its recovery curves to evaluate the function and the excitability of the central jaw motor pathways in awake subjects with signs and symptoms suggestive of SB. These neurophysiological methods have previously been employed together to study the excitability of the trigeminal motor system.[13] The present study used a magnetic peripheral stimulus to provide further original data on the effects of exciting non-nociceptive afferent fibers.[14]

Limitations of the Study

The main limitation of this study was that sleep recording was performed only in 3 subjects to confirm the diagnosis of SB, although in the other cases the clinical examination and interview clearly suggested a diagnosis of SB. Neurophysiologic differences found between normal subjects and the putative SB patients warrant future investigations with a more accurate selection of the patients through sleep ambulatory recordings, with the aim of revealing in confirmed SB patients individual or general correlations between the different neurophysiological

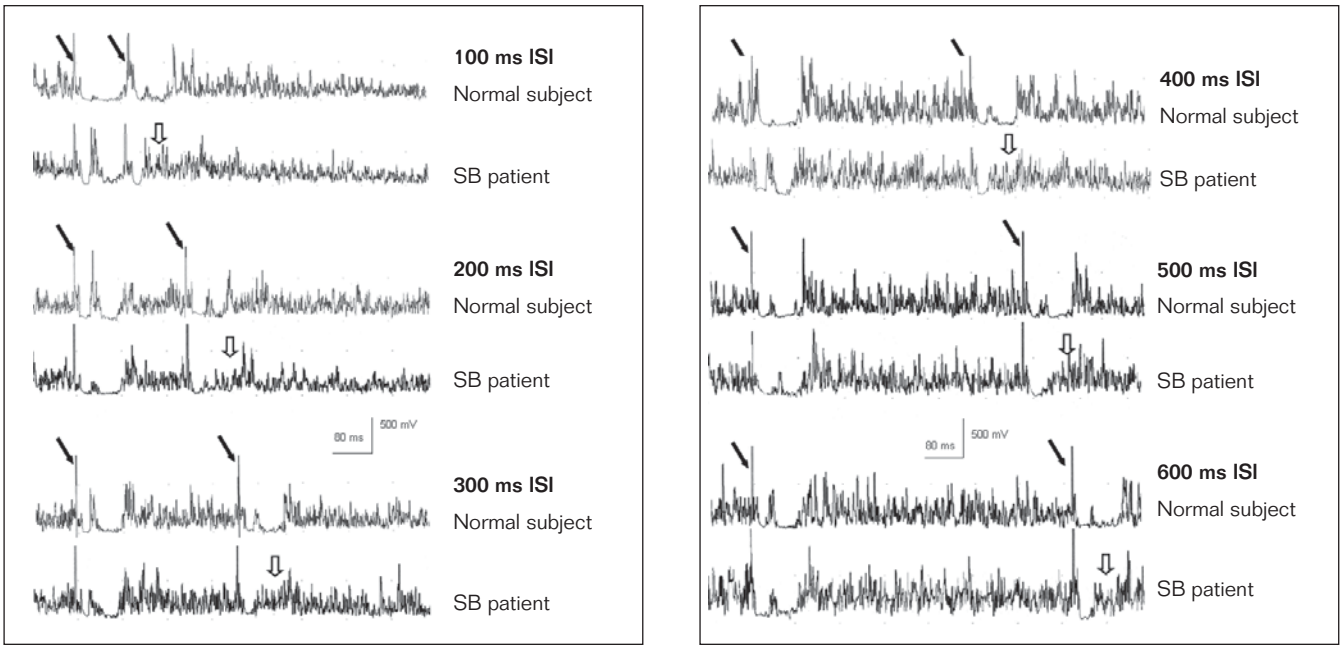

Fig 2 Comparison of the recovery curve of the MIR elicited by magnetic stimulation and recorded in right masseter between a normal subject and a patient. Note the absence of the conditioned SP2 at all ISIs in the patient. The black arrows indicate the stimulus artifacts. The white arrows indicate the hypothetical location of the test SP2.

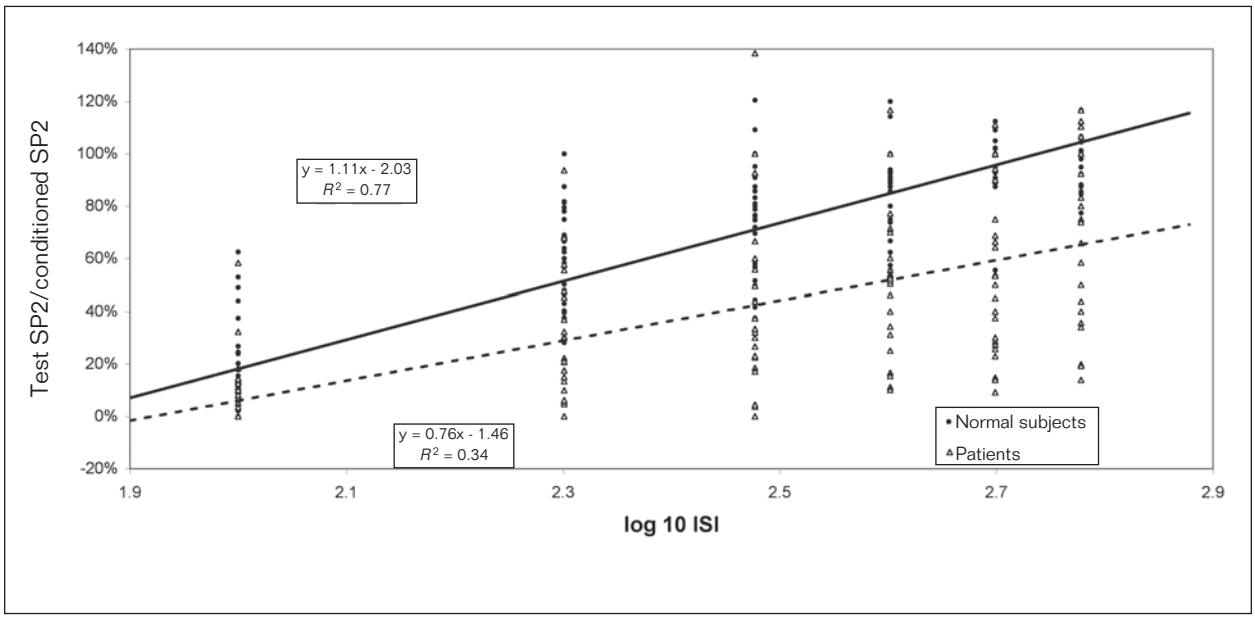

Fig 3 Graph of the recovery function of the MIR elicited by magnetic stimulation in patients and in normal subjects. The y-axis is the area of the test SP2 expressed as percentage of the unconditioned response. The x-axis shows the ISIs (100 to 600 ms) in logarithmic scale. The difference in slopes of the lines (1.11 versus 0.76) was statistically significant ($P < .01$).

parameters (ie, jaw clenching, repetitive phasic jaw muscle activity, and degree of recovery of the MIR). Another limitation was the assessment of the trigeminal motor system parameters in awake subjects. While it would have been interesting to measure trigeminal motor excitability during sleep in the patients, these tests (both TMS and MIR) cannot be used while the subject is asleep, as voluntary contraction of the jaw-closing muscles is required.[16–18] However, a study of a condition related to SB which also occurs at night, the primary restless legs syndrome, was performed with TMS in awake patients. The study revealed the presence of an altered excitability of central motor pathways, supporting the view that the periodic leg movements result from a sleep-related disinhibition of descending central motor inhibitory pathways.[31] Furthermore, the authors are confident that the difference between the recovery curves of the MIRs of the patients and normal subjects did not derive from technical bias. Many factors can modify the SP and its recovery curves. In particular, higher clenching levels tend to reduce SP2 duration,[32] whereas higher stimulation intensities increase it.[33] In order to minimize these factors, the level of clenching was monitored and kept stable. The intensities of both the electrical and the magnetic stimuli were similar in patients and in normal subjects and resulted in equivalent subjective measures (VAS). Particular attention was paid to the subjects' feelings throughout the examinations in order to reduce other conditioning factors that influence the inhibitory trigeminal reflexes, such as levels of attention, levels of arousal, presence of discomfort, nociceptive and non-nociceptive afferent inputs.[32,34–40]

Main Findings

The use of TMS permits an evaluation of the functionality of the trigeminal motor system at the cortical level. The necessity for voluntary muscle contraction in order to elicit MEPs could mask a change of cortical excitability. However, the low TMS intensities used to assess the MEP threshold likely activate the so-called I-waves, due to indirect or trans-synaptic activation of corticobulbar axons, therefore allowing the identification of possible variations in cortical excitability.[25]

Thus it can be concluded that the absence, in the present study, of any MEP alteration, either in terms of amplitude, latency, or CCT of the MEP, or in the active motor threshold, indicated a normal function of the corticobulbar tract in the putative SB patients and the absence of any subclinical pathology or alteration of the excitability of the cortical motor system in bruxism.

Consequently, the cortical motor control of the masticatory system does not appear to be directly involved in pathophysiology of SB, at least when evaluated with TMS. Furthermore, the absence of any alteration of the early SP of the MIR on either side evoked by a single electrical or magnetic peripheral stimulus in the patients indicates that the afferent fibers, the neuronal brainstem circuits responsible for the MIR, and the efferent masseteric fibers were undamaged.[17,41] In response to a question expressed by Bader and Lavigne,[10] this study suggests that chronic and severe SB (as reported by the patients in the present study) cannot induce localized neuropathies secondary to microtrauma in the third branch of the trigeminal nerve. Moreover, the absence of any significant differences between normal subjects and patients in the stimulus intensities and subjective sensations indicate that the perioral sensory acuity during wakefulness in SB patients is normal.[42] This seems to exclude any different sensibility or a higher tolerance for pain.[10]

The absence of SP2 in 4 of 30 patients, and its presence in all normal subjects, is noteworthy, since another study that used the MIR in SB and TMD patients[43] showed that SP2 was absent in SB patients and was smaller or absent in patients with myogenous pain. That study, however, used mechanical tooth stimulation to evoke the MIR, which probably excited different pathways compared to electrical or magnetic peripheral stimulation. Nonetheless, these results indicate a reduced capacity for inhibition by the circuits responsible for the SP2 in SB, which is consistent with the data from the present study.

Regarding the recovery curve of the MIR, it is important to note that the neural mechanisms underlying SP2 are probably mediated by A-beta afferents[44] that reach the spinal trigeminal tract and activate a polysynaptic chain of interneurons that, through ipsilateral and contralateral collaterals, inhibit masseteric motoneurons.[16,29,45–47] The afferent inputs, both nociceptive and non-nociceptive, converge onto neurons in subnucleus caudalis and in the more rostral part of the trigeminal brainstem complex.[48–51] In the present study, the recovery of the test SP2 was reduced in the patients at all ISIs, with both types of stimulation, which might have occurred because of a reduction of the excitability of lateral reticular interneurons at the ponto-medullary level,[22] reducing in turn the activity of the last inhibitory interneuron and consequently giving a reduced degree of suppression

of the MIR at all ISIs. In other words, this finding might indicate that the inhibitory circuits to the trigeminal motoneurons are less excitable in SB patients than in normal subjects, but this would require more detailed study.

The higher statistical significance of the MIR data obtained with magnetic stimulation in comparison to the MIR data obtained with the electrical stimulation could be explained by a more specific contribution of non-nociceptive neurons to the reduced excitability of the inhibitory circuits in SB. While the electrical stimuli could activate both nociceptive and non-nociceptive afferent fibers,[52] it is probable that the low-intensity magnetic stimulus depolarizes only the large sensory axons,[53] accounting for the lack of reported pain and the subjective difference of the perceived stimulus between electrical and magnetic stimuli.

How might these results be relevant to the understanding of SB? SB appears to be a sleep-related disorder that can be considered to represent an increased arousal-associated motor response.[54–56] This altered responsiveness could be mediated by an increase of the excitability in the jaw motor system that in turn could lead to an increased incidence and strength of the spontaneous rhythmic masticatory muscle activity (RMMA) following the microarousals during sleep in healthy subjects. The reduced degree of suppression of the MIR recovery curve, ie, the reduced excitability of an inhibitory pathway to the jaw-closing muscles, could be the basis of the enhanced excitability of this motor system. This model is complementary to the "bruxism generator model" formulated by Lavigne and Montplaisir[12] in which SB is seen as an exaggerated expression of normal sleep-related orofacial motor behavior (ie, RMMAs) where several factors increase jaw muscle activity, leading to a pathophysiologic condition.

Since the results of the present study are not explained by peripheral factors, which central structure could be responsible for the increased motor neuronal excitability? The jaw motor system is highly complex and includes the cerebral cortex, basal ganglia, thalamus, limbic system, and various midbrain structures related to the modulation of sensory, autonomic, and emotional functions,[25,34,39,40] such as reticular formation, periaqueductal grey matter, nucleus raphe magnus, and anterior pretectal nucleus.[16,29] The absence of any cortical change in excitability indicated in the present study suggests the involvement of subcortical structures. This hypothesis is consistent with findings in humans and animals of correlations between bruxism and substances linked to the dopaminergic, serotoninergic, and adrenergic systems.[11,57–59] The neural network involved in the modulation of the SP2 is influenced by the basal ganglia and the limbic system,[22,37] and the present results might be explained by modifications at this level that in turn result in an enhanced responsiveness of the trigeminal motor system to the arousals during sleep that participate in the genesis of SB.

Conclusions

Despite the limitations of this study made in awake subjects with signs and symptoms suggestive of SB, the data are consistent with the view that various groups of interneurons are able to modulate the trigeminal motor system. In particular, the data suggest the presence of a group of interneurons receiving peripheral non-nociceptive information that can be centrally modulated, probably by subcortical structures, eg, the basal ganglia, limbic system, and sympathetic nervous system. The results support the view of a central genesis of bruxism, characterized by an alteration of the excitability of this group of interneurons. This alteration could increase firing probability in trigeminal motoneurons during sleep arousals and cause the excessive jaw muscle contractions characteristic of bruxism. These interneurons receive inputs from the motor cortex, the basal ganglia and the limbic system. In addition, from a clinical standpoint, even though SB patients do not show a completely homogeneous behavior, the neurophysiological methods used in this study may be helpful in the diagnosis of SB by excluding any neurological alteration of the trigeminal motor system and by demonstrating hyperexcitability at the subcortical level of the system.

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