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Migraine and Tension-Type Headache Reduction Through Pericranial Muscular Suppression: A Preliminary Report

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ABSTRACT: Migraine and tension-type headaches have always plagued mankind. In spite of all the research dollars spent trying to determine the etiologies of these headaches, the neurology community still has not established a known cause of migraine and tension type headaches. This paper describes a study that was conducted for the U.S. Food and Drug Administration in which the efficacy of the Nociceptive Trigeminal Inhibition Tension Suppression System was evaluated and proved safe and efficacious in the reduction of medically diagnosed migraine and tension-type headache.

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No one denies the impact that migraine and chronic tension-type headaches have upon human suffering and annual financial expenses. Migraines affect one in five females and one in twenty males.¹ While precise estimates vary depending upon the study, lost productivity estimates for the United States work force average each year from \$6.5 to \$17.2 billion.² Perhaps more striking is the estimated annual cost of a migraineur to his or her employer. These costs range from \$5256 to \$6864 per man and \$3168 to \$3600 per woman.² The American Migraine Study³ estimated that 23 million persons twelve years and older suffered with severe migraine headaches and yet, this condition is under treated and under diagnosed world-wide.¹ Whatever the precise numbers, migraine is certainly responsible for millions of sick-days and reduced productivity per year and billions of dollars in medical costs.^{3,4}

Epidemiological data are more difficult to obtain for tension-type headaches simply because the neurological community itself cannot agree on the precise classification of this painful disorder. Many neurologists contend that tension-type headache is nothing more than migraine variant. They base this line of reasoning on the fact that epidemiological studies have failed to identify specific features, especially biochemical differences that could distinguish tension-type headaches from migraines. After great controversy, the *International Headache Society's* classification of headache pain agreed upon the name tension-type headache for what had previously been called tension headache, muscle contraction headache, stress headache, and the ordinary headache.⁵

Migraine and severe tension-type headaches are not limited to adults. The prevalence in children increases from 39% at age 6 to over 70% by age 15. In addition, more than one million days of missed school can be directly attributed to these types of headache pain.⁶

Perhaps even more confusing than the estimated epidemiology of these headaches is the voluminous list of proposed causes of migraine and tension-type headaches. Initially described in the first century A.D. by Aretaeus of Cappadocia,⁷ the causes of migraine headaches have been studied ever since and yet, the exact etiology and pathophysiology are still unknown and the sources of great debate. Although the skin, blood vessels and muscles of the scalp are pain-sensitive, the brain itself (except for large venous sinuses, meningeal arteries and large cerebral arteries) is basically pain-insensitive,⁸ yet migraine and tension-type headaches do exist. If most of the mass of the brain is absent of nociceptive receptors, then what might be the cause or causes of these debilitating headaches? Might the pain originate elsewhere?

For years, and until just recently, anatomists and neurologists have maintained that migraine pain is primarily due to cerebral ischemia from vasoconstriction as the initial event and that the headache pain is a result of intracranial vasodilatation.⁹ However, Olesen and colleagues¹⁰ demonstrated that vasoconstriction theory was not necessarily true. Another prominent theory, the neurogenic or neurovascular theory,¹¹⁻¹⁴ proposes that migraine and tension-type headaches are caused by a disturbance in brain function. According to this theory, dilatation of blood vessels triggers the trigeminal system, producing further vasodilatation. The trigeminal system activates the hypothalamus, causing photophobia, phonophobia, and tightening of the muscles in the head and neck. Although the neurogenic theory is widely accepted today, very little is still known about the actual cause of migraine and tension-type headaches.

Genetic disorders,¹⁵ weather changes,¹⁶ underlying vascular diseases (stroke, hypertension, seizures, etc.),¹⁷ hormonal changes,¹⁸ and other central mechanisms¹⁹ all have been suggested as viable causes of migraine and tension-type headaches. However, recently, and in increasing numbers, reports are entering the scientific literature alluding to one probable cause which may be the development of sustained trigger points in the pericranial and orofacial musculature.^{8,20-30}

Perhaps of more interest to the readers of this journal article is the fact that many researchers have implied that these trigger points are produced by the mandibular parafunctional activity of bruxism³¹⁻⁴³ and this itself may be a major etiologic source of migraine and tension-type headaches. More specifically, many researchers believe

the trigger points actually develop by an over-activity of post ganglionic sympathetic nerves within the muscles of mastication.⁴⁴⁻⁵⁰

Of even further interest is the acknowledgement of pericranial tenderness found in migraine and tension-type headache sufferers. Lous and Olesen reported the presence of pericranial muscle tenderness upon palpation in all headache groups (migraine, tension-type, and mixed migraine/tension-type) and absent in all controls,²³ while Clark recorded the intensity of nocturnal temporalis contraction episodes to be fourteen times greater in tension-type headache patients than in asymptomatic controls.⁵¹ In an attempt to directly reduce the influence of the pericranial musculature, periodic injection of Botox is now being observed as a possible modality for the reduction of migraine. In a double-blind, vehicle-controlled study of 123 subjects with a history of two to eight moderate-to-severe migraine attacks per month, pericranial injection of botulinum toxin type A, 25 U, was found to be a safe treatment that significantly reduced migraine frequency, migraine severity, acute medication usage, and associated vomiting.⁵²

In this article, a recent study, conducted under the supervision of the U.S. Food and Drug Administration (FDA) (Study #K981546), exploring the effects of a new intraoral device, the Nociceptive Trigeminal Inhibition Tension Suppression System (NTI-ss) (NTI-TSS, Inc., Mishawaka, IN) whose specific design is to suppress the intensity of parafunctional pericranial muscular activity, will be described. Data collected and results of using this device will be presented and a probable connection between bruxism and the development of migraine and tension-type headaches proposed.

Material and Methods

The primary objective of this FDA study was to evaluate the safety and effectiveness of the intraoral Nociceptive Trigeminal Inhibition Suppression System (NTI) device for the reduction of frequency and severity of tension-type and migraine headaches, as compared to the known efficacy of the non-commercially available full coverage occlusal splints.

To participate in the study, subjects had to adhere to the following criteria, all of which were determined by the FDA:

1. Diagnosed by a physician, according to the classification of headaches of the International Headache Society, within the last twelve (12) months with tension-type or migraine headaches;
2. Taking sumatriptan as a rescue medication;
3. Have experienced an average of two migraine

- episodes and eight tension-type headaches per month;
4. Have the presence of natural or fixed prosthetic maxillary and natural mandibular anterior incisors;
 5. Exhibit an overbite and overjet within normal limits;
 6. Have stable dentition with no current orthodontic treatment and fully erupted teeth (excluding third molars);
 7. Have no significant periodontal disease or signs and/or symptoms of temporomandibular disorders; and
 8. Be at least 18 years of age.

Baseline data collected consisted of diagnostic opposing study models with an interocclusal record, measurement of tooth mobility and sensitivity (temperature, pressure, contact by dental explorer to the cementoenamel junction) of all maxillary and mandibular anterior teeth, full periodontal charting of all teeth, anterior maxillary and mandibular periapical radiographs, and vitality testing of all maxillary and mandibular anterior teeth.

In addition to the comprehensive dental examination, each subject underwent an extensive examination of the head and neck musculature to record any pericranial, neck, or cervical tenderness. Trigger points (areas of hyperactivity, that, when compressed, are tender at the site and, if sufficiently hypersensitive, give rise to referred pain⁵⁴) were identified simply to verify pericranial muscle tenderness, a common characteristic with chronic headache sufferers. Also, an examination of the temporomandibular joint, including measuring ranges of motion of the mandible and recording any joint noises and tenderness, was performed. Any subject exhibiting a temporomandibular disorder was not included in the study.

Participants in the study were required to keep a daily log for four weeks (to create baseline data) prior to being randomly assigned to one of two groups: control or experimental. A visual analog scale (VAS) was used to report the presence or intensity of head pain three times per day (upon waking, midday, and evening before bedtime) and percentage of waking time with a headache during the previous 24 hours.

Specifically, each study participant recorded:

1. The presence or absence of tension-type headache and VAS to record the intensity;
2. The presence or absence of migraine headache and VAS to record headache intensity;
3. Presence or absence of nausea, photophobia, or phonophobia;
4. Analgesics taken and dosages; and
5. The use of rescue medication sumatriptan.

In addition, during the 8-week treatment phase of the study, each participant also recorded (three times daily)

the degree of compliance (of wearing an appliance) and any adverse events.

At the completion of the four-week pretreatment period, 94 participants were randomly assigned to either the control or experimental group. Sex differences were not monitored as the FDA did not require nor feel these data were required. The experimental group consisted of 51 individuals, 43 were in the control group. For comparison purposes, a full-coverage occlusal splint (similar to a bleaching tray) made of 0.02-inch acrylic was used as a control appliance (in lieu of attempting to provide an intraoral placebo device that could be confirmed to have no intraoral influence on the musculature). Since Lamey had shown that a full-coverage occlusal splint reduces migraine by 40%,⁵⁴ this study chose to gauge the efficacy of the NTI-tss against the known efficacy of the full coverage occlusal splint (and to simultaneously confirm that Lamey's findings were reproducible). This appliance was fabricated in centric occlusion and did not add any additional determinates of occlusion (e.g., cuspid disclusion and/or anterior guidance). It was made, as much as possible, not to interfere with the subjects' existing occlusion. Participants were instructed to insert and wear their device when sleeping and as required during perceived stressful times during the day, for eight consecutive weeks. All baseline data were re-collected following the eighth week of the study and six months after the completion of the clinical trial.

The experimental group (n=51) was given an NTI-tss (Nociceptive Trigeminal Inhibition Tension Suppression System device). This preformed appliance is filled with autopolymerizing acrylic and placed directly over the two maxillary central incisor teeth. After two minutes, the appliance is removed from the mouth, trimmed, and custom fit to the two anterior teeth. The flat disclosing element of the appliance permits a one-point contact of the mandibular anterior teeth (usually, the two central incisors). It was worn each time the subject slept and placed into the mouth when the subject was under increased stress and/or felt that conditions for a headache might be starting.

Results

As is customary when observing the effect of a prophylaxis method of reducing migraine and tension-type headache, at least a month of use is allowed to lapse before an effect (if any) can be realistically observed. The results of the data derived from eight weeks of the study are found in **Table 1** and **Figures 1-7**. Note that in every category, the percentage of reduction of all symptoms decreased for those in the experimental group.

Table 1
Data Obtained Following Eight Weeks of Prophylaxis Use

Description	Percentage reductions of listed symptoms		
	Control	NTI-tss	p-level*
Migraine episodes	38.1†	61.9	<.05
Tension-type headache episodes	15.0	37.3	<.05
All headpain episodes	25.1	46.9	<.01
Imitrex use	17.6	46.8	<.01
Frequency of head pain (% of day with head pain)	14.6	35.3	<.01
Intensity of had pain	23.7	36.9	<.06
Phonophobia	-1.6	68.4	<.002‡
Nausea	40.4	78.0	<.01
Photophobia	22.8	65.6	<.01

*P values calculated for "Substantial equivalence" [Blackwelder WC: Proving the null hypothesis in clinical trials. *Controlled Clinical Trials* 1982;345-353; Laser LL: The "at least as good as" criterion: sample size requirements. *J Dent Res* 1995; 74 [Special Issue]: Abstract 299.

†Consistent with Lamey study which had shown a 40% reduction.

‡Statistically superior.

In addition to those data presented above, the following observations were also made during this study:

1. 16% of NTI-tss users reported an 85-100% reduction of migraine events.
2. Seven percent (7%) of full-coverage splint users reported an 85-100% reduction of migraine events.
3. Twenty-seven percent (27%) of full-coverage splint users reported an average 46% increase in migraine

events following the second month of use, which was twice their reported increase in the first month. Their migraine frequency was increasing.

4. Eleven percent (11%) of NTI-tss users reported an average 12% increase in migraine events following the second month, which was one-half of their reported increase in the first month. Their migraine frequency was decreasing.

Average Migraine Headaches

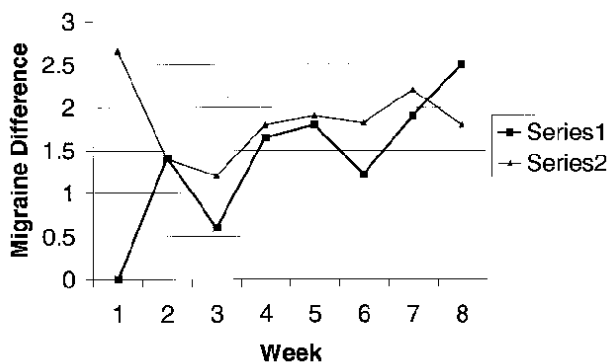


Figure 1
Average reduced number of migraine events per month.

Non-Migraine Headaches

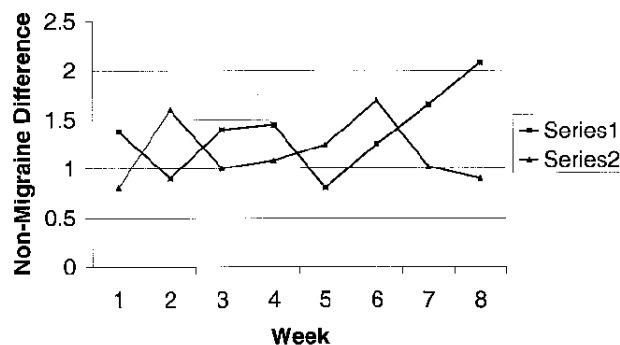


Figure 2
Average reduced number of tension-type headache episodes per month.

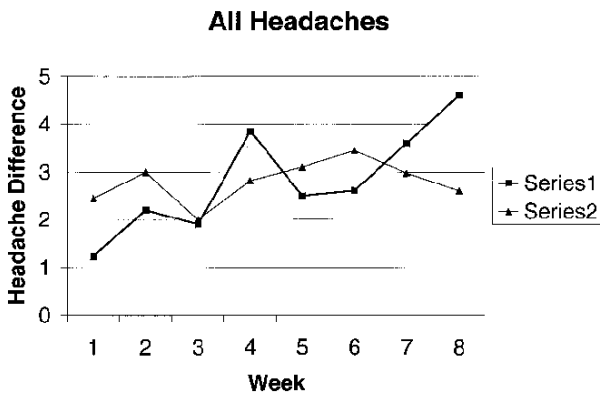


Figure 3
Average reduced number of all headache episodes per month.

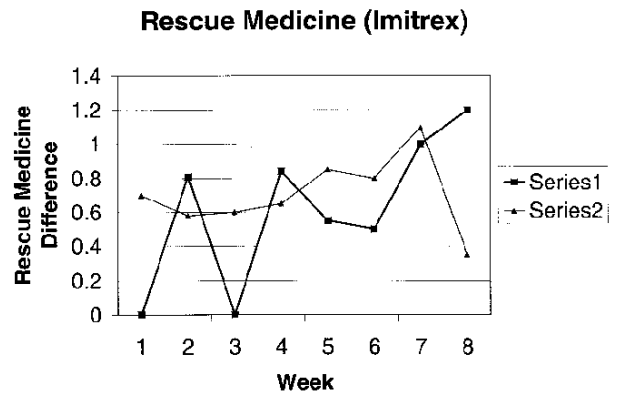


Figure 4
Average reduced Imitrex dosages per month.

Discussion

Boyd, et al. describe bruxism as a function of clenching.⁴⁴ The intensity of clenching dictates the severity of grinding, or lateral movement of the mandible with the teeth in contact, produced by the inferior belly of the lateral pterygoid muscles. There is no grinding unless the jaws are first clenched to some degree. As the clenching intensity increases, resistance to lateral mandibular movement increases and the lateral pterygoids' ability to

move the mandible laterally decreases or is prevented. Hence, only intense clenching can then occur.

With this in mind, realize that the precise etiology of migraine and tension-type headaches is not known, although the scientific data seem to indicate a neurovascular mechanism in combination with stimulation of the trigeminal system and sympathetic nerves innervating the muscles of mastication, neck and cervical muscles.¹¹⁻¹⁶ According to this theory, a trigger prompts a chemical change in the dorsal raphe and locus ceruleus, leading to

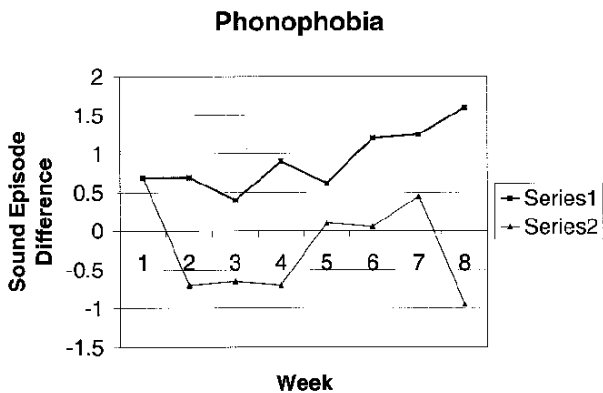


Figure 5
Average reduced number of nausea episodes per month.

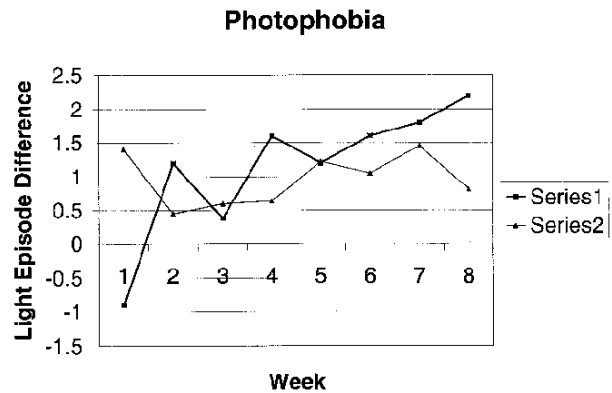


Figure 6
Average number of reduced photophobia episodes per month.

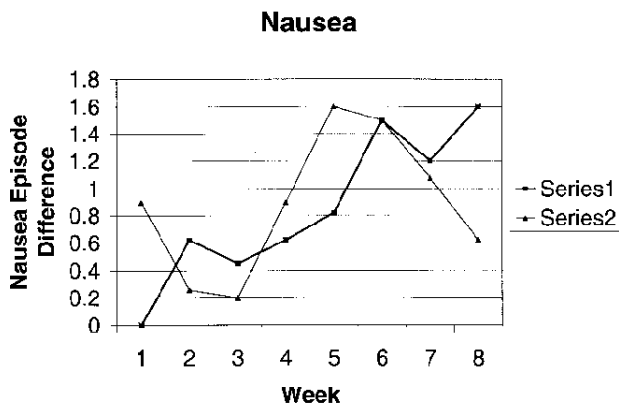


Figure 7
Average number of reduced phonophobia episodes per month.

release of serotonin and norepinephrine respectively. Currently, there is only slight evidence of serotonergic fibers existing in the muscles of mastication.⁵⁵ However, there is no question about the presence of postganglionic sympathetic fibers, which innervate the muscle spindles of these same muscles, using norepinephrine as the neurotransmitter.

Circulating in the blood are catecholamines (norepinephrine and epinephrine), which are excreted from the adrenal cortices. Among other functions, these neurotransmitters activate the sympathetic and parasympathetic muscle spindles within the muscles of mastication, the cervical musculature, and pericranial musculature (**Figure 8**).

The muscle spindles within these mandibular postural muscles that oppose gravity (i.e., the temporalis, the masseter, the zygomandibularis⁵⁶ and the sphenomandibularis⁵⁷) and the cervical muscles, primarily the trapezius, maintain a normal muscle tonus. In those who suffer with migraine and tension-type headaches, these muscles appear to be chronically hypersensitive, often due to chronic parafunction (made possible by the resistance provided by intense jaw clenching).

Headache sufferers are affected by various triggers (e.g., stress, hormonal changes, over-activity, petrochemicals, alcohol, food additives, etc., which can stimulate the sympathetic nervous system) more than non-headache patients. Both migraine and tension-type headaches require a trigger,⁵⁸ and bruxism is known to heighten the sensitivity to such triggers, as well as being a trigger itself,⁵⁹⁻⁶² but by what mechanism?

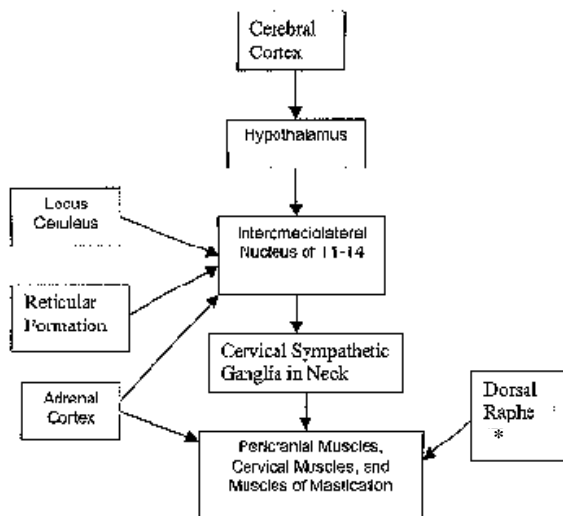


Figure 8
A diagram representing a normal or homeostatic relationship concerning pericranial, neck, and orofacial muscles.*Probable but not proven.

Clenching, acting in some persons as a trigger, produces an increase in norepinephrine release into muscle spindles and vasoconstriction,⁶²⁻⁶⁷ thus increasing muscle fiber contractions,^{68,69} producing isolated hypersensitive regions, or trigger points.⁷⁰ In addition, if one is stressed, additional norepinephrine is released from the adrenal cortex.⁷¹ Further, as the level of norepinephrine in the blood increases, the cervical sympathetic ganglia are stimulated,⁷² producing even more norepinephrine release at the muscle spindle.

This complex cascade of events, produced by a trigger, causing an increase in circulating and localized norepinephrine, can, according to the neurovascular theory, generate a headache. Depending upon the pain intensity (viz, the number of muscle spindles recruited in clenching and sensitized by norepinephrine), either a tension-type headache or migraine develops.⁷³

Adding to the intricacy of these local and systemic events, the central nervous system plays an important part. Responding to various stressors influencing the cerebral cortex through the hypothalamus, the locus coeruleus responds by producing norepinephrine at spinal cord levels, stimulating the sympathetic nervous system (i.e., ultimately, the pericranial muscle spindles). In addition, serotonin, synthesized in the dorsal raphe nucleus and recently implicated in enhanced masseteric contraction,²³ is elevated during stress (**Figure 9**). For years, dentists have attempted to treat headaches by using vari-

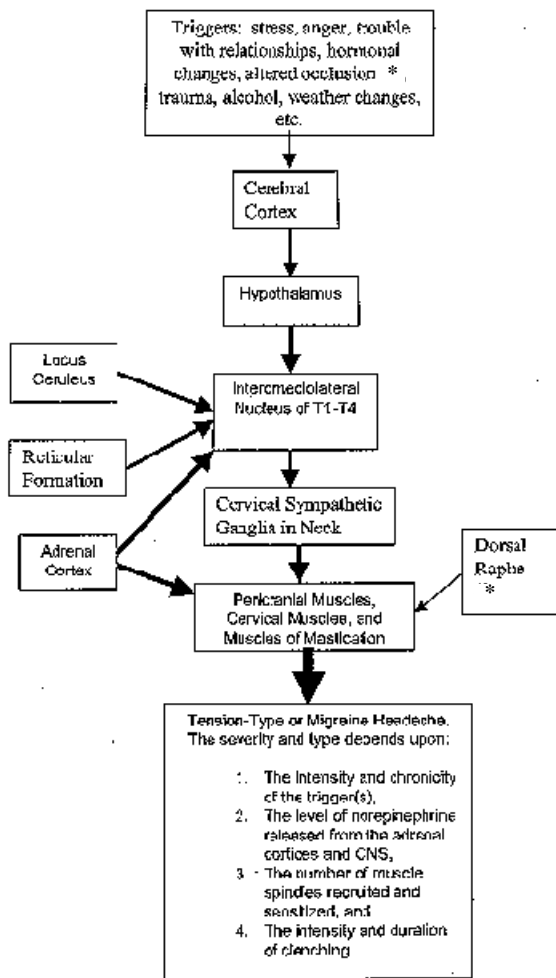


Figure 9
A proposed diagram representing the cascade of events, coupled with clenching, which ultimately can lead to either a tension-type headache or migraine headache. *Probable but not proven.

ous types of intraoral splints. For headaches alone, success has been marginal at best⁷⁴⁻⁸² especially for tension-type headaches.⁸³ Most likely, these flat plane appliances provided more surface on which the bruxer could clench more efficiently, increasing norepinephrine release, thereby producing more pericranial muscle pain.

The NTI-tss appliance, on the other hand, provides only an anterior midline contact or stop (thereby providing no occluding surface for the posterior or canine teeth in any mandibular position, which is required to generate intense clenching⁵⁵) and actually enacts the jaw opening reflex (Figure 10), prohibiting the generation of maximum clenching forces of the elevator muscles. This reflex, the first to develop in the neonate, is stimulated by the anterior point contact of the NTI (Figures 11 A and B and 12). This simple, yet elegant function reduces the

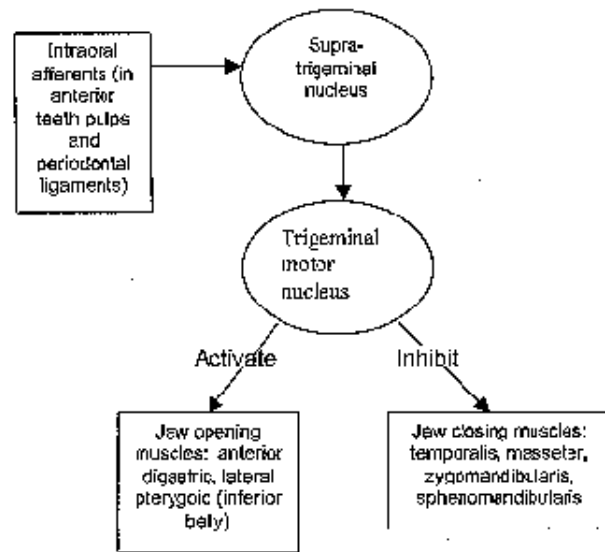


Figure 10
The jaw opening reflex. The NTI appliance not only initiates this reflex when clenching is attempted, but actually exploits or magnifies this reflex.

heightened production of norepinephrine, thus reducing the over-stimulation of the muscle spindles in the pericranial and orofacial muscles. As demonstrated in the data presented, such a decrease in muscle spindle activity (measured by the decrease in frequency and intensity of headache pain) may occur immediately, but most the benefits are not seen until approximately the sixth week of wearing the appliance. It appears, from the data, that the migraine headaches are actually down-graded to tension-type headaches.

The NTI appliance, as stated above, permits only a one-point contact of the mandibular anterior teeth with the appliance. This device is not a device as reported by Lucia,⁸³ as some have proposed. The Lucia jig is an anteriorly placed occlusal appliance. It provides some semblance of anterior guidance and extends from cuspid to cuspid, often permitting cuspid disclusion and therefore, an ability for the wearer to brux on the cuspids, perpetuating and/or precipitating pericranial muscle tenderness. On the other hand, the NTI-tss appliance, providing only a one-point anterior contact, does not permit any occlusal contact other than the one-point anterior contact and prohibits cuspid contact regardless of how much lateral mandibular movement the wearer may exhibit.

Interestingly, the NTI appliance statistically reduced the number of migraine episodes as effectively as the popular migraine prophylactic medication, Depakote (valproic acid, Abbott Laboratories, Abbott Park, IL), but

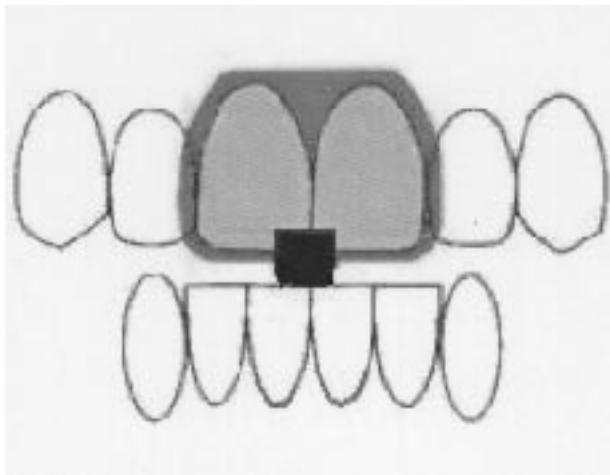


Figure 11A and B

The NTI-tss in place. Note the single, anterior point (or stop) contact which serves to enact the jaw opening reflex, and the lack of canine and posterior contacts (thereby preventing high intensity muscle contraction), which in combination serve to provide the NTI-tss efficacy.

A (above): Diagram representation of NTI-tss in place.

B (below): Actual NTI-tss in place. Note cuspids cannot occlude and note the single anterior point contact with the mandibular anterior teeth.

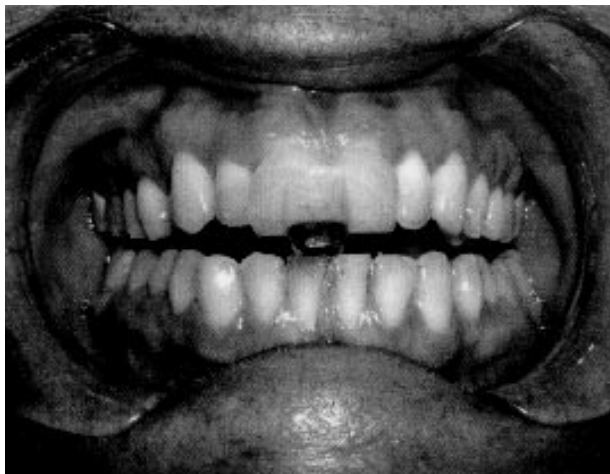


Figure 12

Lateral mandibular movement with the NTI-Tss in place. **Note:** Only one anterior point contact and cuspids are unable to engage.

type headache. While dentistry is not the usual specialty consulted to diagnose migraine or tension-type headache (a complete medical work-up is required to rule-out any potential contributing conditions), dentists, with their vast knowledge of head and neck anatomy and understanding of the parafunctional activity of bruxism, can be of great benefit in the reduction of migraine and tension-type headache suffering.

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without any adverse side-effects (48% of migraineurs who can tolerate the side effects of Depakote, an anti-convulsant, have a 50% reduction of migraine events⁸⁵). Further, no side-effects in any participant (development of periodontal disease or even inflammation, movement of teeth, injury to the temporomandibular joints, development of tooth sensitivity) developed throughout the clinical study.

Summary

Based upon the data derived in this clinical study, the NTI-tss appliance proved safe and efficacious in the reduction of medically diagnosed migraine and tension-

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