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Sleep Disorders & Bruxism – Trigeminal Cardiac Reflex a Missing Link!

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Abstract

The trigeminal cardiac reflex (TCR) is a unique and powerful brainstem reflex that has received a great deal of research interest. Sleep bruxism (SB) is sleep disorder that affects the TCR as well as other brainstem reflexes via stimulation of the brainstem; at the level of the gasserion ganglion (GG). TCR play an important role in sleep bruxism while an exaggerated form of this reflex could be responsible for sleep disorders. This paper will discuss the unusual relationship of Trigeminal cardiac reflex – bruxism – sleep disorders.

Keywords: Trigeminal cardiac reflex, sleep bruxism, sleep disorders, gasserian ganglion, tachycardia, heart rate, micro – arousals.

INTRODUCTION

Trigeminal cardiac reflex (TCR) is one of the most powerful autonomic reflexes of the body that helps reduce heart rate under challenging situations by acting as oxygen-conserving reflex [1-3]. The TCR is commonly defined as suggested by Schaller and colleagues as a sudden drop in heart rate (HR) and mean arterial blood pressure (MABP) of more than 20% as compared with baseline values [27] evoked by a physical (mechanical, electrical) or chemical manipulation of any of the branches of the trigeminal nerve [28, 29]. The trigeminal nerve can be stimulated anywhere along its course and causes sympathetic withdrawal and parasympathetic over activity through the vagus nerve resulting in bradycardia or even asystole, apnea, bradypnea, and hypotension. Various manifestations of the TCR include the naso-cardiac reflex, peripheral TCR, the diving reflex (DR), and the central TCR [4-8]. TCR is also linked to sleep disorders like sleep-related bruxism (SB) [9].

Bruxism is defined as 'repetitive jaw-muscle activity characterised by clenching or grinding of the teeth and/or by bracing or thrusting of the mandible' with 'two distinct circadian manifestations; either occurring during sleep (sleep bruxism) or during wakefulness (awake bruxism) [10] Sleep bruxism (SB) may lead to masticatory muscle hypertrophy, tooth surface loss, fracture of restorations or teeth, hypersensitive or painful teeth [11-14].

Sleep disorders are a common increasing health problem in today's fast life and can have a significant impact on quality of life and of working. They commonly manifest as excessive daytime sleepiness, difficulty initiating or maintaining sleep, or abnormal movements, behaviours and sensations occurring during sleep. Sleep bruxism, thought to be a more intense form of rhythmic masticatory muscle activity (RMMA), has a prevalence of about 8% [14].

SB results in micro – arousals from sleep classifying it as a true sleep disorder it is also associated with inception of chronic myofascial pain [15] affecting the orofacial region, tension and migraine type headaches, and temporomandibular dysfunction syndrome (TMD) affecting the temporomandibular joints [15, 16].

The TCR is a powerful brainstem reflex that manifests as a sudden onset of hemodynamic influences on heart rate (HR); blood pressure (BP) and has been

associated with cardiac arrhythmias; asystole; apnea and gastric mobility [17]. It is an oxygen conserving reflex that was first discovered in 1999 [18]. The reflex may be activated by mechanical or chemical stimulation of the trigeminal nerve at any course along its distribution. Stimulation of the Trigeminal cardiac reflex results in neuronal signals being transmitted via the trigeminal nerve to the gasserian ganglion; continuing to the sensory nucleus of the trigeminal nerve (V5) in the brain stem (mesencephalic nucleus). Signals are then transmitted polysynaptically through the reticular formation (RF); via short internucial fibres; to the dorsal motor nucleus of the vagus nerve (X). This pathway is considered as an afferent to the TCR. Parasympathetic neurons comprise much of reflex; arising in motor nucleus of V5. Stimulation of V5 results in bradycardia; hypotension; as well as apnea and gastric hypermobility [19] the reflex is of utmost importance during surgical procedures adjacent to the branches of the trigeminal nerve as the TCR can inadvertently be stimulated compromising the surgical procedure [20-23]. In the procedures near or in the gasserian ganglion; the opposite effect may be encountered; tachycardia; tachypnoea and hypotension and gastric hypomobility [24, 25].

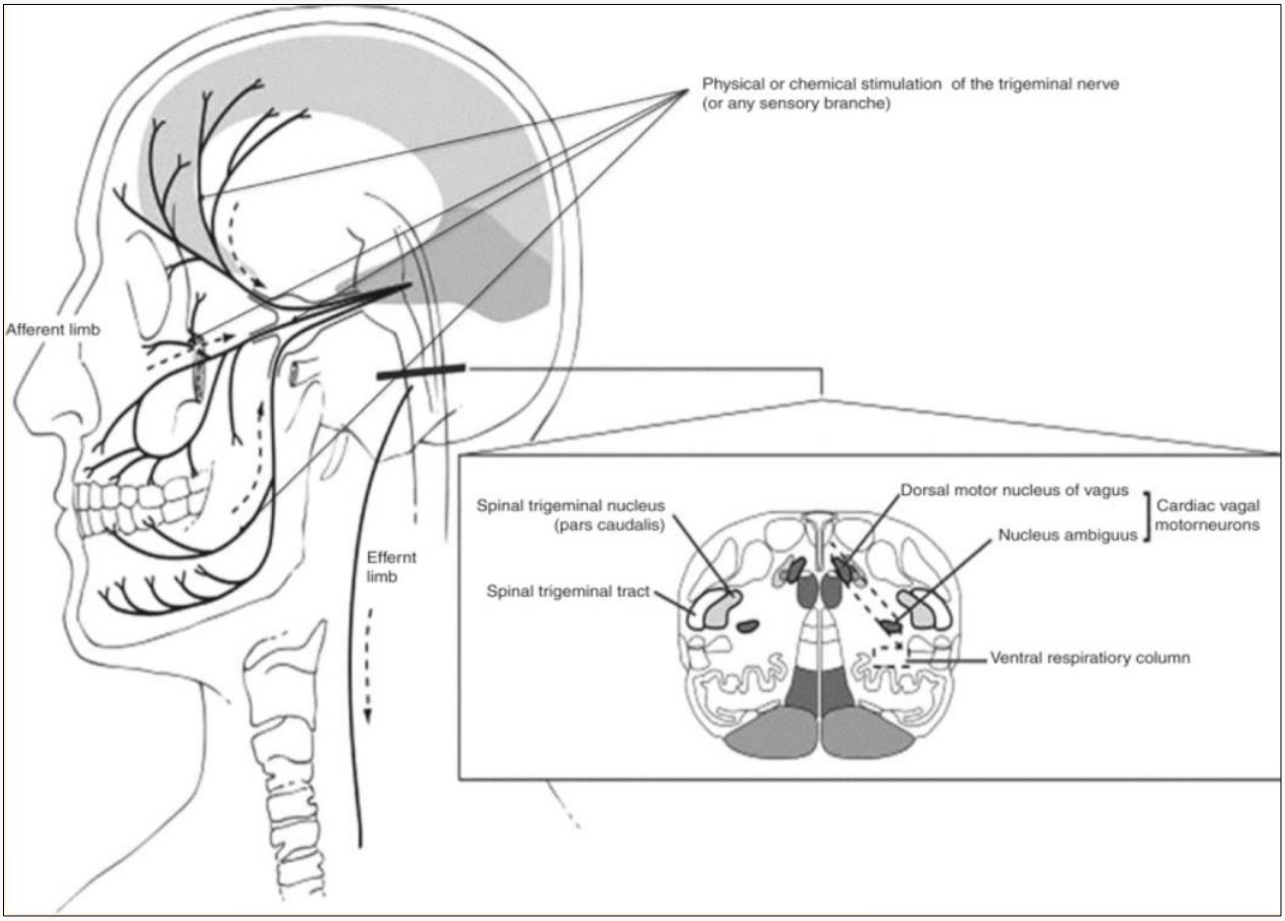

Fig. 1: Pathway of the trigeminal reflex [30]

Table 1: The Extended Classification of the Trigemino - cardiac Reflex [26]

	Skin, nasal mucosa, the Diver's reflex	**Peripheral**		**Gasserion ganglion**	**Central**	**Brainstem**
		Oculocardiac	**Maxilla – mandibular**			
Stimulus	V1	Pressure on globe	V2 and V3	Direct stimulation	Stimulation after ganglion	Direct stimulation on brainstem
Heart rate	Bradycardia	Bradycardia	Bradycardia	Bradycardia and tachycardia	Bradycardia	Bradycardia
Blood pressure	Hypertension	Hypotension, Normotension	Hypotension, Normotension	Hypotension or Hypertension	Hypotension	Hypotension
Respiration	Apnea	Apnea	Apnea	Apnea or Hyperpnea	Apnea	Apnea

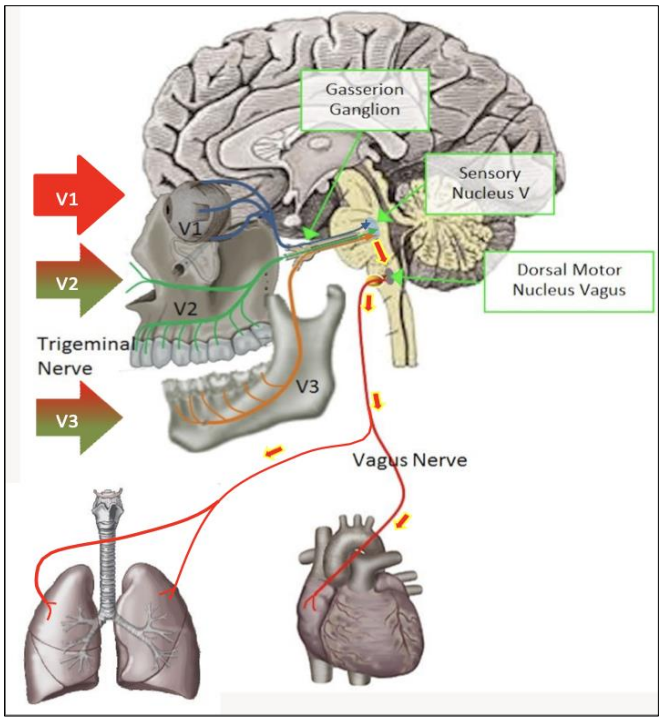

Fig. 2: Trigemino – cardiac reflex [26]

Sleep bruxism affects the trigeminal nerve at the level of the Gasserion ganglion, neurochemically. The stimulation occurs through afferents from the periodontal ligaments of the teeth, the mental nerve of the mandible and muscle spindle organs located in the masseter and temporalis muscles [31]. At this level, both sympathetic and parasympathetic modulation may be observed as tachycardia or bradycardia, a decrease or increase in respiration or as an increase or decrease in blood pressure, gastric motility and cranial pressure. tachycardia, tachypnoea, and inhibition of gastric motility, hypertension, and increased intracranial pressure are seen due to sympathetic hyperstimulation of TCR [32]. Genetic mutations associated with sleep bruxism include the HTR2A C Allele rs2770304 as a polymorphism affected the brain as well as the DRD3 rs6280, also as a polymorphism [33, 34].

Two types of sleep have been described which are non-rapid eye movement (NREM) and rapid eye movement (REM). NREM further has four stages, representing a continuum of relative depth of sleep. NREM and REM cycle throughout the night. Normal individuals first enter sleep in NREM, which progresses through stages 1, 2, 3 and 4, and then enter REM sleep [36].

NREM sleep occupies 75–80% of sleep and REM sleep accounts for 20–25%. The average length of NREM–REM cycles is 70–100 min initially and later increases to 90–120 min as sleep progresses. The duration of REM sleep in each cycle increases as the night progresses [35].

The four stages of NREM sleep have characteristic brain physiology. Stage 1 accounts for 2–5% of total sleep and gets easily disrupted by loud noise. Electroencephalogram (EEG) waves in this stage show transition from alpha waves to low voltage and mixed frequency waves. Stage 2 accounts for 45–55% of total sleep and is characterized by low voltage, mixed frequency waves with sleep spindles and K-complexes. Stages 3 and 4 are together called slow-wave sleep they are characterized by high voltage and slow wave activity. Stage 3 accounts for 3–8% and stage 4 for 10–15% of total sleep. Among all stages of NREM sleep, arousal threshold is highest for stage 4 [35]. REM sleep is characterized by theta waves and slow alpha waves, muscle atonia, and bursts of REMs [35]. Most of dreaming and memory consolidation occur during REM sleep [37]. Non-rapid eye movement and REM sleep vary considerably concerning physiological changes [38, 39]. Broadly, brain activity, heart rate, blood pressure, cerebral blood flow, and respiration decrease during NREM and increase in REM sleep. Muscle tone is absent and the body temperature regulation is disturbed during REM sleep. Airway resistance increases during both NREM and REM sleep, compared to wakefulness [40].

The third edition of International Classification of Sleep Disorders (ICSD-3) classifies sleep disorders into seven major diagnostic sections—insomnia, sleep-related breathing disorders, central disorders of hypersomnolence, circadian rhythm sleep–wake disorders, parasomnias, sleep-related movement disorders, and other sleep disorders [41]. The ICSD-3 classifies obstructive sleep apnea (OSA) as a sleep-related breathing disorder while SB is classified as a sleep-related movement disorder [42]. The etiology of

sleep disorders can be related to social, psychological, and anatomical factors. Insomnia occurs because of a combination of biological, mental, and social factors, stress, old age, and female gender play a major role. OSA occurs due to frequent periods of collapse of the pharyngeal airway. This causes reduction in oxygen saturation of blood leading to cortical and brainstem arousals. Risk factors for OSA include obesity, male sex, alcoholism, increasing age, etc., and it has been found to be associated with higher incidence of hypertension, myocardial infarction, congestive heart failure, and diabetes [43-46]. Patients of sleep bruxism, a more intense form of RMMA, experience higher episodes of RMMA per hour than patients without bruxism [36]. Three types of bruxism have been described: tooth grinding with friction sounds, tooth clenching, and tapping or jaw bracing [47].

It is a well-established fact that the autonomic nervous system plays a critical role in the pathogenesis of various cardiac arrhythmias [57, 58]. For example, atrial fibrillation reportedly has an association with an imbalance between the sympathetic and parasympathetic supply of the heart [59]. Similarly, ventricular fibrillation has been shown to be initiated by sympathetic stimulation, especially in an ischemic heart [60]. A direct relationship between the severity of OSA and the risk of sudden cardiac death at night has been proposed, probably due to greater number of nocturnal ischemic events in these patients [61].

The resulting decrease in heart rate and apnea are the mechanisms through which the TCR can be implicated in causing various sleep disorders the TCR can also be linked to both causation as well as systemic manifestations of OSA. One of the key components of OSA is hypoxemia which itself acts as a potential risk factor for inciting the TCR. Also, hypoxemia is a known cause of sudden death in such patients; therefore may suggest the role of the TCR in victims of sudden death as well [48].

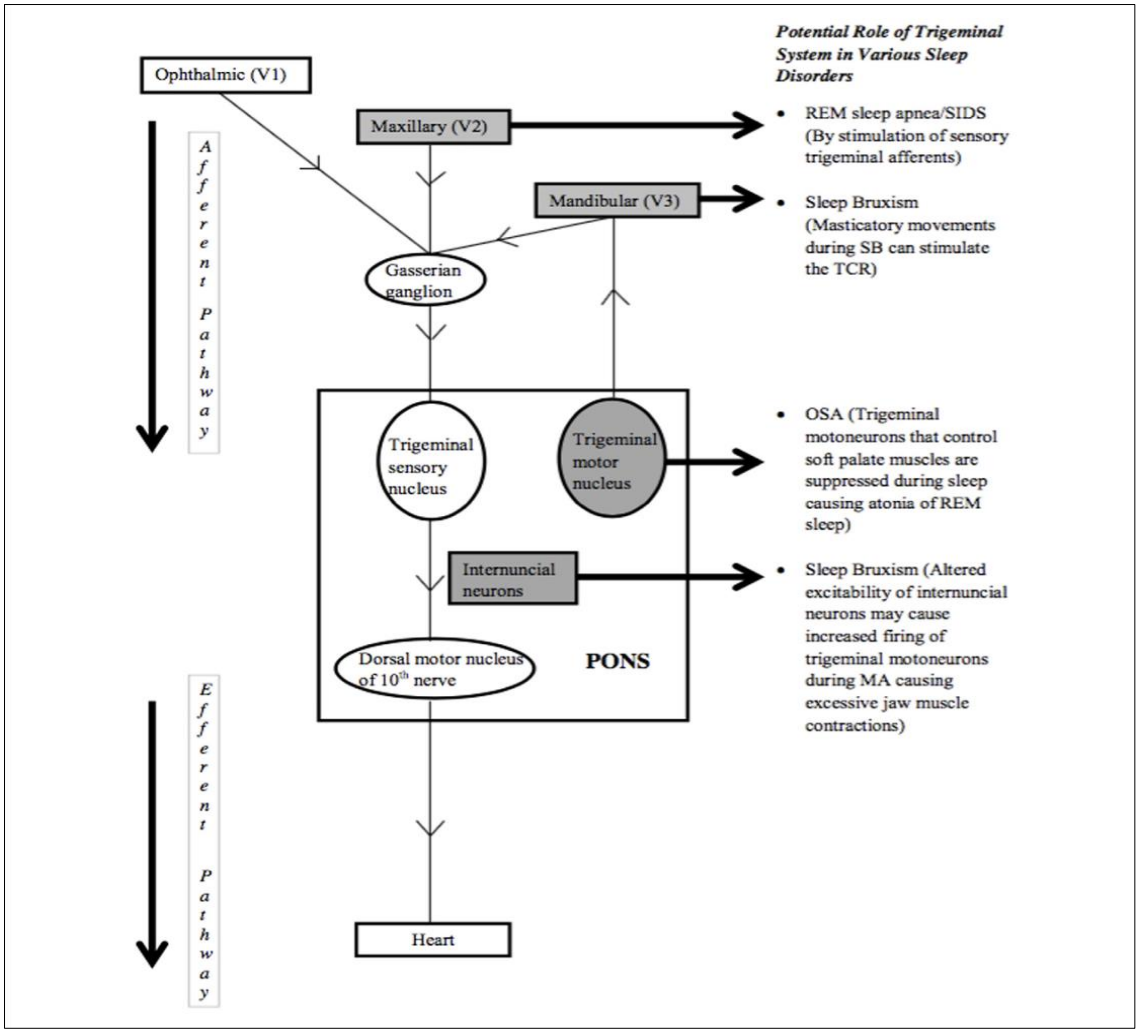

Fig. 3: Trigemino – cardiac reflex pathway and sleep disorders [36]

The naso-trigeminal reflex, a form of peripheral TCR which is known to be a protective response for the upper airways from noxious substances. Dutschmann and Herbert in 1999 tested the hypothesis that

stimulation of sensory trigeminal afferents might contribute to REM sleep apnea. They reported that injection of carbachol (mixed agonist for nicotinic and muscarinic acetyl- choline receptors) into pontine reticular nuclei of anesthetized rats causes marked potentiation of ethmoidal nerve induced respiratory depression and induces REM sleep like respiratory suppression, even apnea in some cases. The authors speculated that activation of sensory trigeminal afferents during REM sleep could easily trigger centrally mediated apnea's and cause pathological conditions like REM sleep apnea or sudden infant death syndrome (SIDS) [49]. An increase in upper airway resistance and increased nasal discharge, as seen in allergic rhinitis and rhino sinusitis, have been found responsible for disordered breathing in sleep and Micro – arousals [50].

Heiser *et al.*, have demonstrated that trigeminal stimulation during sleep leads to arousals in a dose- and time-dependent manner [51, 52]. Several authors have shown earlier that failure to arouse from sleep could be the causative factor for SIDS. Decreased spontaneous arousals during sleep in SIDS victims compared with control infants has been described [53, 54] and has been attributed to the possible immaturity of the autonomic nervous system as shown by Tuladhar *et al.*, in their study, where they examined heart rate responses to arousing and non-arousing trigeminal stimuli [55]. Tuladhar *et al.*, in 2005 reported that the bradycardia occurring in response to non-arousing stimulation of the trigeminal nerve is present in infants up to 6 months of age and is stronger when sleeping in the supine position and the NREM (quiet sleep) sleep stage [56].

CONCLUSION

The TCR might be playing a protective role in the case of sleep bruxism, while an exaggerated form of this reflex could be responsible for SD and SIDS [36]. Based on the available literature and past cases, the TCR can be thought to be playing an important role in various sleep disorders, though further evidence is warranted before it can be definitively implicated [36]. Clinical implications are significant as recognizing the association between TCR, bruxism and sleep disorders could offer new ways for diagnosis and treatment. Healthcare professionals, including dentists, sleep specialists and cardiologists should give importance to know about oral health, sleep quality and cardiovascular well being.

Future research should focus on conducting well designed studies to know the specific mechanism that underlie the TCR – bruxism – sleep disorder relationship. This includes exploring the role of the trigeminal nerve in greater detail during bruxism episodes, understanding the autonomic changes associated with TCR activation and investigating how these interactions impact overall health.

The exploration of the trigeminal cardiac reflex in the context of bruxism and sleep disorders holds promise for advancing our understanding of the intricate connections between oral health, sleep and cardiovascular function. As research progresses, it is anticipated that this knowledge will contribute to more targeted and effective interventions, ultimately improving the comprehensive care provided to individual affected by these interconnected conditions.

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