The relationship of the
trigemino-cardiac reflex and sleep bruxism

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Introduction:

The trigemino-cardiac reflex (TCR) is a unique and powerful brainstem reflex that has received a great deal of research interest. Sleep bruxism (SB) is a sleep disorder that affects the TCR as well as other brainstem reflexes via the Gasserion ganglion (GGa). This paper will discuss the unusual relationship of the TCR and SB as well as the resulting signs and symptoms seen in SB.

Literary Research:

Relevant literature was identified through searching PubMed, Research Gate, Google scholar database and Mendeley web library using the search terms “trigeminocardiac reflex”, “sleep bruxism”, and “GERD”, and “Masseter Inhibitory Reflex”.

Discussion:

Sleep disorders are an increasing health problem in all countries that have a direct effect on quality of life and productivity/safety of workers\(^1\)-\(^3\). Sleep bruxism (SB) is a movement type sleep disorder characterized by transient tachycardia, tachypnea and hypertension occurring slightly before, during or slightly after the bruxism event, resolving immediately after the event ceases (Figures 1 and 2)\(^4\). This increase in sympathetic activity has been shown to result from stimulation of the trigemino-cardiac reflex (TCR) at the level of the GGa\(^5\)-\(^7\). SB can be seen to occur with sleep apnea, just before or after apnea events or may occur independently\(^8\). The sleep bruxism events also result in micro-arousals from sleep, classifying it as a true sleep disorder. Epworth Sleepiness Scale scores of 4 to 9 are characteristic of SB whereas scores of 10 and higher are suggestive of OSA\(^4\). The daytime sleepiness (males) and tiredness (females) seen in SB have similar deleterious effects on alertness, productivity and quality of life to OSA. In
addition, SB is associated with the inception of chronic myofascial pain\(^9\) affecting the orofacial region, tension and migraine type headaches and temporomandibular dysfunction syndrome (TMD) affecting the temporomandibular joints\(^9,10\). (Figures 1, 2)

The trigemino-cardiac reflex (TCR) is a powerful brainstem reflex that manifests as a sudden onset of hemodynamic influences on heart rate (HR), blood pressure (MABP) and has been associated with cardiac arrhythmias, asystole, apnea and gastric mobility\(^{11}\). It is an oxygen-conserving reflex that was first discovered in 1999\(^{12}\), with considerable research ensuing\(^{13}-17\). The reflex can be activated by mechanical or chemical stimulation of the trigeminal nerve at any course along the nerve. Stimulation of the reflex results in neuronal signals being sent via the trigeminal nerve to the GGa. From here, the signals continue to the sensory nucleus of the trigeminal nerve (V5), polysynaptically to the reticular formation (RF) where it is connected rostrally, through short internucial fibers, to the dorsal motor nucleus of the vagus nerve. This pathway is considered as an afferent to the TCR (Figure 1). Parasympathetic neurons comprise much of reflex, arising in the motor nucleus of V5. Stimulation of V5 results in the bradycardia and hypotension seen, as well as apnea and gastric hypermobility\(^{17}\). The reflex is of considerable importance during surgical procedures adjacent to the branches of the trigeminal nerve as the TCR can inadvertently be stimulated resulting in bradycardia, hypoventilation and hypotension compromising the surgical procedure\(^{18}-21\). In procedures near or in the GGa, the opposite can be encountered: tachycardia, tachypnea and hypertension\(^{22,23}\). (Figure 1)

Meuwly, Galoanov et al \(^{17}\), in 2017, have proposed a new classification for the TCR based upon where the trigeminal nerve is stimulated (Table 1). The classic “diver’s reflex” results from
stimulation at the level of the first branch of the trigeminal nerve. This results in the typical TCR response of bradycardia, hypotension and hypopnea. This results from a cutaneous stimulation of the nerve, on the ocular and nasal skin regions. The peripheral classification includes the actual orbit of the eye (by compressing the orbit), the maxillary branch (V2) and the mandibular branch (V3). Only the maxillary and mandibular stimulation regions result in the paradoxical sympathetic response of tachycardia, tachypnea and hypertension (Figures 1, 2). In this classification, the only region of stimulation of the TCR is at the level of the GGa, all other regions do not. Stimulation at the level of the Gasserion ganglion can result in paroxysmal brady or tachycardia, hyper or hypotension and apnea or hyperpnea, depending upon the stimulus. The stimulus of sleep bruxism is at the level of the Gasserion ganglion resulting in the stimulation response of tachycardia, hypertension and hyperpnea. A recent study described this phenomenon and concluded from the research that HR was the most significantly affected and the most useful measurement in the determination of TCR. A diagnostic criterion that is generally accepted is of a heart rate decrease (or increase) of 20% or more from baseline, for a positive TCR diagnosis. Table 2 lists other cause-effect relationship criterion used to diagnose TCR. Sleep bruxism meets the first five criteria of Table 2. GGa nerve blocks are high risk and do not meet ethical standards for trials and anticholinergic drugs fall to suppress the TGR effects of SB or carry significant adverse risks for many. By following this additional criterion and the 20% HR threshold, elimination of other sympathetic and parasympathetic conditions that could affect HR and mimic the TCR is possible, rendering a more accurate diagnosis of the condition 24.
Research has found a genetic commonalty in sleep bruxism sufferers: a polymorphism of the HTR2A gene on chromosome 13\textsuperscript{25,26}. This gene codes for 5-HT (serotonin) receptors. The masseter inhibitory reflex (MIR), another brainstem reflex, is located in the mesencephalic nucleus and has the MIR reflex nucleus affected by this polymorphism\textsuperscript{27,28}. The resulting hypersensitivity to serotonin results in loss of inhibition by the MIR as well as activation of central pattern generators involved with chewing. Extreme muscle contractions of the masseter, temporalis and suprathyroid muscle groups result\textsuperscript{29}. There is a “cascade of events” outlined in table 3 resulting from activation and suppression of other cranial central pattern generators/cranial reflexes involved with sucking and swallowing, in addition to the TCR:\textsuperscript{4} This HTR2A polymorphism seen in most with SB was found to frequently occur in other conditions including obstructive sleep apnea, tension headaches, migraine headaches (without auras) and a myriad of psychiatric disorders\textsuperscript{30-33}. Interesting to note, OSA has headaches as a commonly reported symptom, often upon waking (assumed to be due to hypercapnia). In recent studies it was demonstrated that, with the TCR, at the connection at the level of the reticular formation and nucleus ambiguus, there appeared to be an endogenous modulation. It was also found that the 5-HTR1A and 5-HTR2A serotonin reception genes were involved in mediation (stimulation, depression) of the connections (antagonists altered the TCR)\textsuperscript{17}. With the 5-HTR2A polymorphism known to exist in SB, it is reasonable to assume that this region could also be similarly affected (potentially resulting in hyperactivity of the TCR). Table 3 outlines the cascade of events occurring during SB events. There are a number of cranial reflexes involved including the TCR, the MIR, the sucking reflex\textsuperscript{4} (which can result in trauma of the buccal mucosa and development of linea alba), and the swallowing reflex\textsuperscript{34-36}. Scalloped borders of the tongue are also a common finding in SB, resulting from activation of the genioglossus muscle.
pressing the tongue forcibly against the teeth$^{37,38}$. In other research it has been shown that there is a commonality between SB and gastro-esophageal reflux disorder (GERD) and SB, supporting SB’s influence on the vagus nerve$^{39,40}$. This can manifest as tooth erosions on the inner or lingual surfaces of the teeth and increase susceptibility to dental caries$^{41}$. The 5-HTR2A polymorphism seen in SB and suppression of the MIR, the forces generated during SB events far exceeds those of normal chewing$^{29}$. Damage to the teeth is common including:

- sensitive, loose or broken teeth$^{42}$
- abfraction lesions$^{43}$
- accelerated periodontal disease$^{44}$
- formation of mandibular tori$^{45}$
- elongation of the coronoid processes
- excessive compression of the TMJ, often initiating or accelerating degenerative changes$^{47-49}$.

With the TCR being intertwined with SB, the range of signs and symptoms observed during SB events can be readily interpreted. Restless leg syndrome (RLS) is another movement type sleep disorder that results in activation of the TCR similar to SB. Tachycardia, hyperventilation and hypertension, shown to occur in RLS, have been linked to heart disease in a number of studies$^{50,51}$. To date SB has not been studied to the extent of RLS and it is not known at this time if SB is also a risk factor for heart disease. Further research is certainly warranted.
References

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