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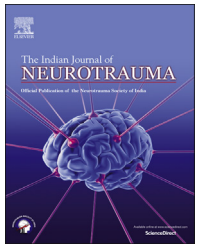

Original Article

Bruxism in patients of moderate to severe traumatic brain injury: Management results suggesting an etiological mechanism

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ABSTRACT

Introduction: Bruxism is an unusual event among patients of altered sensorium after brain injury. Occasionally the bruxism may be so severe as to cause harm to the patients and make nursing difficult. This study presents such cases that were managed by the author. A possible explanation for post-brain injury bruxism is suggested.

Material and method: Twelve patients of brain injury following trauma who were observed to have bruxism were included in the study. The clinical presentation and the response to intervention were studied. Patients less then 16 years were managed with benzodiazepines only. Patients more than 16 years of age were managed with benzodiazepines and pramipexole was administered in addition to benzodiazepines in 5 patients.

Observation: Of the 12 patients 3 subjects were classified as severe brain injury. Nine patients had suffered moderate grade brain injury. 3 (25%) patients were children and the mean age of the rest 9 (75%) patients was 40 years. The children were managed with benzodiazepines. The median time of onset of bruxism from the time of injury was 5.25 days with range of 2 days–12 days. Pramipexole, a dopamine agonist, was useful in management of severe bruxism with a latency period of 2 days. All patients except one recovered within 7 days after starting the treatment.

Conclusion: Bruxism is distressing to a patient-in-recovery following brain injury and cause significant inconvenience to the nursing staff. Effective treatment included the use of benzodiazepines and pramipexole. Pramipexole, a dopamine receptor agonist, should be considered an option for pharmacological management of bruxism after brain trauma. If central pattern generators (CPG) are involved in some of the disabilities of moderate to severe brain injuries like bruxism, there is a rationale for considering a larger study for the use of dopamine receptor agonist in such patients.

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1. Introduction

Bruxism is defined as repetitive jaw muscle activity characterized by clenching and grinding of teeth and/or by bracing or thrusting of the mandible. Bruxism after brain injury is not often mentioned in literature. Though a relatively less harmful consequence of brain injury, it occasionally can cause great discomfort to the patient and the nursing staff. The etiology of bruxism remains unclear to date. However certain speculations based on laboratory findings suggest the possibility of airway maintenance and respiration as underlying physiological mechanisms and the possibility of these events being mediated by a certain state of dopamine (DA) depletion. In the present observation, the author presents 12 cases with brain injury and associated bruxism in the recovery stage and then discusses the treatment for the same.

2. Material and method

The study included the patients of brain injury over the period from January 2006 to August 2013 who were noted to have bruxism during the period of recovery following brain injury. All patients had grinding and clenching of teeth for more than 24-hour period and required intervention either due to excessive motor activity of the muscles of mastication or due to needs of nursing care. The type of injury, time of onset of bruxism after the primary injury, any other associated movement disorders, the response to treatment and the latency of response were noted. The patients were followed up for a minimum period of 6 months. Patients less than 16 years were managed with benzodiazepines only. Patients more than 16 were administered benzodiazepines. After failure of benzodiazepines in effective control of bruxism, pramipexole was additionally administered to 5 patients. Patients were under observation for associated abnormal autonomic presentations.

3. Observation

Twelve patients were among a total of 647 patient (0.018%) of moderate to severe head injury evaluated by the author during a period of about 8 yrs (Table 1). Four (25%) patients were less than 16 yrs of age and 10 (83%) patients were males. The age range was from 2 yrs to 58 yrs. 7 (58%) patients had sustained moderate grade brain injury and 5 (42%) patients had severe brain injury as assessed by the presenting Glasgow Coma Score (GCS). As treatment progressed 3 out of 5 patients of severe brain injury improved to moderate grade. Hence by day 5 post-injury 10 (83%) patients could be classified as moderate grade brain injury. The median time of onset of bruxism from the time of injury was 5.25 days with range of 2 days–12 days. Initially presenting with poor GCS, patients of severe head injury were extubated or tracheostomised by day five of treatment and were gradually weaned off sedation. In such patients the observation of bruxism was delayed. Sedation may be responsible for the delay in presentation. Teeth grinding was loud and masseter contractions were observed in all patients. Though clinically classified as severe (based on persistence of symptoms throughout the day), as Electromyography studies were not done, a grading system suggested for sleep bruxism could not be applied to the cases in this study. Most events continued for several hours at a time and many such events, typically 12–19, would take place in 24 h if not intervened. Yawning interrupted the events for short intervals. A particular event would start with a stimulus or may abort with a stimulus like change in posture. However these responses were not consistent especially in adult patients. Periods of sleep were free of the teeth grinding, typically noted during the later period of recovery.

Associated movements were noted in the subjects. Hypertonic posturing was noted in 3 (25%) patients and coarse tremors of upper limbs were noted in 1 (8.33%) patients. Right forearm extreme pronation was noted in 1 (8.33%) patients. No consistent movement disorder was noted in 7 (58%) patients in this series. In the cases of 2 (16.6%) patients, family member confirmed history suggestive of sleep bruxism and in case of another 2 (16.6%) patients' families reported symptoms suggestive of periodic leg movements before the trauma occurred.

Patients were treated with sedation as a part of standard protocol for management of brain injury. After the onset of bruxism, subjects below the age of 16 years were managed with escalating dosage of benzodiazepine, (dosage starting with 0.15 mg/kg–0.35 mg/kg/dose-administered intravenously initially and later through nasogastric tube) to keep child sedated and provide intermittent relief from bruxism. The patients older than 16 years were administered benzodiazepines (assuming an average age of 40 kg, dosage of 1.5 mg/kg–4 mg/kg) and if the grinding continued beyond 2 days, pramipexole (dosage of 0.00625 mg/kg/dose–0.09 mg/kg/dose using a formulation of 0.375 mg tablets administered through nasogastric tube twice a day, dependant of the weight of patient as known before trauma) was started in addition. Younger patients responded to benzodiazepines better than the older patients. Of the 8 adult patients, 5 required to be administered pramipexole at 0.375 mg two times a day for a period of 3 weeks. It was noted that a latency period of 2 days was required before any improvement was noted in the control of bruxism. Once the patient improved with regard to bruxism, the dose of benzodiazepine could be decreased, thereby decreasing sedation. No adverse effect was noted on administration of pramipexole. 1 of the 5 patients who remained in vegetative state had decreased intensity and frequency of grinding but bruxism never stopped entirely till his last follow-up at 2 years post-injury. He succumbed to his brain injury due to secondary pneumonia. During the period of admission, patient's autonomic parameters were monitored. Tachycardia and diaphoresis were commonly observed. Patients were consistently noted to have tachycardia associated with events of bruxism and 7 (58.3%) out of 12 patients were noted to have facial diaphoresis during the initial 2 weeks. Thereafter the sweating events were less frequent.

4. Discussion

Classified as a parasomnia, bruxism is defined as repetitive jaw muscle activity characterized by clenching and grinding

Table 1 – Clinical profile of patients.

Patient	Age/sex	Type of injury	Onset of bruxism [number days after injury]	Other associated movement disorder	Response to benzodiazapine	Response to pramipexole	Outcome of bruxism
1	3 yrs/m	Fall from height (multiple hemorrhagic contusion and hypoxic encephalopathy)	3	Hypertonic posturing	Bruxism controlled – occasional grinding continues after 2 yrs of injury	–	Persists beyond 2 yrs. Difficult to nurse and dental erosion
2	11 yrs/m	RTA (Diffuse axonal injury)	2	tremors	Bruxism controlled – stopped within 2 weeks of trauma	–	No significant residual problem
3	2 yrs/f	RTA (left temporal EDH)	5	none	Bruxism controlled – stopped within 2 weeks of trauma	–	No significant residual problem
4	14 yrs/m	RTA (diffuse axonal injury)	3	Hypertonic posturing	Bruxism controlled – stopped within 4 weeks of trauma	–	No significant residual problem
5	46 yrs/f	RTA (hemorrhagic contusion bifrontal region)	7	none	Bruxism controlled after addition of pramipexole – stopped within 2 weeks of trauma	Bruxism relieved	No significant residual problem
6	58 yrs/m	Fall in the bathroom (intracerebral hemorrhage)	5	none	Bruxism controlled with addition of pramipexole – stopped within 5 weeks of trauma	Bruxism relieved	No significant residual problem
7	41 yrs/m	RTA (right parietal EDH with tSAH)	5	Right hand dystonia	Bruxism controlled – stopped within 2 weeks of trauma	–	No significant residual problem
8	18 yrs/m	RTA (left fronto-parietal SDH with severe diffuse brain injury with hypoxic encephalopathy)	12	Hypertonic posturing	Bruxism controlled – intensity of bruxism decreased after adding pramipexole. Bruxism continues after 2 years	Bruxism relieved – in frequency and interval	Persists beyond 2 yrs. Difficult to nurse and dental erosion
9	56 yrs/m	RTA (right fronto-parietal thin SDH with coutrecoup brain contusion)	4	none	Bruxism controlled – stopped within 2 weeks of trauma	–	No significant residual problem
10	42 yrs/m	Fall from stairs (left fronto-temporal EDH with right depressed fracture)	5	none	Bruxism controlled – stopped within 2 weeks of trauma	–	No significant residual problem
11	39 yrs/m	RTA (left fronto-temporo-parietal SDH)	6	none	Bruxism controlled stopped after addition of pramipexole – stopped within 2 weeks of trauma	Bruxism relieved	No significant residual problem
12	46 yrs/m	RTA (fronto-basal hemorrhagic contusion)	6	none	Bruxism controlled after addition of pramipexole – stopped within 2 weeks of trauma	Bruxism relieved	No significant residual problem

DAI = Diffuse axonal injury, RTA = Road traffic accident, EDH = Extra dural hematoma.

of teeth and/or by bracing or thrusting of the mandible. Bruxism has two distinct circadian manifestations, it can occur during sleep (sleep bruxism) and during wakefulness (awake bruxism).[1] It has been reported in certain neurological disorders such as cerebellar hemorrhage,[2] anoxic encephalopathy,[3] Rett syndrome[4] and temporal lobe epilepsy.[5] It is also associated with many clinical problems like oro-facial pain, dental restorative treatments and neurological disorders. The entity has been studied extensively by sleep physiologists and sleep medicine experts. In 1985, Pratap Chand et al[3] reported their observations regarding bruxism among 20 comatose patients with various neurological conditions and correlated their relationship with the stages of sleep and the depth of coma. They concluded that bruxism was seen to appear at different levels of consciousness, but to disappear only after a significant improvement in the level of consciousness. A review of the present understanding of the neurobiological mechanism of sleep bruxism has been discussed by Lavigne et al[6] in 2003. They describe the role of brainstem reticular formation in sleep cycles and in jaw movement genesis thereby suggesting the possible role of bruxism as a micro-arousal phenomenon similar to swallowing in sleep. They conclude the possibility of 'maintenance of airway' and 'lubrication of the oro-pharynx' as causes for the triggering of the phenomenon of bruxism.

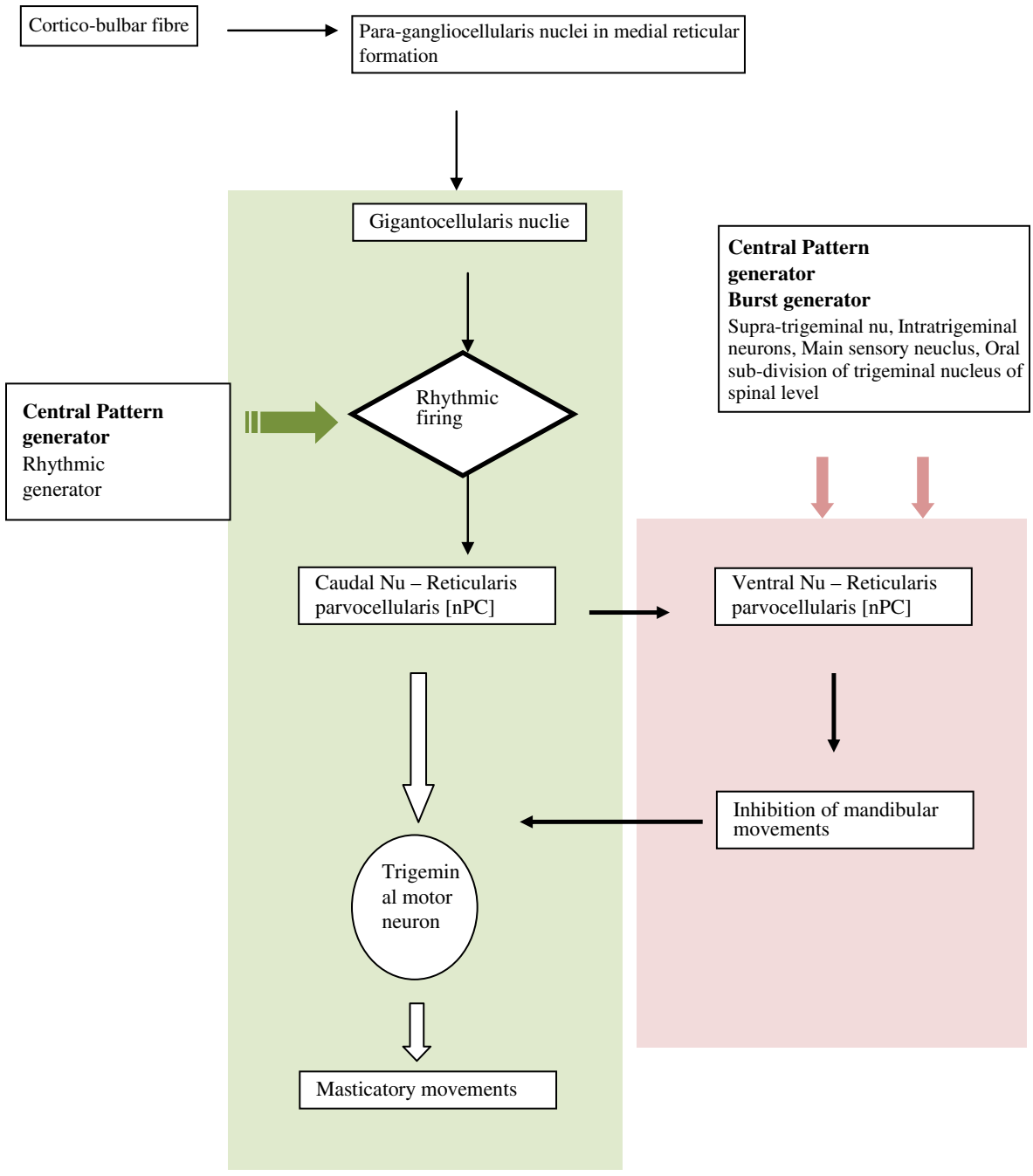

Fig. 1 – Central pattern generator and the proposed mechanism for the RJM and RMMA in sleep.

4.1. *The relation between central pattern generators and mastication must be emphasized in this context*

Our brain controls multiple rhythmic motor activity like swallowing of sputum in sleep, coordination of respiratory pattern during such act, yawning and for that matter even locomotion and respiration in the awake state. The fundamental neuronal physiology of such activity could be explained by the concept of 'Central Pattern Generator' (CPG).[7] These are neuronal networks with specific sensory inputs and precisely patterned motor responses.[8,9] The masticatory CPG is suggested to be composed of two groups: the rhythm generator and the burst generator (Fig. 1). The rhythm generator induces the basic masticatory rhythm while burst generator adapts the rhythm according to sensory inputs from the oral cavity. This is suggested to generate spatio-temporal pattern of burst activity in the masticatory motor neurons supplying the muscles so that movements become appropriate for the food bolus, size, viscosity and temperature. Several elements of the masticatory CPG interact with the respiratory CPG to prevent aspiration and at the same time maintain adequate flow of saliva.[1,10–12] Stimulating and mapping studies have revealed Cortical Masticatory Area (CMA) in addition to primary face motor and somatosensory cortex. CMA also has been demonstrated to be involved in swallowing related activity.[13–15] The act of mastication and the findings of 'Rhythmic Jaw Movements' (RJM) and 'Rhythmic Masticatory Muscle Activity' (RMMA) appear to originate from the same CPG but they differ in the wakefulness pattern and the rhythmic alternate jaw-opening and jaw-closing activity.[15] Its two phases of sustained tonic contraction and phasic relaxation drives are modulated by this CPG. This harmonious integration of respiratory, mastication and swallowing activities is possible through neuron complex in the ventrolateral medullary region.

4.2. *Sleep motor activity has been related to neurotransmitters*

Both Non Rapid Eye Movement (NREM) sleep and Rapid Eye Movement (REM) sleep are associated with motor arousal phenomenon even in the state of atonia during various stages of sleep. Mastication, respiration, swallowing and sleep appear to have a common or overlaying central pattern generator (CPG). Mastication can be triggered by a voluntary motor command from the cortex or by peripheral inputs from the jaw muscle spindles or the sensory receptors of the oral mucosa.[16] These motor afferent cell bodies are placed in the trigeminal mesencephalic nuclei and synapse on the alpha motor neurons in the trigeminal motor nuclei. A wide variety of neurotransmitters have been identified with specific receptors for GABA, $5HT_2$, DA_1 and DA_2.[8,17–19] The neurotransmitters which may be relevant to this study have been cataloged in Table 2. Magee in 1970 reported the influence of L-dopa on sleep bruxism followed by reports of the effect of adrenaline and nor-adrenaline. Such findings, however, were not held by other researchers as a possible cause or therapeutic strategy for bruxism. Later in 1997, Lobbezoo et al[20] published a controlled study with L-dopa showing a modest but significant reduction in sleep bruxism (SB) related motor activity. However, the specificity of dopamine (DA) in the genesis of SB remains equivocal, because an increase in tooth grinding was reported in schizophrenic patients treated with DA receptor antagonist (haloperidol)[21,22] and another controlled study with a modest DA receptor agonist (bromocriptine) did not reveal benefit in SB patients though cognitive function improvements were noted.[21] Amir et al[23] reported an open study to reduce neuroleptic induced bruxism using propranolol, a beta adrenergic receptor blocker and repeated a similar study in patients having bruxism without neuroleptic use by Sjoholm et al.[24] Both studies concluded on the beneficial effect of propranolol thereby suggesting the possible role of adrenaline (Adr) receptors. It is also noteworthy that most drugs

Table 2 – Neurotransmitter and their relation to mastication and sleep.[a]

Neurotransmitter	Relation to mastication	Relation to sleep
Acetylcholine (Ach)	Cortical motor excitability increases.	Activates glutamate and glycine inhibitory neuronal output that reduce REM atonia.
Adrenaline (Adr) or nor-adrenaline (NA)	Facilitates RJM induced by glutamate.	NA triggers above Ach-induced atonia; promotes alertness and arousal.
Angiotensin	Facilitates DA-induced RJM.	
Calcium Channels	Synaptic activation.	Synaptic key events that contributes to GABA inhibition of arousal centre/essential to sleep.
Dopamine	Promotes RJM. DA1 receptors are agonists, DA2 are antagonist.	Promotes arousal and is a major factor in pathophysiology of period leg movement disorder.
GABA	Inhibition of RJM induced by DA.	Promotes sleep onset and non-REM thalamo-cortical EEG pattern. In REM it contributes to NA and 5-HT neuron inhibition that normally facilitates Ach action.
Glutamate/NMDA	Facilitates RJM/dorsal nPC. Blocks phasic RJM/ ventral nPC. Facilitates Jaw-opening motor-neuron.	Involved in reticular activating and arousal.
Glycin	Inhibition of jaw-closing motor-neurons.	Promotes arousal/alertness.
Serotonin (5-HT)	Facilitates RJM; SSRI increases bruxism. 5-HT 2c receptor involved in RJM and CPG facilitation.	Promotes sleep onset. Decreases activity in non-REM and REM.

[a] Ref articles = 6,8,10,24,51–70, nPC = nucleus reticularis parvocellularis.

are likely to have affinity for more than one receptor type related to the neurotransmitter or different neurotransmitter.[6,25,26] For example bromocriptine presents an affinity for DA and Adr receptors. Since SSRI were noted to increase bruxism, 5-HT receptors were studied and concluded to be an active neurotransmitter in the central pattern generator related to jaw movements. Again, the use of either a 5-HT precursor like tryptophan or a selective reuptake inhibitor failed to attenuate or exacerbate sleep bruxism. Hence, from the above studies related to sleep bruxism, it is presently irrational to conclude on a single neuronal pathway or a neurotransmitter as etiology in spite of reasonable indirect evidence of beneficial effect. This justifies the study of more specific dopamine agonists and/or antagonist in the clinical setting.

4.3. *Effect of shear stress upon axons and neurotransmitters in traumatic brain injury*

Diffuse axonal injuries result in the classical retraction ball related neuro-pathological presentation suggesting axonal discontinuity. These lesions are found in high density in the white matter tracts in about 25% of severely brain-injured patients.[27] This causes disruption of axonal membrane and allows unregulated calcium ion (Ca^{2+}) entry. This results in both anatomical and functional disconnection within hours of the traumatic event and is termed delayed or secondary axonotomy.[28] Superimposed on the immediate mechanical injury, multiple complex biochemical events occur over a period of hours to days. These events are in addition to the more commonly known ion channel dysfunction and calcium influx into the cells, mediated by the 'second messenger' linked receptor system. The 'second messengers' are large molecules strategically placed on the inner side of the axonal membrane and have the capability of modulating or amplifying external signals brought to the cell via neurotransmitter and mediators.[28] Classical example includes the glutamate [metabotropic receptor mediated] signal pathway. A number of studies have shown that second messenger system, due to the large size of their molecule and complex stearic interaction, are vulnerable to shear injuries. Some injuries may amplify the effect of the messenger and others may tend to decrease the interactions.[29,30] Bortolotto et al[31] suggest this as a possible

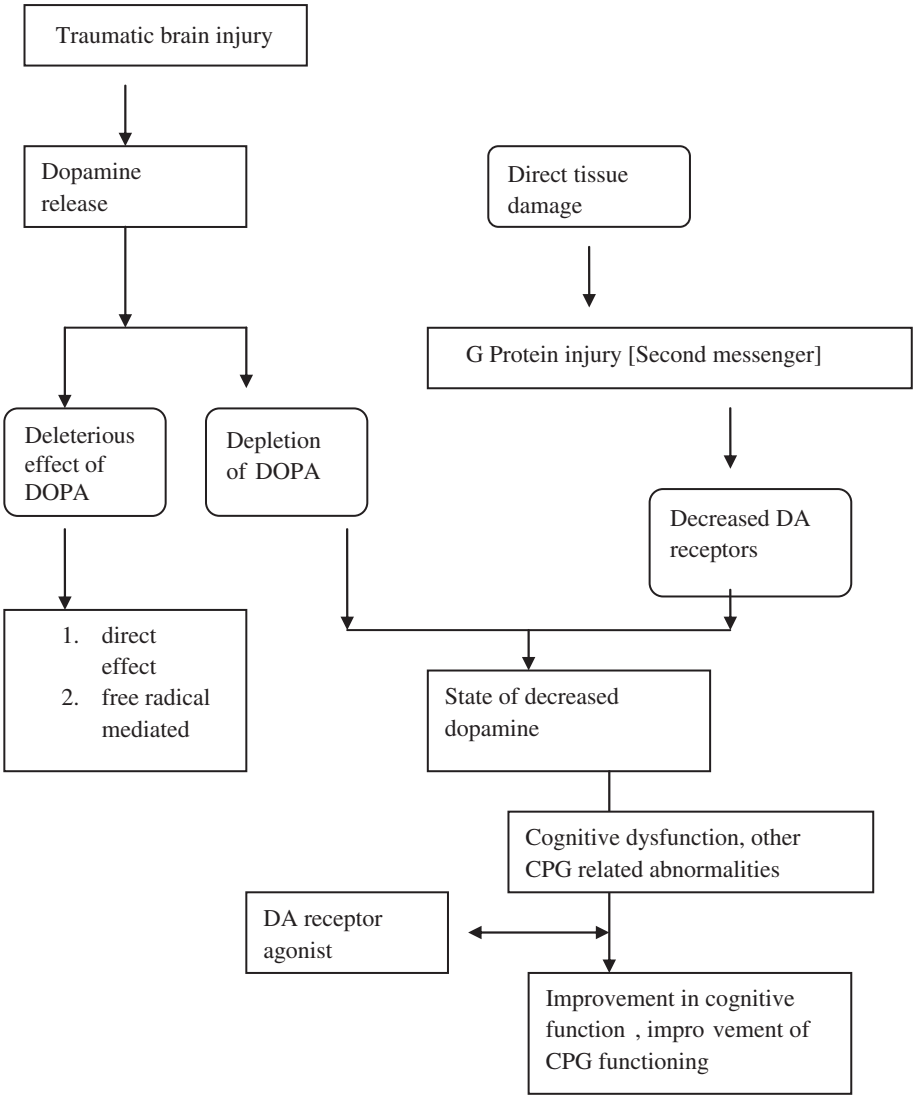

Fig. 2 – Proposed reason for the role of dopamine agonist in the management of TBI induced bruxism.

mechanism for the long lasting behavioral and cognitive changes noted in patients of neurotrauma. The messengers have been found to belong to the 'G-protein' family of molecules. It is noteworthy that DA receptor is a G-protein coupled receptor. Changes in concentration of dopamine, adrenaline and nor-adrenaline receptors have been found in experimental models of Traumatic Brain Injury (TBI).[32]

4.4. *Why dopamine?*

Bales et al[33] in the review manuscript "Targeting dopamine in acute brain injury" published in 2010, reviews the available evidence about the presence and effect of DA on traumatized brain tissue. DA is a critical neurotransmitter in multiple areas of the brain.[34,35] Its role in long term potentiation and long term depression is well documented.[36] DA when discharged in high amounts into the synaptic cleft gets converted to toxic compounds (quinine/semiquinone). These compounds cause detrimental effect due to the formation of free radicals and oxidative stress.[37–41] There is evidence that DA signaling in the DA D2 receptor can induce increase in the release of intracellular Ca^{2+} ions and activation of calcium dependent kinases and phosphatases important for cell death signaling.[42–44] Wagner et al concluded that the initial injury-induced increase in dopamine observed in injured brain may be responsible for precipitating excitotoxic disruption and oxidative damage to dopaminergic cellular function. This then leads to observed change in DA kinetics and decrease in DA release. The above progression of events consolidates the suggestion of eventual depletion of DA among the brain injured patients.[45]

DA plays an important role in the **(a)** regulation of Na/K ATPase, **(b)** cellular metabolism, **(c)** Calcium release and the N-Methyl-D-Aspartate (NMDA) receptor through 'Dopamine cAMP regulated phosphoprotein 32 KDa' (DARPP-32) and 'protein phosphatases -1' (PP-1). Dopamine D2 receptor is known to activate Ca^{2+}/calmodulin-dependent protein phosphatase 3 (calcineurin) by increasing the intracellular Ca^{2+}. The DARPP-32 protein is directly acted upon via calcineurin.[46,47] Thus, calcineurin is a part of regulatory mechanism of dopaminergic neurotransmission. The induction of calcineurin activity following TBI and the alteration in calcineurin subunit distribution makes DA a potential key contributor to therapeutic interventions that act through calcineurin activation or inhibition.[48]

There is also a recognized delayed vulnerability of the dopaminergic (DAergic) neurons to the inflammatory cascade which may be partially explained by the fact that microglia have DA receptors which cause migration and activation to DAergic regions of the brain[31,49,50] in response to released dopamine which transiently increases in the local milieu following brain injury.

These evidences suggest a definitive role of dopamine depletion on the recovery outcome of patient following traumatic brain injury especially when the evidence of shear injury is high Fig. 2 represents this reasoning and the use of a DA agonist for the management of such patient.

4.5. *The role of pramipexole*

Pramipexole is a non-ergot synthetic-organic dopamine agonist with relatively high in-vitro specificity and intrinsic activity at the D2 subfamily of dopamine receptors. Pramipexole acts as a partial or full agonist at the following receptors: D2S receptor [Ki (dissociation constant) = 3.9 nM; IA (Intrinsic Activity) = 130%], D2L receptor [Ki = 2.2 nM;

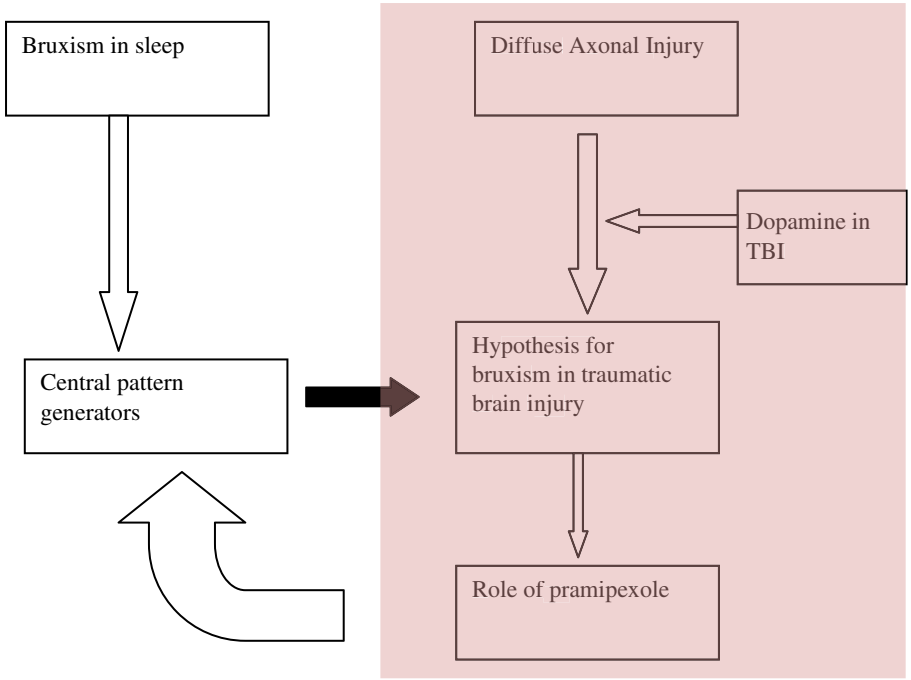

Fig. 3 – Hypothesis to explain the cause of bruxism in TBI. The flow chart suggests link between the existing theory for bruxism and TBI related bruxism and the possible role of pramipexole in treatment.

IA = 70%], D3 receptor [Ki = 0.5 nM; IA = 70%], D4 receptor [Ki = 5.1 nM; IA = 42%]. Pramipexole has been noted to have very negligible or insignificant affinity for the 5-HT_{1A}, 5-HT_{1b}, 5-HT_{1D} and α1-adrenergic receptors in human tissue. By acting as an agonist for the D_2, D_3, and D_4 dopamine receptors, pramipexole may directly stimulate the under-functioning dopamine receptors. This allows pramipexole to be a relatively specific medicine for the management of Parkinson's disease and parasomnia like Restless Leg Syndrome [RLS]. A similar argument may be applied to the use of a specific DAergic receptor agonist for the management of bruxism following brain trauma where there is a relative depletion of both dopamine and the dopamine receptors.

4.6. *Hypothesis for bruxism in head injury*

After a review of the above available evidence related to 1) sleep bruxism and the proposed relation to central pattern generators (CPG), 2) association of Dopamine as an important neurotransmitter in CPG, 3) association of dopamine to traumatized brain and 4) the available data related to the benefits of DA agonists in improvement of cognitive function in patients following TBI and our own observation of improvement of bruxism on administration of DA agonist, an attempt is made to hypothesize a mechanism for bruxism among patients recovering from moderate to severe TBI (Fig. 3). Shear injury resulting from trauma damages multiple CPG in the brain and in some instances a partial damage may result in dysfunctional reciprocal relation in the CPG neurons rather than a complete loss of function (To be more descriptive, this means that the tangential or stretch injuries may actually result in partial damage to a CPG formation. CPG formations are proposed to be typically formed of networks which have groups of neurons with reciprocal functional state – simply exemplified by a perpetual see-saw. On damage to one arm of the network – partial or complete- the functioning of the CPG is tipped off. This then either results in loss of function or 'dysfunctional reciprocal relation' of neurons within the network.). This at the neurotransmitter level may be visualized as a loss of available dopamine or decrease in DA receptors. To be more elaborate, at the sub-cellular level, the same reciprocality needs to be translated from a biophysical functional pattern to a biochemical mechanism. Damage to the cells, partial or complete, results in initial injury-induced increase in dopamine observed in injured brain which may be responsible for precipitating excitotoxic disruption and oxidative damage to dopaminergic cellular function. This leads to observed change in DA kinetics and decrease in stimulated DA release at later time. This explains the suggestion of depletion of DA state among the brain injured patients. At the same time partial injuries may lead to injury of the DA receptors, which belong to the G coupled protein receptor family. These are macromolecules and have been demonstrated to be damaged by change in protein 3-dimesional configuration by mechanical stress or oxidative stress. Hence the dysfunctional state of the CPG may be interpreted as a loss of available dopamine or decrease in DA receptors.

There have been multiple studies dealing with bruxism in sleep but none for bruxism following traumatic injury of the brain. Since bruxism is observed in brain injured patients, the question then arises as to – 'why does it happen?' and if it does, 'why doesn't' it occur to all patients of brain injury? The proposed mechanism based on the conclusions of this study and the available literature answers the questions satisfactorily. Administration of a DA agonist may be able to reverse this apparent down-regulation to a variable extent. This may also be an explanation for the observed inconsistency in response of bruxism to DA agonist therapy. Bruxism in TBI, being a relatively selective expression of CPG damage, may provide a good experimental ground to study the recovery of more complex and wide-spread CPG's like that associated with locomotion and cardio-respiratory activity. Thus, a smarter pharmacotherapy strategy may be considered when brain injury leads to damage to such centers.

5. Conclusion

From this study we conclude the following:

1 Bruxism in patients in recovery from TBI appears to benefit from administration of pramipexole.
2 There is a rationale for considering a larger study for the use of DA agonist in patients of moderate to severe traumatic brain injury.
3 Bruxism in TBI patients should be studied further for understanding the role of CPG damage and long-term outcome of patients with severe brain injuries.

This may allow us to develop other novel therapeutic approaches for the re-regulation of ineffectual CPG with possibility of recovery of such patients.

Conflicts of interest

The author has none to declare.

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