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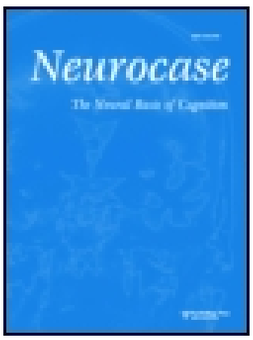

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Cannabidiol in the management of bruxism in behavioral variant of frontotemporal degeneration

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ABSTRACT

Awake bruxism is an understudied feature of behavioral variant of frontotemporal dementia (bvFTD). We present the case of aman who presented with psychiatric, behavioral, cognitive changes, and teeth clenching that resulted in significant changes in his teeth alignment including an underbite. He received multiple treatments with partial response. He then started using acannabidiol (CBD) capsule, and the grinding was almost completely relieved after this intervention. There is still no standardized pharmacology treatment for bruxism in patients with bvFTD. As aconsequence, acase-by-case approach is suggested. CBD can be helpful as an adjunct therapeutic agent for awake bruxism.Not StartedCompletedRejected.

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Introduction

Frontotemporal dementia (FTD) spectrum syndromes are the second most common form of dementia in adults under the age of 65 and behavioral variant FTD (bvFTD) is the most common FTD subtype (Hogan et al., 2016). Patients with bvFTD have been described with awake bruxism (Kwak et al., 2009), an oral parafunctional activity that consists of tooth grinding, bracing, or clenching dystonic movements that occur during wakefulness. Awake bruxism can lead to dental breakdown, muscular jaw pain, and temporal headaches. Severe forms of bruxism can compromise oral functions such as chewing, speaking, and swallowing (Jankovic et al., 2000). There is a paucity of literature regarding the treatment of bruxism in neurodegenerative diseases, particularly with bvFTD. Levodopa-carbidopa, galantamine, and injections of botulinum toxin into the masticatory muscles have been reported as useful in bruxism associated with other neurodegenerative conditions (Guaita & Högl, 2016). There is also some evidence that cannabidiol (CBD), the non-psychoactive component of the plant *Cannabis sativa*, is effective in the treatment of bruxism associated with brain disease (Nitecka-Buchta et al., 2019). Its tolerability and paucity of side effects make CBD (Machado Bergamaschi et al., 2011) an attractive option for patients with dementia. We present a case where CBD was successfully used as a treatment for awake bruxism.

Materials and methods

This subject was referred to the Memory and Aging Center at the University of California, San Francisco, with a clinical diagnosis of FTD and enrolled in a large research study called "Frontotemporal Lobar Degeneration: Genes, Images and Emotions." As part of this study, he underwent a neurological exam with a neurologist and a neuropsychological assessment with a trained neuropsychologist. T1-weighted MP-RAGE images were acquired on a 1.5-T Siemens Magnetom VISION system. The patient signed a consent form approved by the UCSF human protection committee.

Results (case report)

A 52-year-old right-handed man with 16 years of education and a history of repetitive concussive and subconcussive head trauma episodes presented to the clinic with a 4 year history of behavioral and cognitive changes.

At baseline, he was hardworking, family oriented, thoughtful, kind, and loving. His first symptoms appeared in 2015 when he presented with apathy and stopped caring about the upkeep of his house. At the same time, he exhibited executive dysfunction, and he made mistakes with bills, leading to the loss of his job. His symptoms progressed to include disinhibition, loss of empathy, compulsions, and hyperorality. He talked inappropriately to strangers, watched television instead of engaging with his siblings during family gatherings, compulsively visited his brother's house, on one occasion 25 times in a day, and had an increased interest in sweets.

In October 2016, he presented with daily retroocular pain and severe bruxism. The teeth clenching was audible to people around him and resulted in significant changes in his teeth alignment and an underbite. In 2018, he moved to a different state after losing his house due to financial mistakes. In his new home, he was perceived as more anxious and impulsive. The bruxism worsened. He lost his driver's license and walked 10 miles per day and lost 20 pounds despite overeating. In

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addition to his behavior changes, during the year prior to presentation he developed difficulty with language including anomia, semantic paraphasias, and early semantic loss. He became disabled for instrumental activities of daily living and required supervision or assistance with basic tasks, including bathing, dressing, and grooming.

Before coming to UCSF, the patient was initially diagnosed with depression and anxiety as well as post-traumatic stress disorder (PTSD) related to turbulent adolescence. He started taking naltrexone following the PTSD diagnosis, but his family did not notice a clear benefit. He took several SSRIs (sertraline, fluoxetine, paroxetine, and citalopram) as well as aripiprazole until the summer of 2018 with a mild response. He then received divalproex sodium and lithium for his behavioral symptoms with a moderate response. In 2019, he received botulinum toxin A injections for his bruxism which decreased by 90% for about 6 weeks and then increased back to 50%. He then started using a CBD capsule containing 4.8 mg of CBD and 0.31 mg of THC in the morning and the grinding was almost completely relieved after this intervention.

The patient's bedside mental status testing was notable for poor recall of recent events, semantic paraphasias, and semantic loss with slight oral buccal apraxia but preserved motor speech. During neurological examinations, the cranial nerve exam showed normal eye movements but abnormal slight facial weakness, right eye ptosis, and asymmetric nasolabial folds. Dysarthria was absent. Motor exams revealed paratonia but no parkinsonism and normal bulk without fasciculations. He had no cerebellar dysfunction and a normal gait. Neuropsychological testing revealed moderate deficits in executive function tasks with mild deficits in memory and language function and sparing of visuospatial function. Brain imaging showed marked bilateral frontotemporal atrophy. A diagnosis of bvFTD was made.

At the time of this report, the patient's bruxism had remained under control for 6 months.

Discussion

This single case shows that CBD might have efficacy for bruxism in non-Alzheimer´s syndromes such as FTD. Awake bruxism has been observed in patients with FTD (Kwak et al., 2009). The underlying mechanism might be a dopaminergic deficiency. Patients with FTD present a loss of presynaptic dopaminergic neurons, reduced dopamine transporter binding, and abnormal dopamine receptor binding in the nigrostriatal pathways (Murley & Rowe, 2018). Interactions between the dopaminergic and endocannabinoid systems are hypothesized to enable phytocannabinoids such as CBD to influence movement. This extract from *C. sativa* has several molecular targets. It antagonizes the action of CB1 and CB2 receptor agonists and acts as an inverse agonist of these receptors (Pertwee, 2008) (Laprairie et al., 2015) (Martínez-Pinilla et al., 2017). CBD is also an agonist of TRPV1 and, in parallel, inhibits the enzymatic hydrolysis and the uptake of anandamide (Peres et al., 2018). These action mechanisms might contribute to normalizing dopaminergic transmission and reducing bruxism. Additionally, CBD has a local myorelaxant effect on the masseter muscles when administered topically compared to placebo as shown by Nitecka-Buchta et al. (2019).

In this patient, another neurotransmitter that might have been involved in the awake bruxism is serotonin. It has been hypothesized that SSRIs modulate serotonergic action on the mesocortical neurons arising from the ventral tegmental area, causing a physiological dopaminergic deficit that leads to bruxism (Kishi, 2007). Also, they can cause dystonia through an inhibitory effect of serotonergic inputs on the dopaminergic pathways of the striatum (Raveendranathan & Rao, 2015). The endogenous cannabinoid system reduces central serotonin release through the activation of CB1 receptors (Mackie, 2005). Blocking these receptors with CBD could potentially enhance the dopaminergic deficit. Conversely, CBD has an additive or synergistic effect, increasing serotonin levels when administered concomitantly with SSRIs. Yet, CBD is less effective in modulating serotonin levels when serotonin levels in the central nervous system are low (Sales et al., 2018).

The lasting effects of CBD on bruxism observed in this patient still need evaluation in a placebo-controlled study. However, we present a relatively benign therapeutic alternative for a symptom that has been understudied in patients with FTD and that, as in this case, can negatively impact the health and quality of life of the patient and the family.

Disclosure statement

No potential conflict of interest was reported by the authors.

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