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ABSTRACT: Introduction: Major depressive disorder (MDD) is a highly prevalent and often debilitating condition with a vast impact on modern societies worldwide. Although it interferes significantly with functioning, MDD is frequently unresponsive to conventional treatment approaches and pharmacotherapy failure has been reported in approximately one third of patients. Current knowledge of the exact underlying disease mechanisms is insufficient, and may thus largely contribute to such therapeutic limitations. Optogenetics, a novel study field employing the expression of genetically-encodable light-sensitive proteins in specific cell types, circumvents the limitations of other forms of neuromodulation and enables temporally precise, bidirectional control of cellular activity in well-defined neuronal populations. This strategy has been used successfully to dissect neural pathways and circuitries involved in complex mental diseases such as MDD.

METHODS: A systematic literature search was conducted using the terms "Optogenetics", "Depression" and "Major depressive disorder" on the databases MEDLINE, LILACS, SciELO, Pubmed and BIREME. Inclusion criteria were adopted: articles published in the English language from 1971 (description of bacteriorhodopsin as a light-activated regulator of transmembrane ion flow) to 2017 and articles based on experimental studies were selected.

RESULTS: By using highly validated animal models based on the exposure of phenotypically susceptible rodents to different forms of chronic stress, researchers have been able to reproduce the hallmark symptoms of Depression as well as the histopathological abnormalities found in human brain specimens post-mortem. Several brain regions and neuron populations involved in MDD have been identified by use of a variety of molecular resources including viral vectors, genetically engineered animals, multiple promoters and bacterial opsins. Important areas of dysfunction underlying depression including the medial prefrontal cortex, the ventral tegmental area, the nucleus accumbens, the hippocampus and the basolateral amygdala have been investigated by using optogenetic neuromodulation, yielding new insights into the pathological processes underlying MDD. Researchers have been able to pinpoint affected circuitries and employ time-precise light modulation to successfully revert symptoms of MDD, restoring normal function. It is important to highlight that although promising, studies using optogenetics are controversial, largely due to the variable set tools, models and tests employed in research.

CONCLUSION: Light modulation using optogenetics has greatly aided to establish accurate models to unveil the neurobiological basis of Depression. Further research will continue to help build more complete pathophysiological constructs and pave the way for new treatment strategies.

Keywords: Optogenetics, Neuromodulation, Depression, Major Depressive Disorder.

23
"To die, to sleep – to sleep, perchance to dream..." Inhibition of Nightmares with Pramipexole: A Possible Treatment for PTSD

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ABSTRACT: Introduction: The association of sleep disorders and post-traumatic stress disorder (PTSD) is almost universal. Nightmares are not only one of the most commonly associated but also featured as a diagnostic criterion for PTSD. PTSD-related nightmares are particularly distressing, may impair functioning and increase risk of suicide. No specific pharmacologic agent has been demonstrated to impair dreaming. Inhibition of PTSD-related nightmares with pramipexole has not heretofore been described. Such a case is presented.

METHODS: Case study - This 60 year-old male with PTSD and trauma-related nightmares upon introduction of pramipexole 0.5 mg PO qHS for Restless Leg Syndrome (RLS) had total elimination of dreams, which recurred upon discontinuation of this agent as a result of insomnia and increased anxiety. A lower dose of 0.375 mg qHS provided optimal RLS-symptom control and overall improved tolerance despite nightmare recurrence.

RESULTS: Abnormalities on Neurological examination: Recent recall: 2 of 4 objects without improvement with reinforcement. Able to spell the word "world" forwards but not backwards. Abstract thought impaired. Chemosensory testing: Anosmia and normogeusia. Motor: Drift: mild right pronator drift with right cerebellar spooning and right abductor digiti minimi sign. Reflexes: 3+ brachioradialis and biceps bilaterally,

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absent ankle jerks. Other: CT scan with and without contrast: normal.

DISCUSSION: Nightmares related to PTSD may occur during Rapid Eye Movement (REM) sleep and non-REM sleep. Underlying sympathetic activation may lead to disruptive motor behavior similar to that seen in REM sleep behavior disorder. The exact mechanism of action by which inhibition of dreams occurred with use of pramipexole is unclear. Such a response is consistent with prior documented evidence of REM sleep suppression with low-dose pramipexole such as it's efficacy in reducing the intensity and frequency of nightmares and dream enactment related to REM sleep behavior disorder. Further research on therapeutic interventions that target nightmares directly may be beneficial for the management of patients with PTSD.

Key words: PTSD, Pramipexole, Nightmares

24
CerefolinNAC Therapy-Induced Dysgeusia

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ABSTRACT: Introduction: CerefolinNAC (CFLN-NAC) is a prescription medical food reported to help with mild to moderate cognitive impairment [Pamlab 2017]. It contains L-methylfolate calcium (6 mg), methylcobalamin (2 mg), Schizochytrium (90.3 mg), and N-acetylcysteine (NAC) (600 mg) [Pamlab 2017]. However, dysgeusia secondary to CFLN-NAC therapy has not heretofore been described.

METHODS: A 64 year-old female presented with an eight year history of progressively decreased ability to smell and taste of unknown origin. CFLN-NAC was prescribed off-label to treat her hypogeusia and hyposmia. Three days after treatment initiation, her taste sensations gradually returned and she was able to describe food as bitter, salty, sour and sweet. Also, she was able to decipher the taste of different nuts, such as almonds, macadamia, pecans, and peanuts at baseline. However, her taste sensations became distorted and she was unable to distinguish specific foods. She reported that most food tasted bland, but she was still able to sense textures of various foods describing them as, "crunchy, but without taste." She denied any oral pain, xerostomia, hot flashes, and psychological distress. CFLN-NAC was continued for three months and her hypogeusia improved from 20% to 80%. Her dysgeusia persisted, but remitted once CFLN-NAC was discontinued.

RESULTS: Abnormalities in physical examination: General: scalloped tongue, decreased blink frequency, and hypokinesia. Cranial Nerve (CN) Examination: Olfaction (CN I) Testing: Alcohol Sniff Test: 8 (hyposmia). Pocket Smell Test: 2 (hyposmia). Olfactometer Identification Test: Left: 5 (anosmia); Right: 12 (hyposmia). CN III, IV, VI: saccadization on horizontal eye movement. Motor Examination: hypokinetic movements and 1 + cogwheel rigidity in bilateral upper extremities. Drift Test: bilateral abductor digiti minimi signs with cerebellar spooning. Reflexes: absent patellar and Achilles bilaterally. Hoffman's Reflex: present bilaterally. Other: Magnetic resonance imaging (MRI) of the brain with contrast was unremarkable.

CONCLUSION: When treating taste impairments, vitamins and minerals have been found to enhance the effect of non-injured nerves, but they do not repair damaged nerves. The presence of a scalloped tongue may suggest nerve injury of unknown proportion, and can either diminish or alter taste. CFLN-NAC may have enhanced the gustatory stimulus of the non-injured nerves. This transient increase could have either caused her dysgeusia or possibly unmasked the dysgeusia secondary to a scalloped tongue. Notable impairments found in her exam evince Parkinson's disease as a possible etiology, but structural abnormalities were not seen on brain MRI, making this unlikely. Conversely, the relatively rapid resolution after terminating CFLN-NAC strongly suggests that this is not merely a coincidence, but rather an origin. Those initiated on CFLN-NAC should be queried for new onset of dysgeusia and warrant other treatment options.
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25
Ventriculoperitoneal Shunt as a Meteorologist: Medtronics Shunt Headaches Vaticinating Climatic Perturbation

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