schizophrenia and epilepsy, suggesting that the relationship between the 2 disorders occurs at the level of the genome.

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Report of a Case | A man in his late 60s with a 15-year history of PD (Hoehn and Yahr score, 3) and 20-year history of RBD presented with worsening DEB. While the patient’s daytime motor symptoms improved following deep brain stimulation, episodes of DEB became progressively more violent, resulting in assault on his wife and self-injurious behaviors. Yelling occurred multiple times per night. Violent behaviors were reported every other night, such as punching through walls or striking furniture (Figure). Initial polysomnography demonstrated obstructive sleep apnea (OSA), with an Apnea Hypopnea Index score of 8.5. Given the mild severity of OSA, risk of interaction with continuous positive airway pressure device during DEB, and patient preference, conservative treatment was initiated.

Violent behaviors persisted despite treatment with standard agents (clonazepam and melatonin). The patient’s maximum tolerated dose of clonazepam was 1 mg, as higher doses resulted in drowsiness. The addition of melatonin, titrated to 12 mg, also failed to control symptoms. Prazosin, ramelteon, cyproheptadine, and eszopiclone were subsequently added. Despite this extensive regimen, the violent behaviors increased in frequency. One severe episode resulted in a head laceration after striking the wall, requiring emergency department evaluation with unremarkable neuroimaging. Given the persistent threat of violent, potentially fatal behaviors, a trial of sodium oxybate was initiated under supervision during polysomnography. Dosing was titrated to 2.5 g twice nightly, which was based on a case report1 and guidelines for treatment of RBD.2 Treatment with sodium oxybate resulted in complete cessation of DEB episodes for 2 months, representing a reduction from the patient’s previous frequency of nearly every other

Figure. Rapid Eye Movement Behavior Disorder and Violent Events

Despite removing all objects from the bedroom and laying the mattress onto the floor, the patient continued to strike out at walls and the ground, causing self-injury and damage to property during dream enactment behavior.

OBSERVATION

A Case of Rapid Eye Movement Sleep Behavior Disorder in Parkinson Disease Treated With Sodium Oxybate

Rapid eye movement (REM) sleep behavior disorder (RBD) is characterized by altered dream mentation, vocalizations, and dream enactment behavior (DEB). The motor behavior is often aggressive, resulting in potential injury to the patient or bed partner. Clonazepam and melatonin are considered standard treatments. Limited data exist on the use of alternative agents when standard medications fail. We report a case of successfully treated RBD in advanced Parkinson disease (PD) with sodium oxybate in a patient refractory to both standard and alternative pharmacologic agents.

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night. He subsequently had 3 breakthrough episodes during the first half of the night and his first dose was increased to 3 g, with no further violent episodes reported to date. Importantly, the patient tolerated sodium oxybate well, without developing adverse medication events or significant worsening of his OSA. Repeat polysomnography on sodium oxybate demonstrated an Apnea Hypopnea Index score of 12.8, but again, the patient preferred to avoid a trial of continuous positive airway pressure given his improvement in DEB.

The Stanford University institutional review board determined that this project did not meet the federal definition of research with human participants, and institutional review board approval was not required.

Discussion | Rapid eye movement sleep behavior disorder is characterized by DEB, which can result in injury. Limited data exist on the use of alternative agents when standard medications fail in both idiopathic RBD and RBD with PD. Prazosin, an α1-adrenergic antagonist, has documented efficacy in patients with posttraumatic nightmares and disruptive nocturnal behaviors. In one case report of refractory idiopathic RBD, sodium oxybate effectively controlled dream-enactment behavior, with sustained improvement during 12 months of follow-up. Additionally, sodium oxybate was shown to improve daytime sleepiness in PD in an open-label study. Our patient experienced improvement in DEB with sodium oxybate. He tolerated the medication well, without development of serious adverse events.

Conclusions | To our knowledge, this is the first reported case of a patient with advanced PD and severe refractory RBD treated safely and successfully with sodium oxybate. While the exact mechanism by which sodium oxybate suppresses RBD is unclear, this medication may be of benefit to a patient with refractory RBD at risk for serious injuries. The findings from this observation and previous studies suggest the importance of future research to examine the potential therapeutic role of sodium oxybate in PD and RBD.

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COMMENT & RESPONSE

Computer-aided Therapeutics in Treating Autoimmune Encephalitis

To the Editor | I read with great interest the article in JAMA Neurology by Joubert and colleagues that detailed the clinical features of autoimmune encephalitis (AE) mediated by α-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid receptor antibodies. In this regard, the father of modern-day AE research, Josep Dalmau, and his colleagues have published numerous articles that define this category of diseases. Of these disorders, the best characterized, perhaps, is the anti-N-methyl-D-aspartate receptor encephalitis receptor (NMDAR) variant, which is the prototypical AE syndrome. Despite these rapid advances, treatment options for patients with AE remain rather mundane and target-nonspecific. Unfortunately, neurology as a science is driven by discovery rather than therapy—this gap is probably narrowing, if slowly.

A publication of the NMDAR structure revealed x-ray crystal structures of the GluN1/GluN2B NMDAR with the allosteric inhibitor Ro25-6981, partial agonists, and the ion channel blocker MK-801. Receptor subunits demonstrating extensive interactions between the amino terminal and ligand-binding domains, as well as transmembrane domains, were identified. However, to date, and with such specific targets being implicated in disease pathogenesis, not a single in silico technique or method has generated any ligand/peptide or protein that can silence NMDAR antibody. It is time to change that paradigm and deliver some cleverly engineered molecules that can specifically target antibodies involved in AE.

After the discovery of the 3-dimensional structure of human immunodeficiency virus (HIV) protease, an enzyme essential to the HIV reproductive cycle, computational researchers designed molecules in silico to precisely fit the shape of the enzyme’s active site, and the resulting drugs, potent inhibitors of HIV protease and the HIV life cycle, were brought to market in record time and revolutionized the treatment of HIV/AIDS. Hopefully, a similar strategy will bring targeted therapies to AE that will benefit patients.

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