

Treatment of REM Behavior Disorder with Acetylcholinesterase Inhibitors

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Introduction: The author previously reported 3 cases of REM sleep behavior disorder (RBD) that improved by Treatment with acetylcholinesterase inhibitors (Neurology 2000 Sept. 26;55(6):870-1). Now a series of ten cases of RBD are presented that were similarly treated with acetylcholinesterase inhibitors and all of whom also demonstrated improvement in parasomnias. It has become clear that treatment of RBD with acetylcholinesterase inhibitors is a logical and effective treatment approach that can be utilized without the side effect profile of more customary approaches with benzodiazepines.

Methods : Patients ranged from 48 to 70 yrs old with an average age of 63.9 (5F / 5M). Treatment was with the acetylcholinesterase inhibitors donepezil (Aricept) or rivastigmine (Exelon), typically used in the treatment of Alzheimer's disease. Patients that were also found to have OSA or PLMS were included in this study if they continued to exhibit REM parasomnias after Tx of the OSA and PLMS. Duration of Tx at the time of this assessment ranged from 4 to 18 months, ave of 11.5 months. Responses to treatment were based on clinical follow-up, primarily from bed partners observations.

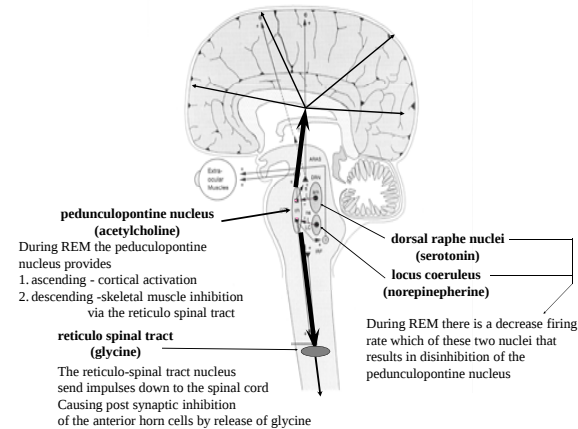
Results : All of the patients placed on acetylcholinesterase inhibitors demonstrated a significant improvement in the magnitude of parasomnic events and/or frequency of observed events. Events in all patients reduced from almost nightly elaborate parasomnias down to subtle movements that were not deemed disturbing, and not on a nightly basis, with only occasional more elaborate breakthrough events. Dosages of medications were as high as 20 mg for donepezil, and if side effects, such as diarrhea developed, then they were switched to rivastigmine and dosages went as high as 6 mg qhs (not bid). Of note many patients with RBD who were also found to have OSA and / or PLMS demonstrated drastic improvement in their parasomnias by treatment of the OSA / PLMS alone and were not included in this study because further treatment was not necessary. Clonazepam was not initiated in any of our patients, but two came to our center already on clonazepam with persistent REM events. These patients were still demonstrating REM parasomnias in spite of Clonazepam usage, but Clonazepam was not withdrawn in these patients. They also demonstrated improvement with the addition of the acetylcholinesterase inhibitors.

Conclusion : This study provides additional evidence that RBD can be treated by enhancing cholinergic neurotransmission. There is considerable evidence that neurons located in the pedunculopontine nuclei play a major role in producing REM sleep and the related atonia of REM sleep. This region sends descending impulses to activate reticulospinal tract nucleus. The reticulo-spinal tract nucleus sends impulses down the spinal cord to the anterior horn motor neurons releasing glycine that causes post synaptic inhibition of motor neurons. Acetylcholinesterase inhibitors work by enhancing the cholinergic activity of the pedunculopontine nucleus to restore the failing network during REM that leads to return of the post synaptic inhibition of the anterior horn cells. GABA neurons also play a role in the muscle atonia of REM, possibly by an interneuronal activity that is involved in this same system leading to post synaptic inhibition of the anterior horn cells. However, treatment to enhance this pathway with clonazepam is frequently accompanied by sedating side effects as well as all of the other long term negative effects on sleep associated with clonazepam. Therefore, it would be reasonable to consider the use of acetylcholinesterase inhibitors as a first line treatment in patients with RBD and then switching to clonazepam if adequate clinical response is not achieved.

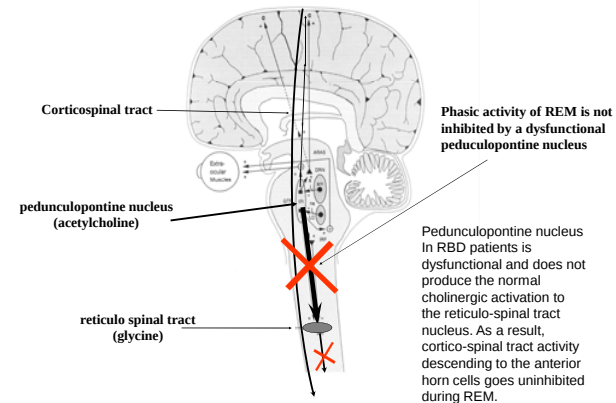
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Brainstem regulation and control of REM



REM Behavior Disorder



REM Atonia reestablished in REM Behavior Disorder

