Rapid Eye Movement Sleep Behavior Disorder: What Is Known and What Should Be Studied

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Rapid eye movement sleep behavior disorder (RBD), characterized by vivid striking dreams and dream-enacting behaviors, can be classified as both young and old. RBD is young in that it was conceptualized as a distinct clinical disorder by Schenck et al. [1] in 1986, and it is old because it mainly affects older people. In Korea, an RBD case, confirmed by polysomnography, was reported in 1994. REM sleep without atonia (RWA) on the polysomnography is requisite for RBD diagnosis. Currently, qualitative analysis of RWA is used as RWA quantification is burdensome and time-consuming. Notably, patients complaining of vigorous dreams and violent behaviors are occasionally diagnosed with obstructive sleep apnea or show no definite RWA, which may negate diagnosis based on clinical history or RBD questionnaires.

Regarding pathophysiology, dopaminergic degeneration was investigated because of its close relationship with alpha-synucleinopathies. Studies using dopamine transporter (DAT) positron emission tomography (PET) or single photon emission computed tomography (SPECT) showed that dopamine (DA) dysfunction might be implicated in RBD. However, several findings suggest that other pathogenic processes can be involved; 1) in managing RBD symptoms, effectiveness of clonazepam with no influence on DA and little effect of dopaminergic drugs, 2) appearance of RBD in narcoleptic patients, 3) young RBD patients without progression to alpha-synucleinopathies, and 4) RBD symptoms induced by antidepressants.

Clonazepam is widely prescribed for the control of RBD symptoms, even if there are few randomized controlled trials on its use and it has not been demonstrated that it is superior to other benzodiazepines. Clonazepam is effective in 80% to 90% of cases with adjuvant therapy such as carbamazepine and zolpidem. Melatonin, having more tolerable side effects but less efficacy than clonazepam [2], is also used singly or in combination with clonazepam. Managing vigorous and violent behaviors is required to prevent injuries to patients themselves and their bed partners, but RBD treatment cannot modify the progression to alpha-synucleinopathies.

Compared to other sleep disorders, much attention is being paid to the clinical course of RBD rather than its treatment. Studies from Spain and Canada have reported the risk of developing neurodegenerative disorders to be about 30% at 5 years and up to 80% at 10 years from the time of RBD diagnosis. Lower phenoconversion rates in Japan, China, and Korea (35.5% at 10 years and 56.5% at 14 years) might suggest racial or geographical differences in conversion [3]. Biomarkers of risk factors for phenoconversion include [4-6]: older age, disease duration, motor dysfunction, mild cognitive impairment, electromyographic tonic activity, and decreased putamen DAT density. These markers can be used to classify and select patients for clinical trials of neuroprotective agents. It will take 2–3 years to complete clinical trial of therapies whose effects are demonstrated in RBD animal models [7].
ics or anti-inflammatory drugs, which have been tested for their efficacy in improving symptoms of Parkinson’s disease, can be candidates for RBD studies. In consideration of the high phenoconversion rate and the absence of available course-modifying agents, the anxieties and worries of RBD patients and their families need to be understood and psychologically supported.

For that, these research issues will be addressed further: 1) To develop neuroprotective agents for delaying or modifying the neurodegeneration process, establishing animal models [8] showing RBD symptoms and converting to alpha-synucleinopathies should be the first step; 2) Follow-up of isolated RBD patients with long-disease duration might give us insight into the heterogeneity of RBD progression and pathogenesis; 3) The cognitive decline related to long-term use of clonazepam is frequently questioned by patients and clinicians, and needs to be studied and addressed; and 4) For reliable automatic quantitative analysis of RWA, which is expected to give valuable information, artificial intelligence can be adopted.

Conflicts of Interest
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REFERENCES