

REM sleep behavior disorder (RBD) should be considered as a precursor and marker for alpha synucleinopathies and promote therapeutic intervention.

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Rapid eye movement sleep behaviour disorder (RBD) is characterized by dream enactment and complex motor behaviours during rapid eye movement (REM) sleep and loss of normal REM sleep muscle atonia during polysomnography. The prevalence of idiopathic RBD (iRBD) was previously estimated to be between 0.38% and 0.5% within the general population; probable RBD (without polysomnographic confirmation) is likely even more frequent, affecting 5%-6.8% of the older general population after age 60-70 years. Postmortem evidence shows that some RBD patients have degeneration within the areas that control REM sleep and have Lewy bodies and neurites in these areas (synucleinopathy was the underlying pathology in 94% of autopsied patients in the largest multicenter autopsy series of RBD). Therefore, it seems most likely that RBD is caused by synucleinopathic degeneration. Consistent with early neurodegeneration, patients with RBD demonstrate subtle motor, cognitive, and autonomic impairments. Approximately 50% of patients with spontaneous RBD will convert to a parkinsonian disorder within a decade. Ultimately, nearly all (81%-90%) patients with RBD develop a neurodegenerative disorder. Among patients with Parkinson disease, RBD predicts a non-tremor-predominant subtype, gait freezing, and an aggressive clinical course. RBD arises from degeneration of the circuits that control healthy REM sleep and the more classic motor and cognitive symptoms associated with synucleinopathies develop as degeneration spreads rostrally into the brain structures that control these behaviors. Although this idea remains speculative, it nonetheless fits well with Braak's classic staging model of Parkinson's disease pathogenesis, which proposes that neurodegeneration starts in the brain stem before ascending rostrally. Neuro-protective strategies for targeting α -synuclein in RBD could be beneficial in slowing or even halting the progression of synucleinopathies.