Relation between rapid eye movement (REM) sleep behavioural disorder (RBD) and the onset of neurodegenerative disorders

Background

Questions:
- During sleep, the brain moves through different stages. One of these stages is REM sleep. During this phase, the eyes move rapidly in various directions. People enter REM sleep within the first 90 minutes of falling asleep and, as the sleep cycle repeats throughout the night, REM sleep occurs several times nightly. It accounts for approximately 20 to 25% of an adult's sleep cycle, and over 50% of an infant's. Most dreams occur during REM sleep, and it is thought to play a role in learning, memory, and mood.
- REM parasomnias includes nightmare disorder, sleep paralysis and REM-sleep behavioural disorder (RBD).
- RBD results from loss of normal muscle atonia during REM sleep [REM sleep without atonia (RSWA)], which can lead to disruptive and potentially injurious dream-enactment behaviours. Usually occur one or two episodes per night, essentially in the second half of the night (when REM sleep progressively lasts longer). Typically, patients have the eyes closed while performing their dreams and rarely leave the bed, when they do so, they usually wake-up. Diagnosis is confirmed by polysomnography (PSG) recording (increased phasic or tonic muscle activity seen on electromyogram). This disorder affects more than 1% of adults older than 40 years, and in middle-aged and older adults, it is a prodromal symptom of neurodegeneration until proven otherwise.

Aim and Methods

- Review the link (risk factor of developing the disease versus initial clinical manifestation of it) between RBD and α-Synucleinopathies, severe neurological disorders, such as Parkinson Disease (PD), Multiple System Atrophy (MSA) and Lewy Body Dementia (LBD).
- A comprehensive search was conducted on the principal medical databases including MEDLINE, Cochrane Library and PubMed. Search terms covered 2 concepts: (1) [REM sleep behaviour disorder] AND (2) [neurodegenerative diseases OR sleep disorders].

Discussion

- Studies found positive predictive values for RBD indicating a synucleinopathy varying from 58% to 100.0%, gradually increasing over time. Clinically suspected and PSG-proven RBD occurs with disproportionally greater frequency in Multiple System Atrophy (MSA), Parkinson Disease (PD), and Lewy Body Dementia (LBD) compared to other neurodegenerative disorders [among these 3, they are ordered by decreasing frequency]. This is in favour that RBD is a manifestation of an evolving synucleinopathy. Within the pathophysiologically hypotheses proposed to explain REM sleep disorders in Synucleinopathies, emphasis is placed on the role of cholinergic neurons of the pedunculopontine and laterodorsal tegmental nuclei, structures shown to be particularly impaired in PD.

Conclusion

- The vast majority of patients initially diagnosed with RBD eventually develop a synucleinopathy, often after a prolonged interval (5 to 29 years). The role of dopaminergic agents (DA), used in the treatment of PD and related disorders, in the appearance of RBD is not negligible. Nevertheless, it cannot explain on their own the presence of REM sleep disorders in PD and other related disorders.
- Actual evidence is in favour that RBD is a manifestation of an evolving synucleinopathy and finding putative neuroprotective actions or agents to delay the emergence of, or halt the progression to Synucleinopathies are necessary.

Bibliography


1 - Centro Hospitalar de Setúbal