REM SLEEP BEHAVIOR DISORDER: IN SEARCH FOR NEUROPSYCHOLOGICAL AND ELECTROPHYSIOLOGICAL BIOMARKERS IN NEURODEGENERATION

Rapid Eye Movement (REM) sleep Behavior Disorder (RBD) is a REM sleep parasomnia characterized by the enactment of unpleasant dreams and vigorous behaviors caused by the loss of physiological atonia during REM sleep, which can cause injuries to the patients or their bedpartners [1]. RBD can manifest as isolated (iRBD) when it occurs in the absence of any other disorder, or as secondary when associated with another neurological disease. However, even iRBD has been demonstrated to predate the insurgence of neurodegenerative diseases, in particular α-synucleinopathies (a class of neurodegenerative diseases characterized by an abnormal accumulation of a protein, namely α-synuclein, in neurons, glia cells and nerve fibres) [2] by many years, with longitudinal studies showing a conversion rate > 80% in a decade or more [3; 4]. In the light of these findings, it becomes of utmost importance to find sensitive biomarkers for a timely prediction of phenoconversion.

Several evidence reported the presence of neuropsychological impairment in iRBD patients. However, the heterogeneity of results and the frequent employment of cross-sectional design severely limit the predictive value of this finding. Among neuropsychological biomarkers, deficits in verbal and non-verbal memory, attention, executive function and visuospatial abilities have been reported in iRBD. In particular, the presence of visuo-spatial and executive dysfunction suggest a cognitive profile comparable to those observed in dementias associated to α-synucleinopathies. A recent study underlined the importance of neuropsychological assessment in predicting specific phenotype of conversion. In particular, patients who developed Dementia with Lewy Body (DLB) presented clear impairment in attention and executive functions 6 years before dementia onset [5].

In addition, electrophysiological studies have been employed to recognize signs of neurodegeneration in iRBD patients. Specifically, polysomnographic (PSG) and electroencephalographic (EEG) quantitative analysis, EEG connectivity, Event-Related Potentials (ERP), REM Sleep Without Atonia (RSWA) quantification have been investigated, providing interesting results. However, not all these methods were used in longitudinal researches therefore limiting the interpretation of the results. Among these variables, EEG slowing (both during wake and sleep) [6] and increased RSWA have been identified as the most efficient in predicting neurodegeneration [7].

In this project, multimodal approach will be used to specifically characterize RBD patients’ neuropsychological and electrophysiological profile in order to predict phenoconversion trajectories. Therefore, we aimed to: (1) provide a comprehensive neuropsychological assessment; (2) perform an ERP study with an attentional task (i.e. Posner cueing task); (3) perform functional connectivity analysis during both attentional task, resting wake and sleep; (4) carry out quantitative and qualitative PSG macro- and micro-structure analysis (slow wave activity, K-complexes, sleep spindles, RSWA).

A large number of iRBD patients (40 patients) will be prospectively recruited for this study along with the possibility to work also on our retrospective cohort. A further advantage and outstanding opportunity for the PhD candidate will be to work in collaboration with the “In vivo structural and molecular neuroimaging Unit” for a more specific evaluation of fluorodeoxyglucose positron emission tomography (FDG-PET) biomarkers. The design of this study is essentially longitudinal and it will be articulated following the 3-year PhD structure. Therefore, a baseline assessment and a follow-up evaluation (mean 1.5 years) of each RBD patients will constitute the foundation of this project. During the first year, patients’ enrollment, acquisition of neurophysiological and neuropsychological data as well as planning of data analysis will be conducted by the student. During the second year, further patients’ enrollment, follow-up evaluation of a first set of patients and analysis of data will be performed. The third year will be fundamental for finalizing follow-up assessment and data analysis, interpreting results in the light of previous literature and thesis writing.

Our ward and laboratories offer the opportunity to investigate this topic from a multidisciplinary perspective comprising neurophysiological recordings and analyses, neuropsychological assessments and paradigms from experimental psychology.


