P55

Circadian rhythm in Parkinson's disease, from chronotype to phenotype: a clinical and biological study

Massimo Marano[1,2], F. Motolese[1], M. Rossi[1], A. Magliozzi[1], M. Iannizzotto[1], G. Sergi[1], A. Casamassa[3], A.L. Vescovi[3], V. Di Lazzaro[1], J. Rosati[3]

[1]Neurology, Neurophysiology and Neurobiology Unit; University Campus Bio-Medico of Rome, Rome, Italy
[2]Fondazione Alberto Sordi, Rome, Italy
[3]CSS Mendel Institute of Human Genetics, IRCCS Casa Sollievo della Sofferenza, Rome, Italy

Introduction: Alterations of the circadian rhythm might play a role in the pathobiology of neurodegenerative diseases. Symptoms of sleep and wakefulness impairment are prominent in Parkinson's disease (PD), being also crucial disease milestones. However, the relationship between the circadian cycle and the clinical and biological disease profile has not been fully elucidated so far [1].

Objective: To explore the relationship between the PD chronotype and the phenotype in a clinical and biological translational setting.

Methods: 50 non demented PD patients entered a cross-sectional and longitudinal study collecting data on chronotype (MEQ-SA), sleep and wakefulness quality (PDSS, RBDQ, ESS), motor and non-motor performances (UPDRS, Hoehn & Yahr, NMSQ, PDQ39), heart rate variability as an index of autonomic nervous system functioning and prospective PD associated events (eg, falls). Five samples of skin fibroblasts obtained by PD patients were cultured and compared to 5 matched controls in a case-control study exploring the expression of the circadian rhythm genetic regulators and the cell growth [2].

Results: PD patients manifested 2 main chronotypes: "moderate morningness" (n=28) and "intermediate" (n=16). No clear association intercurred between the chronotype, the sleep and the wakefulness quality. The "intermediate" group showed (i) a higher Hoehn & Yahr and a worse disease profile overall in various motor and non-motor parameters, (iii) a higher rate of falls after 1 month of follow-up and (iii) a lower HRV parasympathetic activity. Cultured fibroblasts showed a different pattern of expression of the CLOCK-BMAL1 system compared to controls.

Conclusions: Our observations suggest that there is a fascinating interplay between the chronotype and the PD phenotype, which deserves further attention. Moreover, the presence of an altered CLOCK-BMAL1 pattern in fibroblasts is a cue that points toward a role of the circadian rhythm deregulation in the molecular pathobiology of the disease. A study replication on neuronal tissue is warranted.

References:

[1] Pacelli C, et al., 2019. Int J Mol Sci. 2019;20 (11):2772.
[2] Leng Y, et al. 2020 JAMA Neurol. 77 (10):1270-1278.