

## Letter to Editor

### Melatonin, and sudden unexpected death in parkinson's disease: do we have some good news?

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According to epidemiological studies conducted by the UN, the global population of elderly persons is estimated to further increase reaching 1.4 billion by 2030, 2.1 billion by 2050, and 3.2 billion by 2100 [1]. As life-expectancy is increasing, ageing is the most important risk factor for many neurodegenerative diseases driving both morbidity and mortality [1]. A recent review appropriately discussed the current knowledge about both sleep and circadian alterations in Parkinson's disease (PD) and provided recommendations regarding future research directions [2]. Despite recent advances in PD research, some issues have not been deeply debated.

PD is one of the most frequent age-related neurodegenerative disorders with an estimated prevalence increasing by >50% by 2030. However, mortality in PD is not frequently discussed in the neuroscientific community [3]. Generally, PD has a reduced life-expectancy because of its increased mortality compared to the general population [3]. Main causes of death in PD are pneumonia, cerebrovascular diseases, and

cardiovascular diseases. Additionally, sudden unexpected death in PD (SUDPAR) contributes to mortality in PD [3]. SUDPAR is defined as unexpected death of a PD patient without an evident cause on autopsy. Though causes of SUDPAR remain elusive [3], cardiac abnormalities and autonomic dysfunction seem to play key roles [3,4]. Whether age at onset, duration of PD, gender, motor severity and drug treatment (polypharmacy) contribute to the pathogenesis of SUDPAR [3], requires further investigations. Additionally, sleep disorders, such as central sleep apnea syndrome in PD, could be other possible risk factors [2].

Following these considerations, melatonin could be a specific biomarker relating to circadian dysfunction and SUDPAR. Recent studies have shown that melatonin is involved in the regulation of the cardiovascular system. Furthermore, melatonin has cardio-protective properties via antioxidant activity, anti-inflammatory properties, regulating blood pressure, or via anti-atherogenic effects. Moreover, melatonin protects against ischemia/reperfusion induced-arrhythmias in

animal studies. Studies in humans demonstrated that patients with heart failure have lower serum melatonin levels compared to the general population. Another important issue is the putative relationship between melatonin and sudden cardiac death (SCD). As previously reported, there are indications that SCD follows a circadian rhythm, which is inversely correlated with serum melatonin levels. Accordingly, SCD often occurs in the early morning, a time at which serum melatonin levels are low. Coincidentally, melatonin levels in the middle of the night are elevated, when the incidence of SCD is lowest.

Based on experimental and clinical evidence that clearly points to melatonin-mediated cardioprotection, it can be speculated that melatonin concentrations can be considered a potential biomarker for possible cardiac abnormalities in PD. In fact, well-designed studies have shown that melatonin concentrations can be considered as major markers of circadian phases in PD [2]. Since melatonin levels decrease substantially with age (Sahna2002) and heart failure is associated with low serum melatonin levels [5], we speculate that melatonin replacement therapy may attenuate the incidence of SCD especially in elderly and PD patients [5].

Overall, there is a need to improve impaired cardiovascular functions in PD and to prevent SCD or SUDPAR in PD but also to investigate the specific mechanisms of melatonin to improve cardiac functions.

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### **References**

1. Naja S, Makhoulf MM, Chehab MAH (2017) An ageing world of the 21st century: a literature review *Int J Community Med Public Health* 4: 4363-4369.
2. Mantovani S, Smith S. S, Gordon R, O'Sullivan J.D (2018). An overview of sleep and circadian dysfunction in Parkinson's disease. *J Sleep Res.*
3. Scorza F. A, do Carmo, A. C Fiorini, Nejm M. B, Scorza C. A et al. (2017). Sudden unexpected death in Parkinson's disease (SUDPAR): a review of publications since the decade of the brain. *Clinics* 72: 649-651.
4. Scorza F. A, Cavalheiro E. A, Scorza C. A, Ferraz H. B. (2016) Sudden unexpected death in Parkinson's disease: Perspectives on what we have learned about sudden unexpected death in epilepsy (SUDEP). *Epilepsy Behav.* 57: 124-125.
5. Sahna, E., Olmez, E., Acet, A. (2002). Effects of physiological and pharmacological concentrations of melatonin on ischemia-reperfusion arrhythmias in rats: can the incidence of sudden cardiac death be reduced? *J Pineal Res.* 32:194-198.