



## Correspondence

## Sudden death in Parkinson's disease: Unjustifiably forgotten



## A B S T R A C T

Parkinson's disease (PD) is one of the most common age-related neurodegenerative disorders. Epidemiological studies have demonstrated that PD is accompanied by high rates of premature death compared with the general population. The main causes of deaths are related to pneumonia and cardiovascular diseases. Importantly, it has also been recognized that some PD patients may eventually die unexpectedly and suddenly, referred as Sudden Unexpected Death in Parkinson's Disease (SUDPAR). Despite on-going PD research, there are still deficits in our knowledge about the risk factors, mechanisms and prevention of SUDPAR. By some means, current evidence suggests cardiac abnormalities and autonomic dysfunction plays an important role in SUDPAR. Thus, SUDPAR in patients with PD is a real phenomenon and translational studies should be carried out with the aim of elucidating this phenomenon.

In 1887, when the general medical practitioner James Parkinson from London published the first detailed clinical description of Parkinson's disease (PD), he could not imagine the eminent scientific breakthrough that would be achieved in PD research in the 130 years following his description [1]. In addition, James Parkinson could not assume that in the years following his discovery the world's populations would become older at an accelerated rate. According to official UN data, it is estimated that there are 1.4 billion elderly people in the world by 2030, 2.1 billion in 2050 and approximately 3.1 billion in 2100 [2]. Obviously, this increase in the elderly population in our society will increase the incidence and prevalence of neuropsychiatric diseases related to aging, in which PD will take a prominent place. In this sense, PD is the second most common age-related neurodegenerative disorder after Alzheimer's disease and entails a major burden in disability, comorbidities, stigmatisation, and even mortality [1,3].

Following this line of reasoning, the results demonstrated in the elegant article recently published by Zhang and colleagues evaluating the mortality of PD in China [4], stimulated our research group to discuss some aspects with emphasis on mortality in PD. Briefly, Zhang et al. identified a normal survival of patients with PD compared to the control population over ten years follow-up but also indicated that the postural instability gait disorder (PIGD) subtype is a potential predictor for poor outcome [4]. Importantly, during the ten years study period, 9.0% of PD patients died suddenly of unknown cause [4]. Why did the authors not emphasize this very relevant finding?

Recently, some studies have demonstrated that an increasing number of PD patients dies suddenly and unexplained, referred as "Sudden Unexpected Death in Parkinson's Disease" (SUDPAR) [3,5]. Considering that SUDPAR is infrequent, it is a real phenomenon that has attracted the interest of the neurological community since the 1970's [3,5]. Actually, there is no formal definition proposed by specialists for SUDPAR. However, SUDPAR could be didactically defined as an unexpected death in a patient with PD without any satisfactory explanation of death as determined by autopsy studies [3,5]. The epidemiological data of SUDPAR are not yet reliably available in the literature and there is an emerging need to recognize and rank the risk factors of SUDPAR. Currently, it has been suggested that duration of PD, gender, motor severity, sleep disorders, concomitant cardiac and

pulmonary disease, and drug treatment (polypharmacy) could be possible risk factors for SUDPAR, but these possibilities require further investigations in experimental and clinical studies [3,5]. Despite ongoing PD research, there are still deficits in our knowledge about the SUDPAR mechanisms. Current evidence preferentially cardiac abnormalities and autonomic dysfunction, because ~60% of PD patients have cardiovascular disturbances and because of the frequent autonomic dysfunction in PD [3,5]. While the specific risk factors and mechanisms are not yet defined, prevention of SUDPAR is crucial. Thus, cardiac monitoring of individuals with PD, especially in patients considered at high risk, is urgently recommended [3,5]. In doing so, repeated cardiac follow-up investigations should be carried out, including long-term blood pressure monitoring, electrocardiogram (ECG) recordings and echocardiography [5]. Finally and clinically relevant is that neurologists and their multidisciplinary team need to discuss the issue of SUDPAR in an appropriate way with PD patients and their relatives, addressing SUDPAR as an infrequent but serious, possible complication.

## Disclosure

The authors report no conflicts of interest.

## Acknowledgements

Our studies are supported by the following grants: FAPESP (Fundação de Amparo à Pesquisa do Estado de São Paulo); CNPq (Conselho Nacional de Desenvolvimento Científico e Tecnológico); Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES), AFIP (Associação Fundo de Incentivo à Pesquisa).

## References

- [1] W. Poewe, K. Seppi, C.M. Tanner, G. M Halliday, P. Brundin, J. Volkmann, A.E. Schrag, A.E. Lang, Parkinson disease, *Nat. Rev. Dis. Primers*. 3 (2017) 17013.
- [2] United Nations, Department of Economic and Social Affairs, Population Division, World Population Ageing 2015 (ST/ESA/SER.A/390), (2015) Available at [http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015\\_Report.pdf](http://www.un.org/en/development/desa/population/publications/pdf/ageing/WPA2015_Report.pdf), Accessed date: 20 June 2018.

<https://doi.org/10.1016/j.parkreldis.2018.08.012>

Received 21 June 2018; Accepted 24 August 2018

1353-8020/© 2018 Published by Elsevier Ltd.

- [3] F.A. Scorza, A. do Carmo, A.C. Fiorini, M.B. Nejm, C.A. Scorza, J. Finsterer, H.B. Ferraz, Sudden unexpected death in Parkinson's disease (SUDPAR): a review of publications since the decade of the brain, *Clinics* 72 (11) (2017) 649–651.
- [4] Y. Zhang, C. Wang, Y. Wang, Q. Xiao, J. Liu, J. Ma, H. Zhou, J. Pan, Y. Tan, S. Chen, G. Xu, G. Wang, Mortality from Parkinson's disease in China: findings from a ten-year follow up study in Shanghai, *Parkinsonism, Relat Disord* (2018), <https://doi.org/10.1016/j.parkreldis.2018.05.012> Epub ahead of print.
- [5] F.A. Scorza, A.C. Fiorini, C.A. Scorza, J. Finsterer, Cardiac abnormalities in Parkinson's disease and Parkinsonism, *J. Clin. Neurosci.* 53 (2018) 1–5.

Mariana B. Nejm<sup>a,b</sup>, Monica L. Andersen<sup>b</sup>, Sergio Tufik<sup>b</sup>,

Josef Finsterer<sup>c</sup>, Fulvio A. Scorza<sup>a,\*</sup>

<sup>a</sup> *Disciplina de Neurociência, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil*

<sup>b</sup> *Departamento de Psicobiologia, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil*

<sup>c</sup> *Krankenanstalt Rudolfstiftung, Vienna, Austria*

*E-mail address: mbnejm82@gmail.com (F.A. Scorza)*

\* Corresponding author. Rua Pedro de Toledo, 669 1<sup>o</sup> andar. São Paulo, SP, CEP: 04039-032, Brazil.