The Microbiota in Parkinson's Disease: Ranking the Risk of Heart Disease

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Dear Editor,

Gut microbiota, a term that includes microorganisms present in the gastrointestinal tract, is an integral part of the human body and affects the functions of human physiology [1]. Furthermore, recent findings have highlighted that perturbation of the gut microbiome has been linked with chronic diseases ranging from gastrointestinal inflammatory and metabolic conditions to neurological illnesses [2, 3]. Specifically, early findings have revealed that the gut microbiota plays a key role in the pathogenesis of Parkinson's disease (PD) via the gut-brain axis [4]. Given these considerations, we enjoyed reading the elegant review article entitled, "Parkinson's Disease and Gut Microbiota" by Hirayama and Ohno [5] published in your esteemed journal. In brief, the authors properly discussed the recent research on possible mechanisms of how gut dysbiosis is causally associated with the development and progression of PD [5]. However, we would like to add some thoughts that may open the debate about the relationship between gut microbiome dysbiosis and cardiac disorders, highlighting the possible role of this association with the occurrence of some cases of sudden death in PD (SUDPAR).

PD is a progressive, incurable, and symptomatically devastating neurodegenerative disorder with high mortality rates when compared to the general population [6]. Additionally, SUDPAR has been considered an important cause of death in PD [6]. A general analysis of relevant studies on SUDPAR has shown that an average of 14% of PD individuals die suddenly [6]. A number of risk factors may be directly related to SUDPAR, such as age at onset, duration of PD, gender, motor severity, and drug treatment (polypharmacy) [6]. The "direct" mechanisms of SUDPAR include cardiac abnormalities and autonomic dysfunction, even because ~60% of PD patients have structural and functional heart changes [6]. Thus, it has been clearly demonstrated that myocardial infarction, ischemic stroke, congestive heart failure, and even SUDPAR represents a relevant burden and considerably increases mortality in PD [6]. Really, it has been speculated that gastrointestinal microbiome alteration may be one of the triggering factors that contribute to the pathogenesis of PD, affecting symptoms and response to therapy and perhaps modifying progression or even disease initiation [7, 8]. Regarding the cardiovascular system, the scenario is quite similar. In fact, as advancing age is accompanied

by changes in the gut microbiota and by a decline in immune system function, these intrinsic factors are proposed to be a significant determinant of age-associated pathological states, including cardiovascular diseases [9, 10]. In this sense, recent translational studies suggest that alterations in the gut microbiome could play a role in cardiovascular disease [11]. Really, it is presumed that trimethylamine N-oxide, a molecular metabolite that is derived from the gut microbiota, may play an important role in the pathogenesis of multiple cardiovascular diseases such as atherosclerosis, hypertension, diabetes, and myocardial infarction [12, 13]. Another interesting proposal is that translocation of microbiome-derived lipopolysaccharide to the bloodstream promotes the onset of “metabolic endotoxemia,” which triggers inflammation and in severe cases could cause cardiovascular diseases [13, 14].

Overall, where do we go from here? First, it becomes clear that PD is a systemic disease [6]. Second, there is an emerging consensus that cardiovascular dysfunction in PD patients imposes a considerable burden on mortality [6]. Third, although such data are merely associative, aging has physiological effects on both the host and the microbiome, especially in those individuals with PD [15–17]. Finally, as gut microbiome perturbation may also impact on brain and heart function in PD individuals, it

is quite plausible that variation in the human gut microbiome may be considered as an independent risk factor for SUDPAR. Obviously, we are totally convinced that more convergence research is urgently needed on these issues.

Conflict of Interest Statement

The authors report no conflicts of interest.

Funding Sources

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); and Fundação de Amparo à Pesquisa do Estado de Minas Gerais (FAPEMIG).

Author Contributions

Authors’ contributions to the manuscript: F.A.S. was responsible for design, writing, and final content, and A.C.G., C.A.S., and J.F. had read and approved the final version. All authors participated in data interpretation and manuscript review. All authors contributed to the scientific discussion.

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