Reply to the Letter to the Editor “The Microbiota in Parkinson’s Disease: Ranking the Risk of Heart Disease”

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Dear Editor,

Thank you for sharing an interesting thought with us. Dr. Scorza and colleagues state that changes in gut microbiota may also affect the cardiac functions in patients with Parkinson’s disease (PD). Especially, they suggest that sudden death in PD may be associated with alterations in gut microbiota. They recently wrote a review article on cardiac abnormalities in PD [1]. They concluded that cardiac autonomic dysfunction is the most prominent feature in the heart in PD. We indeed reported the impairment of cardiac sympathetic nerves in PD using MIBG myocardial scintigraphy first in the world [2]. In addition, we reported that sympathetic nerves in peripheral blood vessels throughout the body are impaired in PD patients with severe orthostatic hypotension [3]. In PD, the cardiac sympathetic nervous system is overreacted to sympathomimetic drugs [4], and the circulatory response to exercise is impaired [5], indicating that the heart in PD exhibits the disruption of homeostasis to external stimuli. Impairment of blood pressure regulation is not limited to orthostatic hypotension. Even in the supine position, the occurrence of postprandial hypotension with fainting can cause trauma and aspiration pneumonia associated with prolonged circulatory failure and loss of conscious-

ness [6]. Furthermore, these autonomic disturbances are associated with hyposmia in early-stage PD [7]. We agree that sudden death in PD can be causally associated with autonomic failure in PD. Autonomic neuropathy can be associated with gut dysbiosis, since animal experiments show that administration of alpha-synuclein to the intestinal tract propagates alpha-synuclein to the heart and sympathetic ganglia [8]. An article cited by Dr. Scorza and colleagues shows that *Bacteroides*, *Enterobacteriaceae*, and *Streptococcus* were increased in coronary atherosclerosis. We, however, showed that *Bacteroides* was rather decreased in PD, and the other taxa were not changed in PD [9]. As introduced by Dr. Scorza and colleagues, trimethylamine is converted from choline and carnitine by gut microbiota, and trimethylamine-N-oxide promotes atherosclerosis [10]. The production of trimethylamine-N-oxide is high in subjects with the *Bacteroides* type of enterotype [11]. Again, this is different from what we observed in PD. In heart failure, pathogenic bacteria such as *Campylobacter*, *Salmonella*, and *Enterobacteriaceae* are increased in the intestine [12], which is also different from the changes in gut microbiota in PD. As far as we know, gut microbiota in cardiac diseases is different from what we observe in PD. We have not evaluated de-

tailed cardiac functions except for MIBG scintigraphy in our PD patients, and the association of gut microbiota and cardiac functions in PD remains elusive. We agree that a possibility proposed by Dr. Scorza and colleagues needs to be further analyzed in detail in the future.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Both authors contributed equally.

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