

Introduction

Introduction: The Gut-Brain Axis in Parkinson's Disease

Teus van Laar

Department of Neurology, University Medical Center Groningen, Groningen, The Netherlands

This special edition on the gut-brain axis in Parkinson's disease is one in a very long list of publications on this theme during recent years. If one searches in PubMed on 'Parkinson and Gut', the data show that especially the last 3 years the interest in this topic has grown tremendously. From 1969, showing the first 2 references on this topic, up to 2008, the number of publications stayed below 10 per year. However, since 2008 the number of publications has increased to over 110 in 2019.

This interest fits in the overall increased attention of researchers and the public on the role of food and other environmental factors on health. The gut-brain axis discussion therefore is not restricted to PD, but also includes other neurodegenerative- and brain diseases like autism, depression, multiple sclerosis and Alzheimer disease, which directly gives rise to questions about causal relationships. Are we looking at epiphenomena in different diseases, or could it be that specific changes in the gut are the pivotal factor in the pathogenesis of multiple brain disorders, and if so, how?

The current edition of JPD has become a comprehensive and up to date summary of the most important PD-related discussions at this moment, revealing the enormous complexity of the topic, which unfortunately leaves several questions open. Does PD start in all patients in the gut, or is this route related to a small subgroup of patients? Is there a peripheral and a central route of getting PD? What is the role of constipation, and what does it mean if patients do not have constipation? What is the effect of constipation on the

microbiome and what other factors might be related to constipation.? Does the presence of constipation lead to a different subtype of PD?

Changes in microbiome composition between PD and healthy controls (HC) are extensively discussed. It is clear that, despite all the methodological issues, the microbiome in PD is really different from HC. This is supported by data showing that these differences become more significant over time. This suggests that microbiome changes are not only a starting point of PD, but part of the disease progression. However, the inhomogeneity in study design, sampling, lab processes, sequencing methods and the variety in confounders really impair the final conclusions.

The most complex part of this special edition is about the interplay between microbiome changes, metabolomics, local-, systemic- and brain inflammation, gut wall permeability, aSyn production, -accumulation and -transport, and the risk on PD or PD progression.

The problem here is how to establish causality. What is first, and do the causal events vary between the different subtypes of PD? The complexity is partially caused by the fact that multiple systems take part in the communication between gut and brain, existing of neuronal pathways, besides endocrine- and immunological connections.

Finally the role of aSyn is discussed extensively. On one hand aSyn is discussed as a toxic agent if aggregates are being formed, but on the other hand intriguing data are presented on aSyn as a media-

tor of immunological responses, preventing and/or reducing inflammation.

The ultimate question is if this bunch of data will lead to new therapeutic options. Several trials are running at this moment, but so far no definite new treatments have become available.

Hopefully, this special issue will contribute to new insights and new trials, finally leading to a better life for patients with PD.

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