

## Gut Bacteria May Influence Parkinson's Risk, Phenotype

Pauline Anderson | April 06, 2015

Researchers in Finland have discovered what could be an important clue to what drives Parkinson's disease (PD). Their new study has shown a reduced abundance of the Prevotellaceae bacteria family in the gut microbiome of PD patients compared with healthy control persons.

Although the new findings only "scrape the surface," they "give us good reason to dig deeper," said lead author Filip Scheperjans, MD, PhD, Department of Neurology, Helsinki University Central Hospital, and Department of Neurological Sciences, University of Helsinki, Finland.

If further research verifies that PD is caused by a diminished number of Prevotellaceae in the gut, boosting levels of these bacteria might slow the progression of the disease, or even prevent it.

Their findings are published in the March issue of *Movement Disorders*.

### "Intriguing" Theory

"It's an intriguing theory," said Dr Scheperjans. "I think it's something we will be looking at, because the ultimate goal of why we're doing the study is that we want to find something that we can correct."

However, perhaps a more pressing goal is to confirm that these changes in gut microbiome occur before patients develop PD.

It has already been shown that PD patients tend to have gastrointestinal dysfunction, particularly constipation, and that these symptoms may precede motor symptoms by several years. "So from a clinical point of view, we know that the gut is basically affected very early in PD, but we actually haven't a clue really what is causing it," said Dr Scheperjans.

According to background information in the article, the human body contains some 10 times more microbial cells than human cells, and these microbes carry about 100 to 200 times more protein-coding genes than the human genome. Almost all of these genes are of bacterial origin.

Intestinal microbiota influence the immune system and the absorption of nutrients, vitamins, medications, and toxic compounds.

There is mounting evidence of an intense bidirectional interaction between gut microbiota and the nervous system, influencing brain activity, behavior, and levels of neurotransmitter receptors and neurotrophic factors.

The new study included 72 PD patients (mean age, 65.3 years; 48.6% women), and 72 age- and sex-matched control individuals who were without signs of parkinsonism or potential premotor symptoms (mean age, 64.5 years; 50.0% women). The median time from motor symptom onset in PD patients was 5 years. All but two patients were receiving an antiparkinsonian medication.

The study excluded individuals living in the same household and so presumably having a similar diet.

From fecal samples collected from each study participant, researchers pyro-sequenced the V1-V3 regions of the bacterial 16S ribosomal RNA gene. They used random subsamples of 4500 sequences for analysis.



**Dr Filip  
Scheperjans**

They found that the mean abundance of Prevotellaceae in the feces of PD patients was reduced by 77.6% compared with control individuals. This bacteria "is a normal inhabitant of the human gut," with people having varying amounts of it, said Dr Scheperjans.

"It's important to note that based on our data, PD patients have less of Prevotellaceae, but there were also controls who had low levels, so that alone doesn't explain PD."

The researchers did not find significant associations of bacterial abundances with age, body mass index, total Unified Parkinson's Disease Rating Scale, and time from motor or nonmotor symptom onset.

The decreased abundance of Prevotellaceae was not explained by more severe constipation in PD patients, although the abundance of other bacteria, but not Prevotellaceae, was associated with degree of constipation, or by differences in comorbidities.

Less abundance of the bacteria also was not affected by medications. Dr Scheperjans noted that the COMT (catechol-O-methyl transferase) inhibitor was the only PD drug that was associated with changes in the gut microbiome.

"That was interesting, because that drug causes GI side effects like diarrhea," he said. "But we accounted for that in our analysis, so the basic finding of the difference between PD patients and controls is not explained by the medications that patients are using."

The study showed that another type of intestinal bacteria — Enterobacteriaceae — was linked to the severity of postural instability and gait difficulty (PIGD). These bacteria were significantly more abundant in patients with a PIGD phenotype than in patients with tremor dominant (TD) phenotype.

There is a wide variation in clinical manifestations in PD patients — with some having mostly tremor, and others, rigidity — and the question is whether these phenotypes represent the same disease. It is possible, said Dr Scheperjans, that different PD subtypes are linked to different bacteria.

Dr Scheperjans noted that it is not clear from this study whether the bacterial changes were present before patients developed PD or occurred after.

### **Role of Diet?**

The role of diet is also not clear. Evidence in the literature does not suggest major differences between the diet of PD patients and that of other people, and studies of the impact on PD of particular nutrients or foods — maybe with the exception of coffee — have shown small effect sizes and contradictory results, said Dr Scheperjans.

What is known is that the level of Prevotellaceae bacteria increases when people consume foods high in fiber and certain carbohydrates — for example, fruits and vegetables. And this bacteria has been found in oral plaque and has been linked to periodontal disease, although this could be a different strain of the bacteria.

"The difference between bacterial strains at the genetic level can be huge," said Dr Scheperjans. "We don't know if it's the same bug that is healthy in the gut but bad in the mouth."

Dr Scheperjans and his colleagues are now studying the dietary habits of patients and will be reporting on this later this year.

The idea that gut bacteria is involved in PD is intriguing, according to the authors. Alpha-synuclein, which is the hallmark protein for PD, has been found not only in the brain as the main component of Lewy bodies but also in the gut.

There is evidence, said Dr Scheperjans, that the alpha-synuclein "protein pathology" progresses "in a prionlike fashion," migrating from the enteric nervous system to the central nervous system.

"There is a hypothesis that these pathological proteins can jump from one neuron to the next," and that the vagal nerve is involved in the spread of the pathology, he said.

In the last 2 to 3 years, scientists have learned a lot about the presence and amount of these intestinal bacteria, "but we don't know a lot about what they're actually doing; that's the next step," said Dr Scheperjans.

To that end, he and his colleagues are following the study participants for 2 years to see whether the Prevotellaceae level continues to be reduced in PD patients or if it was just a temporary phenomenon.

"We're specifically interested in seeing how they progressed," said Dr Scheperjans. "We want to see if there's an association between the microbiome configuration and disease progression."

### Remarkable Finding

In an accompanying editorial, a group of authors, including Alberto Espay, MD, University of Cincinnati, in Ohio, point out that the demonstration that selected bacterial populations could influence disease and phenotype "is a remarkable finding" and could have important implications.

"For starters, Scheperjans and colleagues have given us the opportunity to envision a future in which specific motor features of PD could be modified by controlling the relative populations of certain species of microbiota."

In addition to helping to shape novel treatment paradigms, gut microbiota also have the potential to inform the understanding of the etiopathogenesis of PD, they write.

It is "tempting" to speculate that gut microbiota might be in the pathogenic pathway that determines disease phenotypes and is "poised to become a target" for disease-modifying pharmacology, they note. "Gut microbiota may even have a role explaining the differences in PD prevalence between rural and urban environments, between countries and perhaps even between sexes."

The study could not rule out the possibility that PD itself may change the microbial composition of the gut — instead of vice versa — or even that a third factor, such as an environmental trigger, initiates both PD and microbiota changes. But the new information adds to the evidence suggesting "that this may be the beginning of a leap forward in our understanding of and treatment options for PD," the editorialists conclude.

*Dr Scheperjans is an inventor on a Finnish patent application. The editorial writers have reported no relevant financial relationships.*

*Mov Disord.* 2015;30:350-358, 296-298. Abstract, Editorial

Medscape Medical News © 2015 WebMD, LLC

Send comments and news tips to [news@medscape.net](mailto:news@medscape.net).

Cite this article: Gut Bacteria May Influence Parkinson's Risk, Phenotype. *Medscape*. Apr 06, 2015.

This website uses cookies to deliver its services as described in our Cookie Policy. By using this website, you agree to the use of cookies.  
close