“The affected individuals had a high intake of cassava and consumed protein-rich foods less frequently than once a week on average”

mothers seemed to be particularly vulnerable to konzo, possibly owing to their high protein needs.

“With climate change, we could see more konzo cases in Zambia and other countries in Africa that have not had them before,” comments Siddiqi. “Konzo is ultimately a disease of extreme poverty and would benefit from researchers and advocates in the scientific community taking on a larger role.”

Heather Wood

ORIGINAL ARTICLE Siddiqi, O. K. et al. Konzo outbreak in the Western Province of Zambia. *Neurology* <https://doi.org/10.1212/WNL.00000000000009017> (2020)

“brain-derived exosomal α -synuclein measurements could distinguish between individuals with early-stage PD and healthy controls”

with early-stage PD and healthy controls with a sensitivity of 100% and a specificity of 57.1%.

The researchers followed up some of the participants from the early-stage PD group an average of 22 months after the initial sample was collected. An increase in exosomal α -synuclein between the first and second time points was associated with a worsening of motor symptoms during that period.

“We found that α -synuclein in plasma neuronal exosomes performed well as a biomarker for early diagnosis of PD and also as a prognostic marker for the motor aspects of the disease,” says Liu. “Next, we plan to set up cohorts with a larger sample size and longer follow-up to confirm our findings in individuals with early-stage PD.”

Sarah Lemprière

ORIGINAL ARTICLE Niu, M. et al. A longitudinal study on α -synuclein in plasma neuronal exosomes as a biomarker for Parkinson's disease development and progression. *Eur. J. Neurol.* <https://doi.org/10.1111/ene.14208> (2020)

RELATED ARTICLE Thompson, A. G. et al. Extracellular vesicles in neurodegenerative disease — pathogenesis to biomarkers. *Nat. Rev. Neurol.* **12**, 346–357 (2016)

MULTIPLE SCLEROSIS

Microbiome varies between multiple sclerosis subtypes

Variations in the composition of the microbiota are associated with different multiple sclerosis (MS) phenotypes, according to a new study published in *Annals of Clinical and Translational Neurology*. The findings demonstrate the importance of patient stratification in studies of the microbiota in MS and also identify potential therapeutic targets for some patients.

Accumulating evidence suggests that alterations in the microbiota are important in MS, but the results of studies to date have varied. However, in most of these previous studies, patients with relapsing–remitting MS (RRMS) that had been exposed to various MS treatments were compared with healthy controls. In the new study, led by Marie D’hooghe and Jeroen Raes, the microbiome profiles of patients with different MS phenotypes were compared.

“By making subgroups based on clinical phenotype and disease course, this research project allowed us to investigate gut microbiome signals that could be related to clinical disease characteristics in MS,” says D’hooghe.

The study included 98 patients with MS and 120 healthy controls, 98 of whom were participants in the existing Flemish Gut Flora Project. Patients with MS were divided into five subgroups on the basis of their clinical phenotypes: untreated RRMS, untreated RRMS during a relapse, untreated benign MS, interferon-treated RRMS and non-active primary progressive MS.

Stool samples from the patients and controls were analysed to determine the composition of their microbiota. “We used 16S amplicon sequencing, a technique in which a specific region of the 16S ribosomal RNA gene is amplified and sequenced,” explains Jeroen Raes. “Using this, we are able to build microbiota composition profiles.”

No measures of microbiota composition differed significantly between all patients with MS and healthy controls. However, measures of microbial richness and the abundance of several microbial taxa did differ between MS phenotypes.

Patients were also classified into one of four enterotypes — groups defined by specific clusters of bacterial species that make up the microbiota. An enterotype known as Bacteroides2 (Bact2) was enriched among patients with interferon-treated RRMS and untreated RRMS during a relapse.

“The Bact2 enterotype is considered dysbiotic and has previously been found enriched in inflammatory diseases, such as ulcerative colitis, Crohn’s disease and primary sclerosing cholangitis,” explains Raes. “Its presence is correlated with increased systemic and intestinal inflammation, even in the healthy population, and it’s exactly the patients with more ‘inflammatory’ MS — those experiencing a relapse — in whom we find enriched Bact2.”

The findings provide important information for the development of disease-modifying strategies that target the microbiota. For example, Raes points out the potential of one specific finding that low levels of the bacterial genus *Butyricicoccus* were associated with greater disease severity. “Causality still needs to be established, but if that can be proven, the road is open to develop *Butyricicoccus* as a probiotic.”

“I’m convinced that, at least for a subset of patients, we will one day be able to influence the disease course through the microbiome,” continues Raes. “Our study clearly shows that that strategy needs to be personalized to the specific patient phenotype.”

Ian Fyfe

ORIGINAL ARTICLE Reynders, T. et al. Gut microbiome variation is associated to multiple sclerosis phenotypic subtypes. *Ann. Clin. Transl. Neurol.* <https://doi.org/10.1002/actn.3.51004> (2020)