

This study explores the possible, even subtle, impacts of a gluten-free diet (GFD) in comparison to a standard diet in the 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP) mouse model of human Parkinson's disease (PD), utilizing male C57Bl6 mice. The research involves the establishment of both acute and chronic MPTP mouse models, accompanied by a set of flow cytometry assessments, such as the proportions of regulatory T cells (CD4+Foxp3+ Tregs), cytokines - interleukin-10 (IL-10), and interferon-gamma (IFN γ) in CD4 and CD8 T cells, respectively, regulatory CD4+CD45RB-low T cells, $\gamma\delta$ T cells as well as subsets of natural killer (NK) cells in mucosal and non-mucosal lymphoid organs in the chronic MPTP mouse model of PD.

Preliminary results indicate subtle positive effects of the gluten-free diet (GFD) in the chronic MPTP mouse model of PD. A tendency to increased proportion of CD4+Foxp3 Tregs in almost all lymphoid organs studied (spleen, mesenteric, inguinal lymph nodes, and Peyer's patches, but with exception of pancreatic lymph nodes), in animals on the GFD may indicate some subtle effect of the GFD on Tregs. In addition, similarly to the effect of GFD in some other immune-mediated diseases, this study also reveals generally increased proportion of $\gamma\delta$ T cells (irrespective of CD8 expression) in the mice fed GFD, suggesting a potential role for immunomodulation through $\gamma\delta$ T cells in PD. No changes were observed in proportions of CD4+CD45RB-low T cells, IL-10-positive CD4 and IFN γ -positive CD8 T cells as well as various subsets of NK cells.

Besides flow cytometry findings, this study also employed behavioral testing. Mice fed the GFD exhibited higher exploration values in the open field test, indicating increased willingness to engage with their environment. Further research is necessary to dissect the dietary effects on the neuroinflammatory conditions in PD, both in the clinical/neurological and immune parameters. These first findings indeed warrant cautious interpretation and further in-depth studies are needed to establish a more comprehensive understanding of the observed dietary effects in PD. The integration of behavioral assessments, immunofluorescence histology, and immunological analyses underlines the multidimensional nature of this study that seems to be necessary for address the complex interplay among diet, gut, brain, and neuroinflammation.