

## Transmural remodelling of colonic wall following dopaminergic nigrostriatal neurodegeneration

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**Background and Aim.** Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor clinical signs, among which gastrointestinal disturbances represent relevant manifestations [1]. Nevertheless, the morphological alterations associated with intestinal dysfunctions in PD have been barely investigated [2]. The present study was aimed at investigating the remodelling of colonic wall in a rat model of PD with central dopaminergic denervation by intra-nigral injection of the neuro-toxin 6-hydroxydopamine (6-OHDA).

**Methods.** Histopathological analysis of the whole colonic wall was performed 4 and 8 weeks after central 6-OHDA injection. Inflammatory infiltrates, collagen deposition as well as the remodelling of intestinal epithelial barrier and *tunica muscularis* were examined by microscopic techniques (histochemistry/immunohistochemistry/confocal immunofluorescence).

**Results.** Colonic tissue from 8-week 6-OHDA rats were significantly altered, as compared with controls. The *tunica mucosa* showed: eosinophil infiltration; altered lining epithelium (reduced claudin-1 and transmembrane 16A protein expression) and goblet cells (increased mucus expression); enhanced glial fibrillar acid protein-positive cells and vimentin-positive fibroblast-like cells. Along with transmural collagen deposition, significant changes were observed also in the *tunica muscularis*: reduced expression of alpha-smooth muscle actin/desmin and increased proliferation index in smooth muscle cells; increased vimentin expression and proliferative phenotype in myenteric ganglia.

**Conclusions.** A full-thickness structural remodelling occurs in the colon of PD rats 8 weeks after central dopaminergic denervation; the main changes include an alteration of the colonic epithelial barrier along with the activation of the mucosal defence and fibrotic switch of the colonic wall. Overall, these findings suggest that: a) early histological modifications occur in the colon of rats with experimental PD at both mucosal and muscular level; b) these changes and the fibrotic alterations might contribute to bowel motor dysfunctions associated with PD.

### References

- [1] Cloud LJ and Greene JG. *Curr Neurol Neurosci Rep* 2011, 11:379  
 [2] Pellegrini C et al. *Neurogastroenterol Motil* 2016, 28(12):1781

### Keywords

Parkinson's disease, rat model, intestinal dysfunctions, colon, morphological remodelling, histochemistry/immunohistochemistry/immunofluorescence