808

MODULATION OF NEUROGLIAL MYENTERIC PHENOTYPE BY MECHANICAL STRESS

E. Robert[1], **N. Khen-Dunlop**[1,2], C. Grosos[1], Y. Révillon[2], N. Cerf-Bensussan[1], M. Neunlist[3], S. Sarnacki[1,2]

[1]Inserm U989, [2]Pediatric Surgery, Hôpital Necker-Enfants Malades, Paris, [3]Inserm U913, Nantes, France

Background and aims: Intestinal motility disorders may impair the post-operative course after stoma closure and delay digestive autonomy recovery. Faecal stream diversion leads to the presence of an upper functional intestinal segment and an excluded defunctionalized distal segment. We studied enteric nervous system (ENS) phenotype for each segment and the impact of excluded segment stimulation after milk irrigation.

Methods: Analyses were performed on intestinal tissues from 24 children, under two years of age, collected at the time of stoma closure. After stoma realization, 12 underwent distal segment irrigation. Transcriptomic analyses were performed by quantitative RT-PCR for ChAT and nNOS (excitatory and inhibitory neurons markers), GFAP (glial cells marker) and for BDNF and GDNF (neurotrophic factors). Whole mounts preparations of myenteric plexus were also studied with antibodies against ChAT and nNOS. Comparisons between both segments used paired two-tailed test (Wilcoxon's test). Clinical data were also collected.

Results: In the non-instilled patients (n=12), there was an increased expression of nNOS ($p=0.02$), consistent with an increase in nNOS-immunoreactive neurons proportion ($p=0,03$), in distal segments compared to upper segments. In contrast, BDNF and GDNF expression were decreased in distal segments ($p< 0.05$). When distal stomas were irrigated before surgery (n=12), differences between upper and distal segments disappeared. These results were associated to a shorter time for transit recovery in instilled patients ($p=0.02$).

Conclusion: This study demonstrates that intestinal motility disorders can modulate ENS phenotype. It also shows that stimulation of defunctionalized gut may reverse the observed changes and leads to clinical improvement.