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up to 80% of Parkinson's disease (PD) patients (PD/CC) usually refractory to laxative. The molecular mechanisms of PD/CC are still unclear, although changes of enteric nervous system and intestinal epithelial barrier (IEB) have been suggested as involved in its pathogenesis. In this study, functional and molecular traits of PD/CC, CC and Ctrl were analyzed and compared. 12 PD/CC (2 F; 51-80 yrs), 20 CC (15 F; 27-78 yrs) and 23 controls (Ctrls; 11 F; 32-74 yrs) were enrolled. PD was diagnosed according to the United Kingdom Parkinson's Disease Society Brain Bank clinical diagnostic criteria, whereas CC was established with Rome IV criteria. Ctrl were asymptomatic subjects. 10 PD/CC and 10 CC were functionally characterized by anorectal manometry (AM) and transit time (TT). Colonic biopsies were obtained in all subjects and tested for possible IEB abnormalities and vasoactive intestinal polypeptide (VIP) levels by RT-qPCR, immunoblot and immunofluorescence labelling. IEB markers assessed were claudin-4 (CLDN4), occludin-1 (OCCL-1) and zonula occludens-1 (ZO-1). Based on functional tests, PD/CC were clustered in patients with delayed TT and altered AM (60%), or with altered AM only (40%). The analysis of the specimens showed that CLDN4 mRNA was significantly increased in PD/CC vs Ctrl and CC, whereas a reduction of the protein was observed in PD/CC vs Ctrl and CC. The OCCL-1 mRNA was significantly increased in PD/CC vs Ctrl and CC. ZO-1 mRNA relative levels were consistent with those of OCCL-1. Notably, OCCL-1 and ZO-1 mRNAs were comparable in CC vs Ctrl. Immunofluorescence for OCCL-1 showed a decrease of structural organization in PD/CC vs CC and Ctrl. ZO-1 immunoreactivity pattern was conserved in PD/CC vs Ctrl, whereas it was compromised in CC. VIP mRNA levels were significantly higher in CC vs Ctrl and PD/CC, whereas a decreasing trend was observed in PD/CC vs Ctrl, confirmed by both immunofluorescence and immunoblot analysis that showed a 15% drop in VIP protein (PD/CC vs Ctrl). Our data show that PD/CC patients are characterized by transit and/or anorectal dysfunctions, ZO-1, OCCL-1, CLDN4 and VIP changes, thus supporting the role of an altered IEB as a contributory mechanism to the neuroenteric abnormalities. Our findings also suggest that IEB markers are subject to regulatory mechanisms presumably distinct in CC and PD/CC.

POSTNATAL GENISTEIN DIET ACTS ON ANXIOUS BEHAVIORS AND 5-HT SYSTEM IN MICE

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Genistein (GEN) is a phytoestrogen found in leguminous plants, particularly soy, which is used in postnatal weaning of infants, as soy milk. GEN's molecular structure similar, like that of estrogens, allows binding to their receptors (ERs) altering their estrogenic functions. Previous studies have shown that serotonergic (5-HT) system, which is strongly regulated by estrogen, is affected by postnatal GEN exposure, inducing an anxiolytic effect in males and anxiogenic in female animal models.

Therefore, the aims of this work are twofold: to understand which receptor is involved in altering the organizational effect of GEN in

the postnatal period and to evaluate how such exposure may affect the 5-HT system.

CD1 male and female mice were treated daily from PND5 to PND12 with corn oil (control group), GEN and GEN associated separately (MPP, ER α antagonist; PHTPP, ER β antagonist, and G15, GPR30 antagonist) or all together (mix group) with each of ERs antagonist. In adulthood the animals were tested with different behavioral tests to assess anxiety and stress state. Finally, they were sacrificed at PND90 to analyze the 5-HT system within the dorsal and median Raphe nucleus.

The behavioral tests showed an anxiogenic behavior in GEN and GEN + PHTPP only in males and a high locomotor activity along with anxiolytic behavior in all treated females. In 5-HT analyses, no significant differences were observed between males and females, but emerged that ER α receptors was most affected by postnatal GEN treatment playing a crucial role in the pathways that regulate mood. The results show that the 5-HT system was most altered by treatment in the rostral part of the Raphe, suggesting that in that region the system is particularly sensitive to estrogen regulation. Thus, data obtained confirmed that postnatal GEN's administration has effects on estrogen receptors and on 5-HT system, altering the mood pathways.