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Title:

EARLY MATERNAL SEPARATION INDUCED COMMENSAL *E. COLI* OVERGROWTH TRIGGERING VISCERAL SENSITIVITY AND SPECIFIC HUMORAL RESPONSE IN ADULT MICE

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Small Intestinal Bacteria Overgrowth (SIBO) in favor of *Enterobacteriaceae* is highly associated to Irritable Bowel Syndrome (IBS) a functional gastrointestinal pathology where a specific humoral response toward bacterial antigens has been observed. Symptoms of IBS and SIBO are similar consisting in abdominal pain, bloating and altered stool forms. Further, IBS symptoms can be generated and/or exacerbated by early life stressful events. In this study, using the well described rodent model of IBS: maternal separation, we developed a mouse model of SIBO and studied its consequences on IBS symptom and on humoral response toward microbiota. MS increased visceral sensitivity and induced ileal and fecal overgrowth of *E.coli* in adult female mice. This overgrowth was associated with a decrease of fecal lysozyme antimicrobial activity and increase of anti-*E.coli* IgG and IgA. In order to decipher whether or not those alterations were a consequence of *E. coli* overgrowth, adult mice were force fed daily with 10^9 commensal *E.coli* for 15 days. *E.coli* gavage reproduced ileal and fecal overgrowth as well as visceral hypersensitivity and increased anti-*E.coli* IgG and IgA. However, *E.coli* gavage didn't decrease lysozyme antimicrobial activity in feces suggesting that lysozyme defect is a consequence of MS that can participate to the *E.coli* overgrowth.

This study shows for the first time that (i) maternal separation in mice weakened intestinal antimicrobial defense that might result to intestinal *E.coli* overgrowth and (ii) intestinal *E.coli* overgrowth was responsible for visceral hypersensitivity and systemic humoral response toward microbiota.

Keywords: MS, *E.coli* intestinal overgrowth, humoral response toward microbiota, visceral hypersensitivity