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## EARLY MATERNAL SEPARATION IN MICE TRIGGERED A SPECIFIC IgG RESPONSE AGAINST SOLUBLE FOOD ANTIGENS

A. Riba, C. Cartier, V. Bacquié, C. Lencina, V. Mallet, C. Harkat, M. Gillet, H. Eutamène, V. Théodorou, S. Ménard.

Neurogastroentérologie & Nutrition, Toxalim, UMR 1331 INRA / INP, Toulouse, France.

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**INTRODUCTION:** In the last two decades, non IgE reaction to food called hypersensitivity has been incriminated in the symptomatology of functional gastrointestinal disorders (FGD) such as irritable bowel syndrome (IBS). Early life stressful events contribute to IBS symptoms emergence later in life. Accordingly the rodent maternal separation (MS) stress resulting to visceral hypersensitivity and increased gut permeability at adulthood is commonly used as an animal IBS model. As perinatal period is a critical window for immune system development, we investigated whether a neonatal maternal separation stress (MS) in mice may trigger food hypersensitivity at adulthood. **METHODS:** MS was applied for 10 days starting at post natal day (PND) 2 and consisted of mice pups isolation from litter and dam 3h/day. Adult male mice were studied at PND42. Total intestinal paracellular permeability was measured in plasma 4h after oral gavage with 4kDa dextran FITC. Visceral sensitivity in response to colorectal distension (CRD) was evaluated in mice previously equipped with NiCr electrodes implanted in the abdominal muscle. CRD was performed using an embolectomy probe inserted into the rectum and inflated with 0.02ml step increasing volumes from 0 to 0.10ml. Abdominal response, as criterion of visceral sensitivity was recorded by electromyography (EMG). Plasmatic immunoglobulins (Ig) concentrations and specificity against soluble food antigens were measured by ELISA. **RESULTS:** MS increased intestinal total paracellular permeability in adult MS mice ( $17.7 \pm 4.2 \mu\text{g/ml}$  vs  $8.1 \pm 0.8 \mu\text{g/ml}$ ,  $P < 0.05$ ). Furthermore, MS increased the EMG response to CRD at volumes 0.02ml to 0.06ml compared to controls ( $4.0 \pm 0.6 \text{ mV.s}$  vs  $0.98 \pm 0.2 \text{ mV.s}$ ,  $P < 0.05$ , 0.02ml;  $5.3 \pm 1.1 \text{ mV.s}$  vs  $2.0 \pm 0.4 \text{ mV.s}$ ,  $P < 0.05$ , 0.04ml and  $6.3 \pm 0.9 \text{ mV.s}$  vs  $3.1 \pm 0.6 \text{ mV.s}$ ,  $P < 0.05$ , 0.06ml). Total IgG concentrations but not IgA nor IgE were increased in MS mice ( $241 \pm 11 \mu\text{g/ml}$  vs  $199 \pm 11 \mu\text{g/ml}$ ,  $P < 0.05$ ). Thereof, Ig specificity against soluble food antigens was assessed by normalizing Ig concentrations between samples. MS induced increase of IgG reactivity against a soluble lysate of rodent standard food (optical density  $0.68 \pm 0.08$  vs  $0.47 \pm 0.07$ ,  $P < 0.05$ ). IgE and IgA reactivity against soluble food antigens was not affected by MS. **CONCLUSION:** MS not only induced IBS-like symptoms such as increased paracellular intestinal permeability and visceral hypersensitivity in adult offspring but also a specific IgG response to soluble food antigens. These data reinforce the concept that early life stressful events affecting IBS patients may also trigger food hypersensitivity.