PERINATAL EXPOSURE TO LOW DOSES OF BISPHENOL A IMPAIRS IMMUNE HOMEOSTASIS AND PROMOTES INTESTINAL PARASITE INFECTION IN YOUNG RATS

S. Ménard, C. Lencina, M. Leveque, M. Olier, M. Naturel, S. Sekkal, C. Harkat, V. Bezirard, V. Theodorou, E. Houdeau
(sandrine.menard@toulouse.inra.fr)
Team 04, Neuro-gastroenterology and Nutrition Group, UMR 1331 INRA Toxalim, Toulouse, France

Background

Bisphenol A (BPA): xenoestrogen, food contaminant

WHERE?

polycarbonate — résine époxy

STATUTE LAW / HUMAN EXPOSITION IN EU

NOAEL : No Observed Adverse Effect Level **= 5 mg/kg/day**

TDI : Tolerable Daily Intake = NOAEL/100 **=50 µg/kg/day**

Human exposition in European Union =0.2-0.6µg/kg/day

PREVIOUS WORKS

1-Perinatal exposure to BPA $_{NOAEL}$ worsened experimental immune colitis in adult F1 female rats
Braniste *et al.* PNAS 2010

2-Perinatal exposure to 5µg/kg/day of BPA impaired oral tolerance in adult F1 female rats (45 days)
Ménard *et al.* Oral communication PNRPE 2012

OVA-tolerized OVA-immunized

- Increase anti-OVA IgG response
- Increase proliferation of cells isolated from spleen and mesenteric lymph nodes
- Increase OVA-induced secretion of IFNγ

OVA challenge following oral tolerance protocol
Colon sampling:

- Increase neutrophil recruitment
- Increase pro-inflammatory response (IFNγ)
- Decrease anti-inflammatory response (TGFβ)

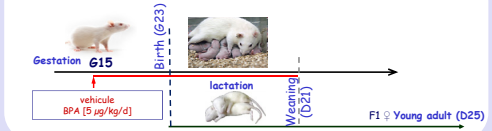
Ménard et al., submitted

AIM OF THIS STUDY

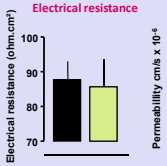
Analyse consequences of perinatal exposure to 5µg/kg/d of BPA on immune homeostasis in young rats at weaning (25 days) (oral tolerance and parasitic infection)

Methods & Results

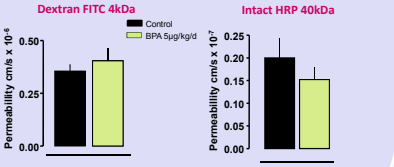
Perinatal treatment with BPA



Paracellular permeability (jejunum)

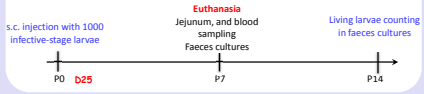


Transcellular permeability (jejunum)

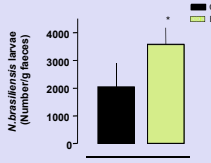


➢ BPA perinatal exposure did not affect jejunal permeability at D25

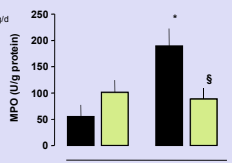
Parasitic infection with *Nippostrongylus brasiliensis*



Parasite burden in faeces



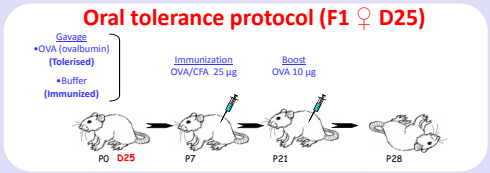
MPO activity in jejunum



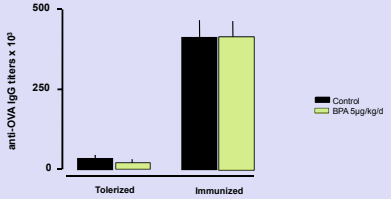
* Compared to without *N. brasiliensis*
§ Compared to control group

➢ BPA exposure increased *N. brasiliensis* burden in faeces
➢ BPA exposure blocked *N. brasiliensis*-induced neutrophil recruitment in jejunum

Oral tolerance protocol (F1 ♀ D25)

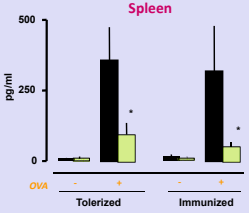


Anti-OVA IgG

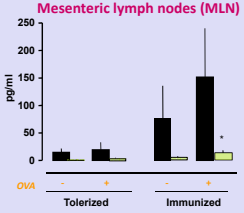


IFNγ

Spleen

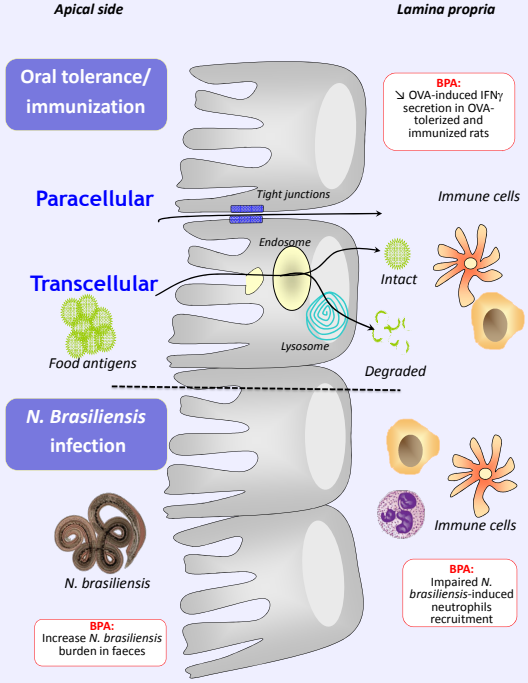


Mesenteric lymph nodes (MLN)



➢ BPA perinatal exposure did not affect humoral response to OVA, but dramatically decreased OVA-induced IFNγ secretion by spleen and MLN immune cells in tolerized and immunized rats

Conclusion



BPA perinatal exposure at 5µg/kg/day impaired immune homeostasis in young rats at weaning:

- Lack of specific cellular response to food antigens without alteration of the humoral response
- Impaired defense mechanisms triggered during parasitic infection (neutrophil recruitment)