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Bisphenol S chronic exposure interacted with ewe metabolic status to impair female reproduction

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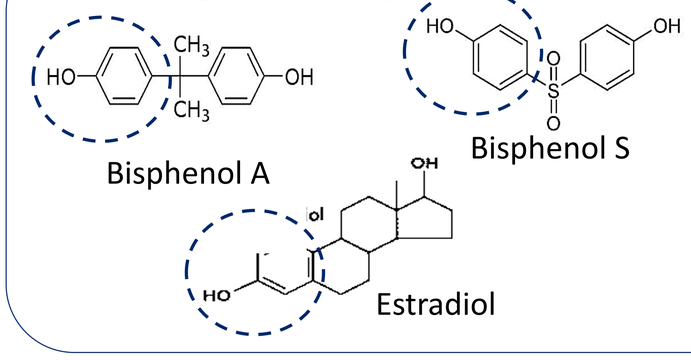
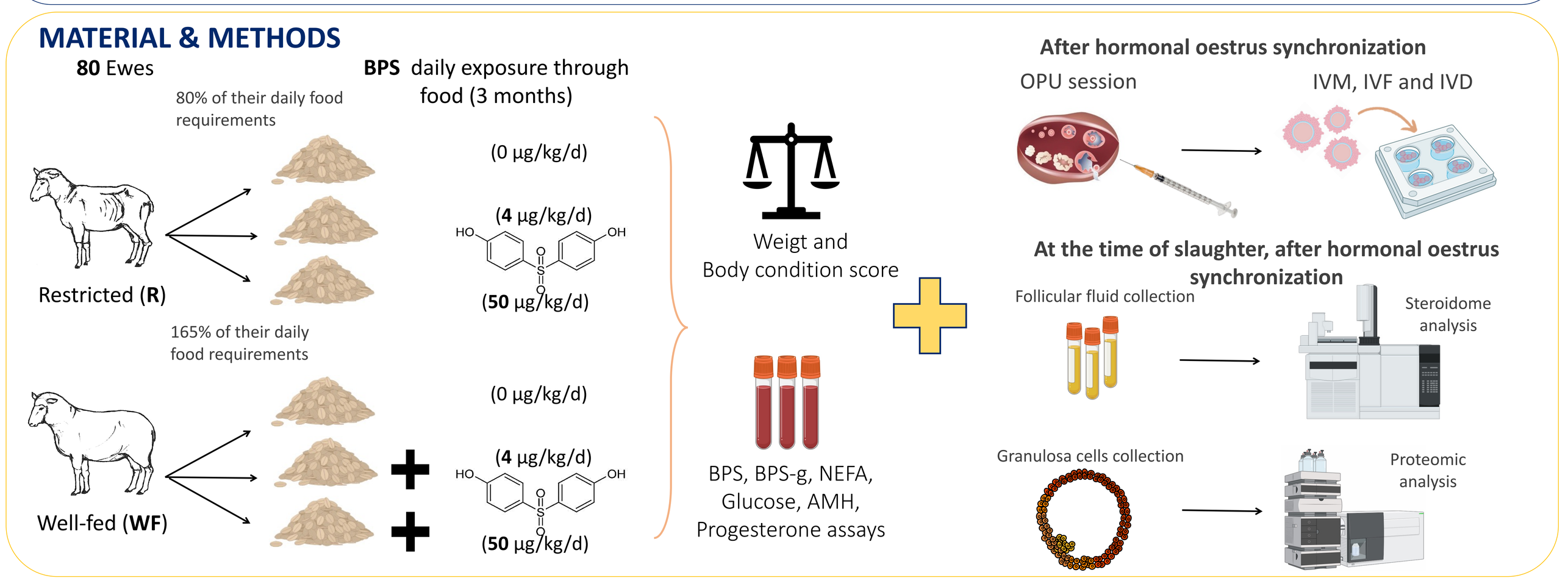
INTRODUCTION



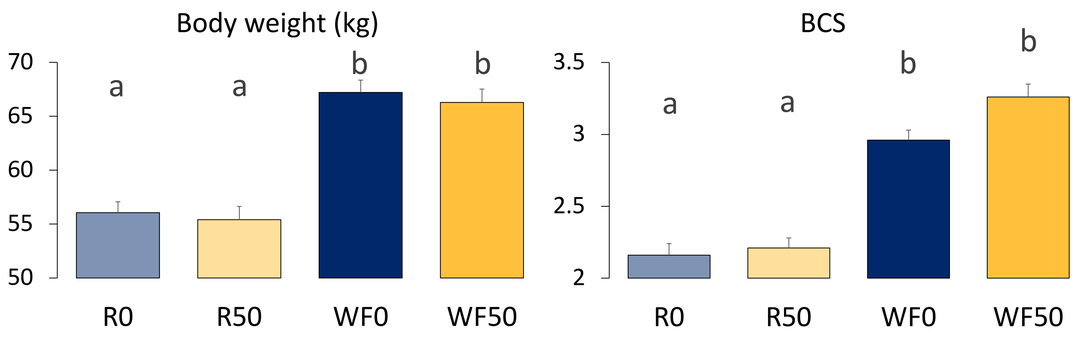
Bisphenol A (BPA), a plasticizer used in the food industry, is reported to be an **estrogenomimetic endocrine disruptor**[1], involved in deleterious effects on oocyte meiosis and maturation as well as in steroigegenesis impairment[2,3]. BPA being regulated, structural analogs emerged including bisphenol S (BPS). Studies on fish and rodent species reported that BPS affects reproduction similarly to BPA[4]. Moreover, because metabolism affects the ovarian functioning, we hypothesized that the metabolic status could interact with the effects of environmental factors.

This study assessed BPS 50 µg/kg/d chronic exposure on oocyte quality, steroidogenesis and granulosa cell proteomic data

MATERIAL & METHODS

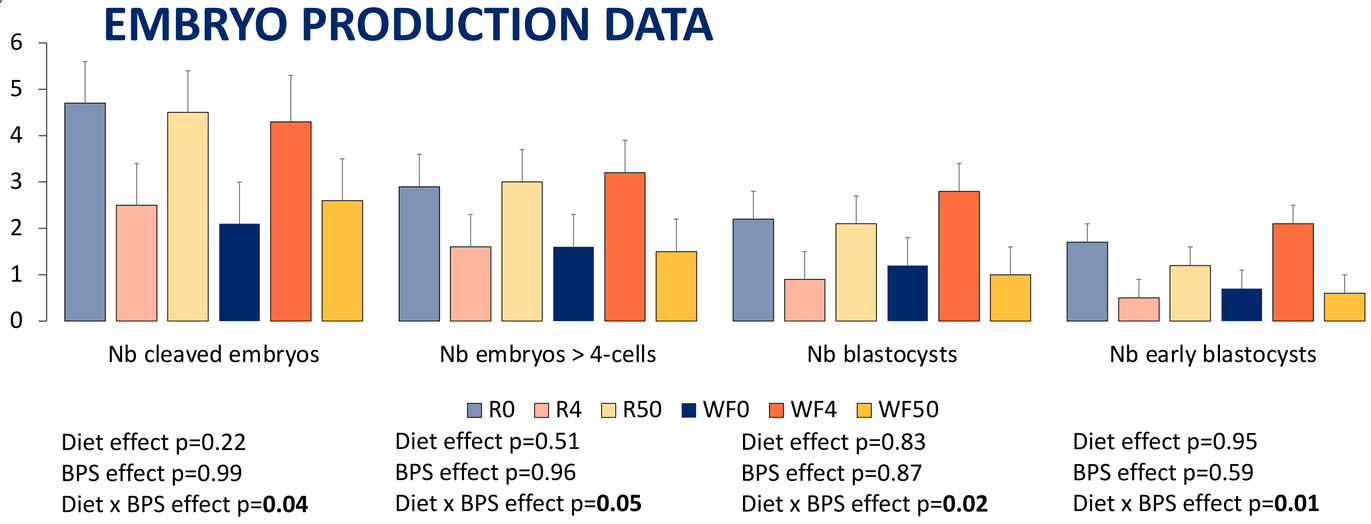


DIET MODEL VALIDATION



Body weight and body condition score (BCS) **differ according** to ewe **diet**

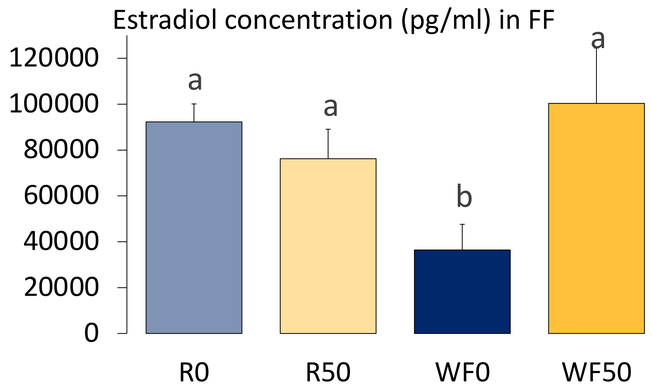
EMBRYO PRODUCTION DATA



	Diet effect	BPS effect	Diet x BPS effect
Nb cleaved embryos	p=0.22	p=0.99	p=**0.04**
Nb embryos > 4-cells	p=0.51	p=0.96	p=**0.05**
Nb blastocysts	p=0.83	p=0.87	p=**0.02**
Nb early blastocysts	p=0.95	p=0.59	p=**0.01**

Significant effect of **diet x BPS dose interaction** for **cleaved embryos**, embryos with **more than 4 cells**, number of **blastocysts** and **early blastocysts**.

FOLLICULAR STEROIDOME DATA

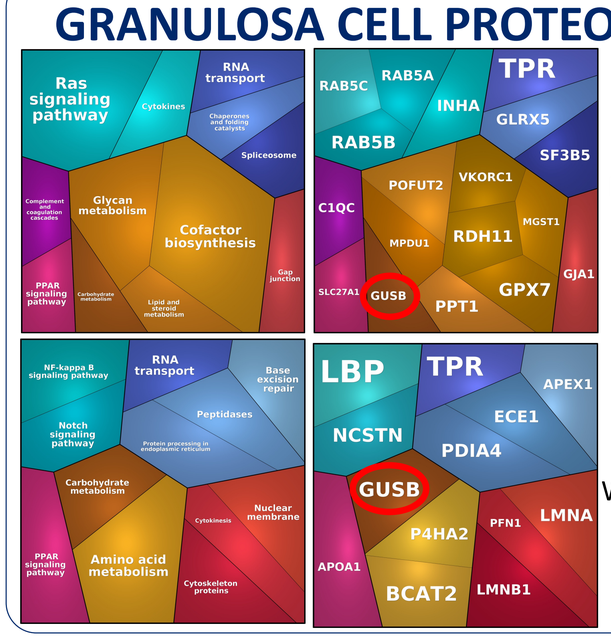


Significant effect of the interaction between metabolic status and exposure to BPS for 7 steroids, including estradiol.

➪ ↗**estradiol** concentration in **WF** ewes **exposed** to BPS

Steroids	Mean concentration (ng/mL) ± SEM R0	R50	WF0	WF50	p-value Diet effect	BPS effect	Diet x BPS effect	Compartment
17α-OH PREG	38,4 ± 9,4^{a}	20,6 ± 4,9^{ab}	11,2 ± 5,1^{b}	23,3 ± 5,1^{ab}	**0,07**	0,65	**0,03**	Follicular Fluid
PROG	0,1 ± 0,01^{a}	0,06 ± 0,01^{b}	0,04 ± 0,01^{b}	0,06 ± 0,01^{ab}	**0,04**	0,32	**0,03**	Plasma
5α-DHT	0,2 ± 0,1^{a}	0,05 ± 0,02^{b}	0,08 ± 0,02^{b}	0,1 ± 0,01^{b}	**0,08**	**0,01**	**0,001**	Follicular Fluid
Estradiol	92,3 ± 7,8^{a}	76,2 ± 12,9^{a}	36,4 ± 11,2^{b}	100,3 ± 24,1^{a}	0,34	0,16	**0,02**	Follicular Fluid
E1	< 0,001^{a}	0,01 ± 0,01^{b}	0,01 ± 0,003^{b}	0,01 ± 0,001^{b}	0,42	0,46	**0,01**	Plasma

GRANULOSA CELL PROTEOME DATA



R0 vs R50

WF0 vs WF50

➪ Effect of the **interaction** between **metabolic status** and **BPS exposure** most of the proteins corresponding to the effect of diet (21 and 30 proteins) **differ according** to exposure to BPS.

➪ **GUSB** which is capable of **deglucuronidating BPA**, is **overabundant** after **BPS exposure** and could **prolonged** the **estrogenic activity of BPS** at the ovarian level. According to the literature and our data, **<u>GUSB expression increases with adiposity.</u>**

CONCLUSIONS & PERSPECTIVES

➪ The **deleterious effects of BPS** and its interaction with **metabolic status** indicate that **its use in food packaging should be regulated.**

➪ Our data also suggest that **people** with a **high level of adiposity** may be **more sensitive to the effects of bisphenols**[5,6]**.**

References: [1]**Moreman** *et al.,* **2017**. *Environ. Sci. Technol.* 2017, 51 (21): 12796–12805; [2]**Ma** *et al.* **2019**. *Environmental Research* 176: 108575 ; [3]**Grasselli** et al. **2010.** *Domest. Anim. Endocrinol.* 39 (1): 34-39 ; [4]**European Food Safety Authority, 2015**. EFSA Journal 13; [5]**Desmarchais** et al. **2022** *Ecotoxicology and Environmental Safety* 229: 113096 ; [6]**Téteau** et al. **2022** *Front. Endocrinol.* 13: 892213