Establishment of a rodent model of endometriosis to evaluate the effect of new therapeutic strategies

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OBJECTIVES

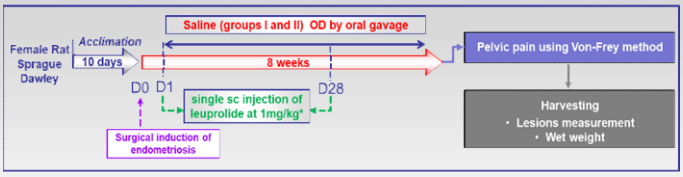
- Endometriosis affects 10-15% of women at reproductive years with no curative treatment
- Main symptoms: debilitating pelvic/abdominal pain (but also dyspareunia, severe dysmenorrhea, dysuria etc…)
- Non-fatal but negative impact on quality of life, work productivity, sexual relationship and self-esteem.
- Current therapeutic options : limited insight into the disease mechanism and include drugs and/or surgery, which may be ineffective over the long term with unwanted 2ndary effects.
- A need for more effective and less invasive therapeutic curative strategies.

Aim of the study:

To establish **a translational rodent endometriosis model,** based on previously described models. The validity of the model was confirmed by investigating the effect of the clinically-used GnRH agonist, leuprolide.

MATERIALS & METHODS

Summary of research design



Experimental groups

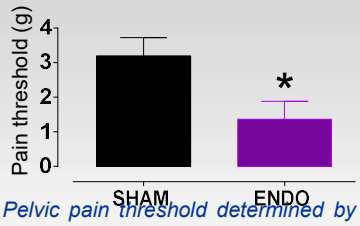
Groups ID		Surgical auto transplantation	Treatment	N
I	Control	sham	saline	10
II	ENDO	Homologous Uterus fragments	saline	10
IV	ENDO+ positive control	Homologous Uterus fragments	GnRH agonist leuprolide 1mg/kg single injection every 4 weeks	10

Endometriosis was induced by a surgical procedure in anesthetized adult female SD rats in diestrus. Six 2x2 pieces from midleft uterine horn were sutured to the mesenteric arteries. Sham rats underwent the same procedure except for suturing. Assessment of the abdominal pain was performed 8 weeks post surgery using Von-Frey, in contrast to previous reports of the indirect pain i.e., paw withdrawal. Then, the lesions were excised and measured.

All procedures are performed in compliance with the legislation on the use of laboratory animals (NIH publication N°85-23, revised 1996) and Animal Care Regulations in force in France as of 1988 (authorization from competent French Ministry of Agriculture - Agreement No. B78-423-1, July 2017

RESULTS

Effect of surgical induction of endometriosis



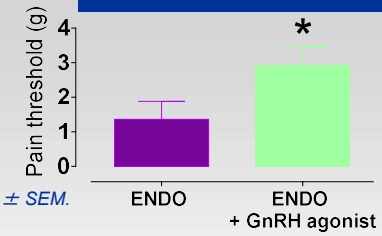
Pelvic pain threshold determined by Von Frey experiments for Sham (n=10) and ENDO rats (n=10)

Data are mean ± SEM.

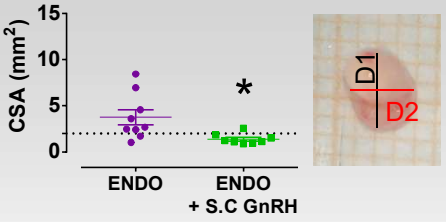
**p<0.05 Student's t-test.*

Abdominal pain threshold was decreased by 2 fold in rats with endometriosis *vs.* sham rats

Validation of the model : Effect of leuprolide



Pelvic pain threshold determined by Von Frey experiments for ENDO rats (n=10), and ENDO rats treated with leuprolide (n=10)



Average lesion area (= D1xD2x π/4) determined for ENDO rats (n=10), and ENDO treated rats with leuprolide (n=10)

Leuprolide significantly increased the threshold force required to elicit a behavioural withdrawal response in rats suffering from endometriosis. The pelvic floor mechanical hyperalgesia is correlated to the growth of lesions

CONCLUSIONS

we have established, based on previously reported rodent models, a model of endometriosis-associated pain that responds to clinically active drugs and can, therefore, be used to identify novel therapies and investigate some of the pathophysiological mechanisms involved in endometriosis.