Stress Promotes the Development of Endometriosis

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Women with endometriosis (EM) experience elevated stress

- Dysmenorrhea
- Chronic pelvic pain
- Infertility
- Psychoemotional distress

Chronic stress

- Higher serum cortisol level in women with endometriosis

Does stress promotes the development of endometriosis?

**In Rats**

In an animal research, female rats were subjected to swim stress for 10 consecutive days prior to the surgical induction of endometriosis.

The results showed that: **prior exposure to stress increased both the number and severity of endometriotic vesicles found in animals with endometriosis.**

• **In Humans**

  • Up-regulated encoding gene expressions of corticotropin-releasing hormone (CRH), urocortin, and glucocorticoid receptor (GR) in ectopic endometrium.

  • Improved symptoms after interventions which reduces stress level in women with endometriosis.

Does psychological stress promote the development of endometriosis?
32 female C57 mice

Control (N=8)

SHAM (N=8)

EM (N=16)

Control (N=8)

Stress (N=8)

Lesion size, Immunohistochemistry (ADRB2, VEGF, PCNA, CD31)

Day 0 Induction

Stress

Day 14 Sacrifice
Psychological stress

• Mice were exposed to the one-year-old male cats every other day for 14 days.

• Mice were in a cage placed in another bigger cage that housed the cat for 24 hours.

• This cat had received no food and water for 12 hours.

• Change the cat every 8 hours.

• Make sure that all mice cannot be physically attacked by the cat, but will be under constant gaze and harassment from the cat.
Total lesion size

![Box plot showing total lesion size for two groups (STRS and USTRS).]
Immunohistochemistry

A: Beta2 receptor

B: VEGF

C: MVD-CD31

D: PCNA
Does the timing of the stress make any difference?
Experimental Design

- 36 female mice
  - Control (N=9)
  - Stress-before-induction (N=9)
  - Stress-after-induction (N=9)
  - Stress before-and-after induction (N=9)

Day -14
- Day 0 Induction
- Day 14 Sacrifice

Lesion weight, Immunohistochemistry (ADRB2, VEGF, PCNA, CD31)
Animal Model

• 8-week female BALB/c mice

• Endometriosis Model: Endometrium fragments of donor mice were intraperitoneally injected to recipient mice.

Chronic Immobilization Stress:

The mice were immobilized in the fixator for 2 hours per day without food and water.
Results

Lesion weight (g)

[Graph showing lesion weight for Control, Before, After, and Entire categories, with statistical significance marked by * and **]
<table>
<thead>
<tr>
<th>Protein</th>
<th>Control</th>
<th>Before</th>
<th>After</th>
<th>Entire</th>
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<tbody>
<tr>
<td>ADRB2</td>
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<tr>
<td>PCNA</td>
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**ADRB2**

- Control
- Before
- After
- Entire

**PCNA**

- Control
- Before
- After
- Entire

**VEGF**

- Control
- Before
- After
- Entire

**CD31**

- Control
- Before
- After
- Entire

*Note: The asterisks indicate statistical significance.*
Is it possible to mitigate the promotional effect of stress by β-blockers?
Experimental Design

PBS(C) (N=10) → Propranolol(P) (N=10) → Propranolol + stress(PS) (N=10) → PBS + stress(S) (N=10) → stress

Day 0 Induction, Implantation of Alzet pumps

Day 14 Sacrifice

Lesion weight, Immunohistochemistry (ADRB2, VEGF, PCNA, CD31)
Results

Lesion weight (g)

The graph shows the comparison of lesion weight among different groups: PBS, Propranolol, Propranolol+stress, and PBS+stress. The PBS+stress group has the highest lesion weight, significantly higher than the other groups. There are no significant differences among the PBS, Propranolol, and Propranolol+stress groups.
### Immunohistochemistry

<table>
<thead>
<tr>
<th></th>
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• Stress promotes the development of endometriosis.

• Timing of the stress does not seem to make much difference.

• Increased duration of the stress may further promote the development of endometriosis.

• β-blockers may be effective in mitigating such a promotional effect.
Acknowlegement

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