Influence of ovarian hormones on development of ingestive responding to alterations in fatty acid oxidation in female rats

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Terminology

- **2-DG**: 2-Deoxy-D-glucose, a glucose molecule
- **MA** (mercaptoacetate): lipoprivic drugs. Interferes the oxidation of fatty acids.

- Administration of those drugs=increase in food intake in male rats.
This study tested to see the effects of administration of lipoprivic drug on food intake of F rats is affected by---

- 1) fat level of the maintenance diet?
- 2) ovarian hormone status?
- 3) previous hormonal history
Experiment 1: high fat OR standard maintenance diet
Experiment 2: following OVX by injection of EB?
Experiment 3: OVX prior to puberty
Experiment 4: OVX prior to puberty + EB injection during puberty?

I looked at Experiment 3 and 4 in particular!
Experiment 3

✿ Subjects
--- 33 Sprague-Dawley female rats
   weaned on Day 23
   OVX (17) or sham (16) performed Day 25-28
   maintained on a standard diet
• Injected none or 69mg/kg of MA
• Intake testing
   --- 1, 2, and 4 hours
• Followed by 200mg/kg 2DG or 0.15 M NaCl
• Date & Time = within subjects
• Surgery = between subjects
Administration of MA (69 mg/kg, i.p.) at time 0 did not stimulate food intake in (A) gonadally-intact (sham OVX; n=16) adult female rats but did produce increased food intake in (B) adult female rats that had been OVX prior to P30, n=17). Administration of 2-DG (200 mg/kg i.p. at time 0) stimulated food intake in both (C) gonadally-intact (sham OVX) adult female rats, n= 16 and (D) adult female rats that had been OVX prior P30, n=16.

* p < 0.05 compared to NaCl
Exposure to ovarian hormones at “puberty” MAY persistently alter ingestive responding to lipoprivic signals in female rats.

TO TEST THIS...

OVX prior to puberty → give either EB or oil (control)

Then compare the effects of administration of MA in female rats.
Subjects
--16 experimentally and sexually naïve Sprague-Dawley female rats, 20-21 days of age
* Bilateral OVX performed in all of them during 27-28 days maintained on a standard diet
• 10 days after surgery
-9 received EB every 4 days for 7 cycles
-7 received oil every 4 days for 7 cycles
• Body weights---recorded every 2 days
  (during the injections and 12 weeks after the last injection)
• Food intake---tested 12 weeks after the last injection
**Experiment 4**

- Administration of either 69mg/kg MA or saline (control)
- Then re-tested 4 days later in opposite condition (those got injected MA---got saline, those got saline---got MA)

Food intake after 1, 2, or 4 hours was analyzed

--Dose=within subjects

--Hormone= between subjects
The amount of weight gain between
1) first---last time of hormone injection
2) last injection---the time of testing at 12 weeks later
…..was measured!
Administration of MA (69 mg/kg, i.p.) at time 0 did not stimulate food intake in adult female rats OVX prior to P30 given cyclic s.c. injections of EB (every 4 days between P35 and P63, n = 9) but did stimulate food intake in adult female rats OVX prior to P30 given cyclic s.c. injections of the oil vehicle (every 4 days between P35 and P63, n=7).

*p < 0.05 compared to Oil - NaCl
Based on both experiments..

- when ovarian hormones are removed prior to puberty, female rats continued to show increased intake, following administration of MA when tested as adults.
  = like MALES!

- Exposure to ovarian hormones may play a role in altering ingestive responses to lipoprivic signals after 30 days (puberty) of age in female rats.
- “exposure to estrogens during puberty”
Females need significantly greater long-term energy in reproductive behavior than males.

* For males
  signal of low long-term energy stores
  = stimulate food intake
  (no suppression in reproductive behavior)
* For females
If she were to reproduce, short-term suppression of reproductive behavior would be adaptive
Onset of puberty—highly related to nutritional status
Fat-related signals appear to play a particularly important role in sexual maturation.
Other studies

- 1) vaginal opening and estrus are accelerated with high fat diet (Frisch, Hegsted et al. 1975; Frisch 1980)
- 2) onset of puberty can be accelerated by administration of the leptin (Ahima, Dushay et al. 1997; Chehab, Mounzih et al. 1997; Gruaz, Lalaoui et al. 1998)
- 3) food deprivation in females before puberty delays the onset of puberty (Bronson 1986)
  ---- decreased uterine and ovarian weights, absence of LH release
**Limitation?**

* **Mechanisms** that underlie the developmental changes in ingestive behavior following the administration of MA in female rats—UNKNOWN

* How estrogens might influence the development of neural circuitry underlying ingestive responses to lipoprivic signals—NOT CLEAR

* The role of potential peripheral consequences of exposure to estrogens—NEEDS TO BE DETERMINED
Take home message

- Future work will need to investigate if alteration in neural circuit/function contribute to this developmental differences.

- Examining whether the peripubertal period represents a critical or sensitive phase during which exposure to estrogens produces more pronounced effects compared to other period----will provide better understandings!

- For females, reproductive behavior is such a work!