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

4Experients in this study

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

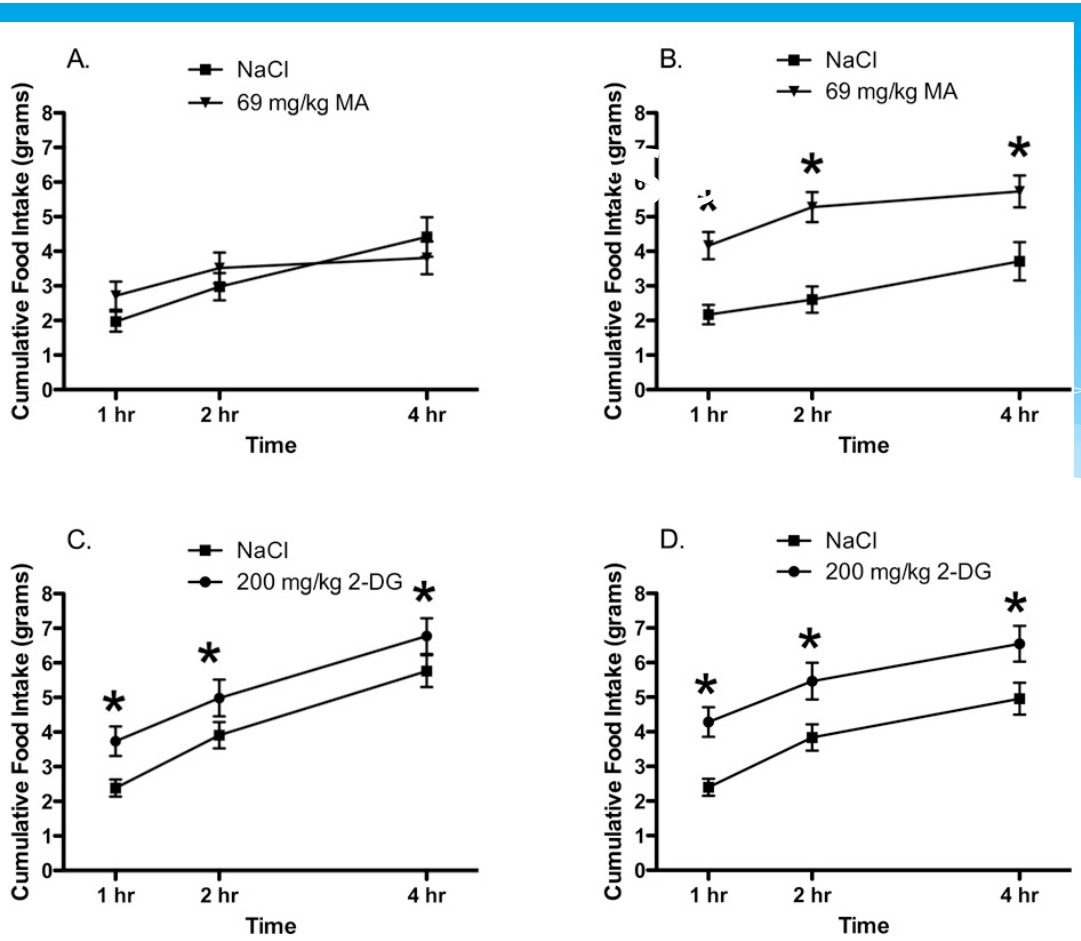
OVX (17) or sham (16) performed Day25-28

maintained on a standard diet

- Injected none or 69mg/kg of MA
- Intake testing

--- 1,2,and 4hours

- 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

Meaning….

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.

Experiment 4

* Subjects

--16 experimentally and sexually naïve Sprague-Dawley female rats , 20-21 days of age

* Bilateral OVX performed in all of them during 27-28days

maintained on a standard diet

- 10 days after surgery

-9 received EB every 4 days for 7cycles

-7received oil every 4days for 7cycles

- Body weights---recorded every 2days

  (during the injections and 12weeks after the last injection)

- Food intake---tested 12weeks after the last injection

Experiment 4

* Administration of either 69mg/kg MA or saline (control)
* Then re-tested 4days 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

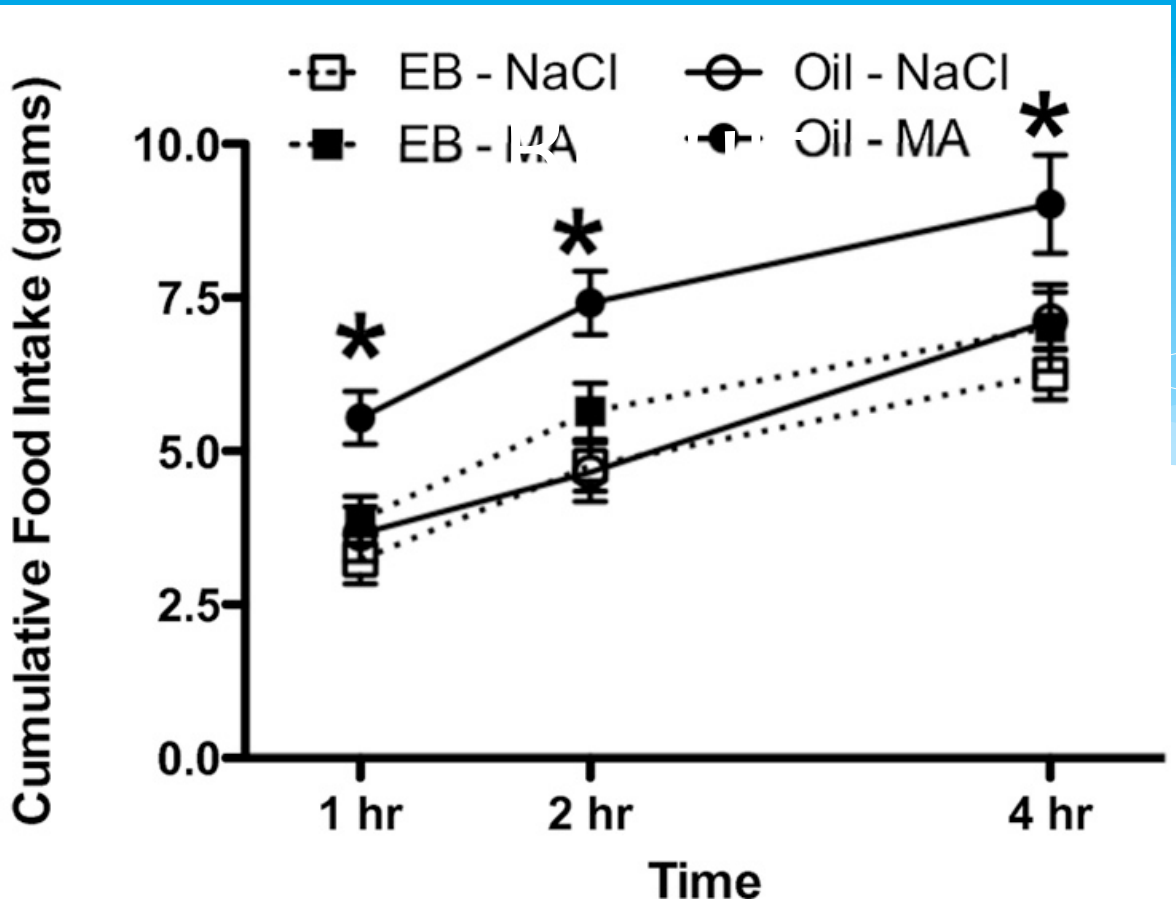
--Hormone= between subjects

Experiment 4

* The amount of weight gain between

1) first---last time of hormone injection
2) last injection---the time of testing at 12weeks 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 30days (puberty) of age in female rats.
- “exposure to estrogens during puberty”

Male and Female difference in energy expanse

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 peropheral 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!