Chronic Mild Stress Produces Sex Differences in Anxiety-like Behavior and Synaptic Plasticity

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Introduction

- Stress can lead to the development of depression. Prevalence of depression among women is twice that of men, most studies have exclusively used males (Kornstein 1997, Sandanger 2004).
- Sex differences in stress, depression, and anxiety are inconsistent.
- Limited studies use CMS in rats of both sexes (Franceschelli et al 2014).
- We hypothesize that CMS will produce sex differences in anxiety-like behavior and synaptic plasticity.

Materials and Methods

- Long Evans rats (males and females ~3 months old) were used.
- Chronic mild stress (CMS) was administered for 5 weeks.
- Sucrose preference test (SPT) and coat state were measured
- Open field test (OFT), Elevated plus maze (EPM), Forced swim test (FST) were recorded.
- Hippocampal extracellular EPSP's were recorded from CA1 region following behavioral assays.

Results

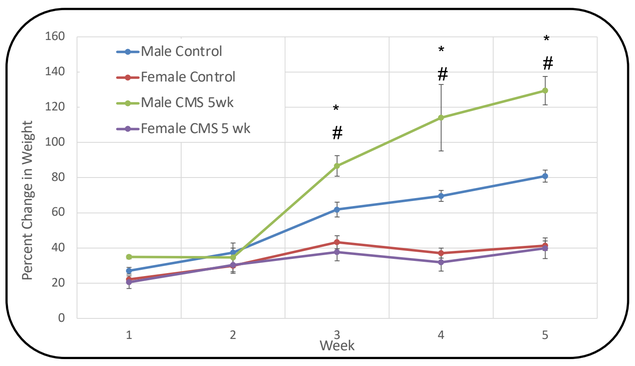

Figure 1. Rat weights over the duration of the experiment. Male control n=11, female control n=4, male CMS 5 wk n=6, female CMS 5 wk n=6. * male CMS different than female CMS, # male control different than female and male CMS ($p < 0.05$).

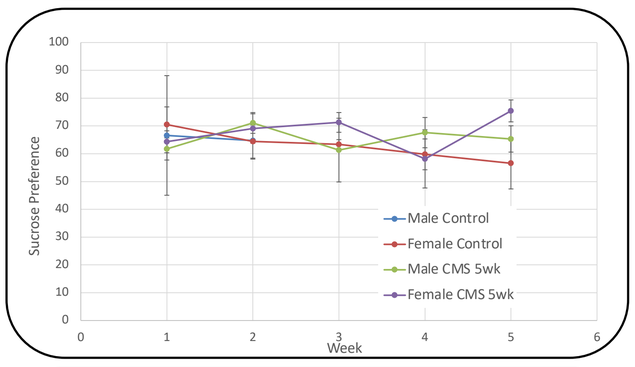

Figure 2. Sucrose preference measured as percentage sucrose consumption over total consumption (1% sucrose + water) for all groups tested. Male control n=2, female control n=4, male CMS 5 wk n=4, female CMS 5 wk n=6.

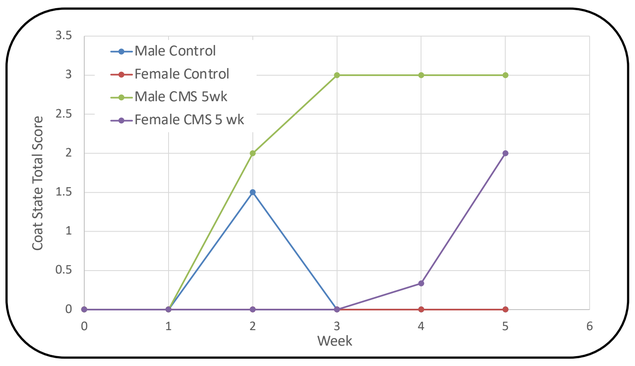

Figure 3. Coat state during the 5-week CMS. Coat state was carried out by assessment of eight different body parts: head, neck, dorsal coat, ventral coat, tail, forepaws, hind paws and genital region. A score of 0 for a coat in a good state or a score of 1 for a dirty coat were given for each area. Total score was calculated from the sum of the score of each body part.

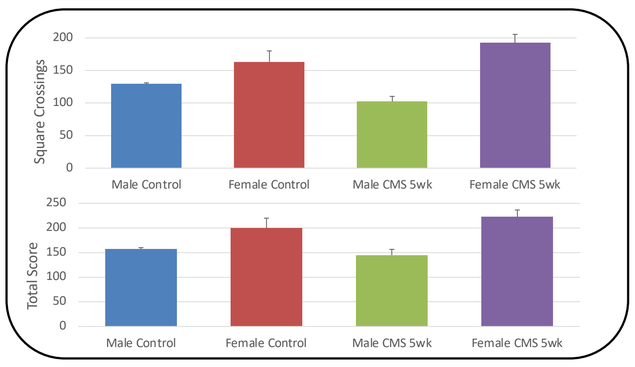

Figure 4. Open field test conducted at end of 5 week CMS. Four groups were tested: Male control (n=2), female control (n=4), female CMS (n=6), male CMS (n=4). For square crossing and total score- male CMS different than female CMS, female control different than male CMS ($p < 0.05$).

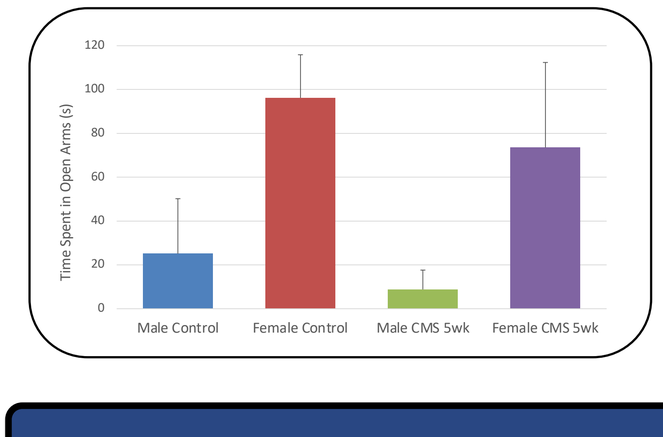

Figure 5. Elevated plus maze conducted at end of 5 week CMS. Time spent in open arms was measured for 5 minutes. Four groups were tested: Male control (n=2), female control (n=4), female CMS (n=6), male CMS (n=4).

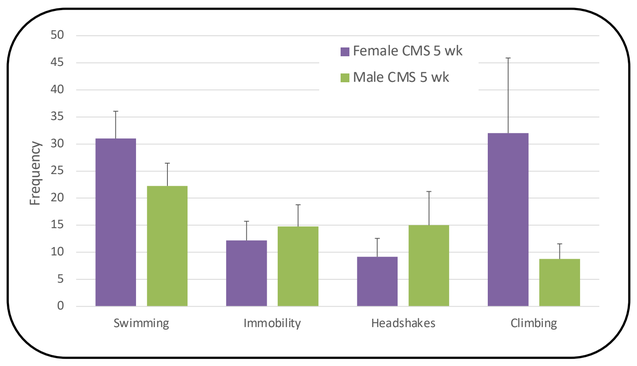

Figure 6. Forced swim test conducted at end of 5 week CMS. Frequency of swimming, immobility, headshakes, and climbing were measured for 5 minutes. Total frequency was calculated. Two groups were tested, female CMS (n=6), male CMS (n=4)

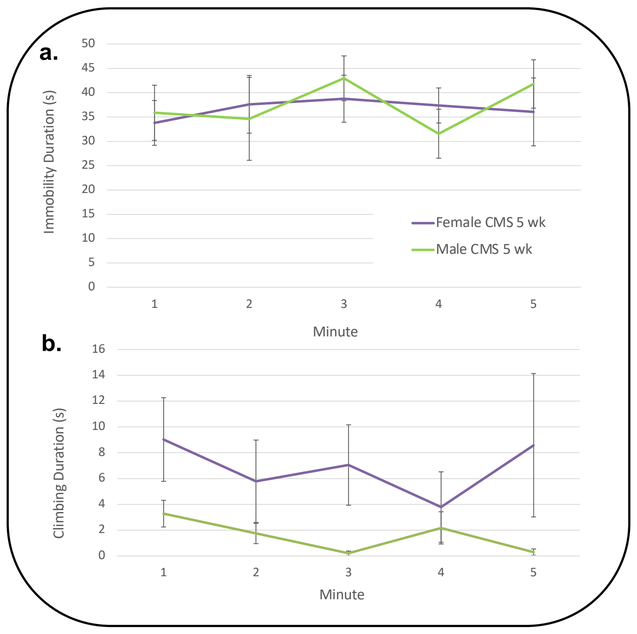

Figure 7.
Forced swim test conducted at end of 5 week CMS. Two groups were tested, female CMS (n=6), male CMS (n=4).

a. Immobility duration was measured for each minute of the assay.
b. Climbing duration was measured for each minute of the assay.

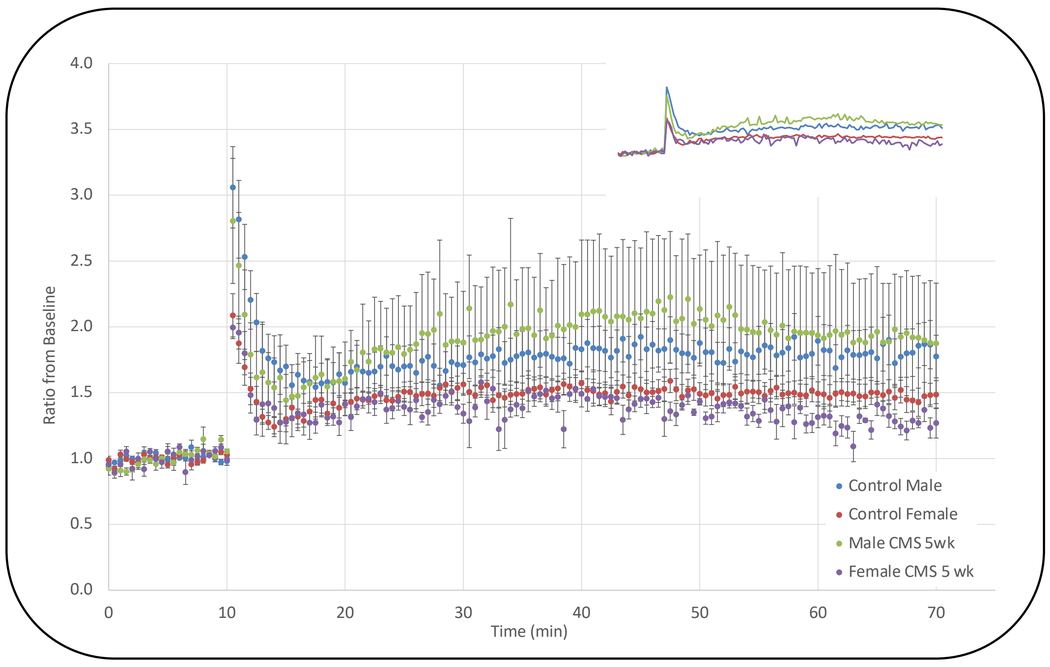

Figure 8. Extracellular EPSP were recorded from CA1 region of rat hippocampus. EPSP slopes are plotted as ratio of EPSP to the mean baseline slope ± SEM. Compiled traces for the four groups tested: male control (n=13 slices from 9 animals), female control (n=15 slices from 9 animals), male CMS (n=3 slices from 3 animals), female CMS (n=4 slices from 4 animals). Upper right inset – display of data for clarity.

Discussion

- Visual assessment of rat estrous cycle did not produce reliable results.
- CMS male increased weight compared to female CMS, (weeks 3-5).
- CMS did not have a consistent effect on sucrose preference.
- The coat state of the male CMS group was affected sooner than the female CMS group.
- **For OFT**: male CMS group had decreased square crossings vs. female CMS group. And for for additional behaviors observed.
- **For EPM**: there was a trend of increased time in open arms for the female CMS group compared to the male CMS group.
- **For FST**: differences in climbing and swimming frequency were observed between CMS groups.
- **For LTP:** CMS males had a slight increase in synaptic plasticity compared with other groups.
- There is an overall indication that CMS affects females and males differently in different assays. This suggests a sex difference in how CMS impacts anxiety- like behavior and synaptic plasticity.
- Future experiments should explore different behavioral parameters, automate analysis, increase sample size, examine sex differences in LTP.

Works Cited

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