The Effect of Early Life Stress on Depressive-Like Behaviors in Adolescent Long Evans Rats

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Results

Sucrose Preference Testing

During the sucrose preference testing, there was a main effect of sex on sucrose consumption [$F(1,54)=39.33$, $p<0.001$] (See Figure 1A,D), such that males consumed a greater amount of sucrose. There was, however, no main effect of stress on sucrose consumption [$F(2,54)=1.43$, $p=0.25$] and no sex*stress interaction for sucrose consumption [$F(2,54)=0.56$, $p=0.58$]. For water consumption, there were no main effects of sex [$F(1,54)=0.02$, $p=0.89$] or stress [$F(2,54)=1.75$, $p=0.18$] and there was no interaction [$F(2,54)=0.91$, $p=0.41$] (see Figure 1B,E). Sucrose preference data were calculated by comparing the amount of sucrose consumed to the total consumption. There were no main effects of sex [$F(1,54)=0.54$, $p=0.47$] or stress [$F(2,54)=1.44$, $p=0.25$] on sucrose preference and there was no interaction [$F(2,54)=0.84$, $p=0.44$] (see Figure 1C,F). All rats showed a sucrose preference greater than 88 percent (see Figure 1C,F) The only significant effect of this test was the main effect of sex on raw sucrose consumption based on the Repeated Measures ANOVAs run with sex and stress as between-subjects variables, across the within-subjects factor of day.

Forced Swim Test

Behaviors of the rats during FST were separated and analyzed by the categories of immobility, swimming, and climbing/struggling using a factorial ANOVA with sex and stress as between-subjects factors.

Immobility.

There was a main effect of sex on immobility in the FST (see Figure 2A), such that females showed greater immobility compared to males [$F(1,54)=36.87$, $p<0.001$]. However, there was no main effect of stress [$F(2,54)=0.22$, $p=0.81$] and no sex*stress interaction [$F(2,54)=0.87$, $p=0.43$].

Swimming.

There was a main effect of sex on swimming in the FST (see Figure 2B), such that males showed more swimming behavior compared to females [$F(1,54)=6.52$, $p=0.014$]. However, there was no main effect of stress [$F(2,54)=0.15$, $p=0.86$] and no sex*stress interaction [$F(2,54)=0.36$, $p=0.70$].

Climbing/Struggling.

There was a main effect of sex on climbing/struggling behaviors in the FST (see Figure 2C), such that males showed more climbing/struggling behavior compared to females [$F(1,54)=20.50$, $p<0.001$]. However, there was no main effect of stress [$F(2,54)=0.79$, $p=0.46$] and no sex*stress interaction [$F(2,54)=1.43$, $p=0.25$].

Discussion

After a total of sixty adolescent Long Evans rats were tested for depressive-like behaviors using a sucrose preference test and Forced Swim Test, the data were analyzed by stress condition (acute, chronic, control) and sex (male, female). Significant main effects of sex were found in FST behaviors and in raw sucrose consumption, but there were no effects for sucrose preference.

The researchers hypothesized that Early Life Stress would have an impact on depressive-like behavior which would be detectable in adolescent Long Evans rats. From the results of the sucrose preference test and Forced Swim Test, there was no main effect of stress. The data therefore do not support this hypothesis. None of the hypotheses regarding sucrose preference were supported either, as there was no sucrose preference effect or interaction with sex and stress. Every group strongly preferred sucrose to water, a preference that may be related to the age of the rats.

It was also predicted that females would show more depressive-like behaviors as a result of ELS. While females showed increased immobility compared to males, this was a main effect

not moderated by stress condition. Thus, the behavior is not additionally impacted by stress and the hypothesis is not supported. Increased immobility in females has been repeatedly demonstrated in the literature when the water depth is between 30cm and 50cm, as consistent with this study (Ma, Xu, Wang, and Li, 2019).

Anhedonia was anticipated to have been measured by a reduced sucrose preference. In adult rats, males in a chronic stress condition have displayed reduced sucrose consumption and significantly reduced sucrose preference (Molet, 2016). Stress condition did not have a main effect on sucrose or water consumption or on sucrose preference. This reduction did not appear in the fourteen-day span of testing in the adolescent rats, but this does not necessarily mean that the ELS was ineffectual in producing depressive-like behaviors. Based on Molet's 2016 study, at seven weeks of age the chronic stress condition should show an observable reduction in preference. Perhaps measuring this beginning at PND38 was too soon to see a significant effect of ELS on this depressive-like behavior, which indicates that this behavior emerges between PND51 and weeks seven through eight of age.

Duman has shown that depressive-like behaviors emerge over time (2010). This understanding is crucial for the next steps in this area of research. I propose that under the same stress conditions, the Forced Swim Test should be administered beginning at PND49 for half of the rats and beginning at PND42 for half of the rats. If there is a significant difference between these two groups in indications of depressive-like behavior, the window of time for emergence of these behaviors can be narrowed.

Ma, Xu, Wang, and Li (2019) reported that females may be more sensitive to single-housing conditions and to light/dark schedules. Female rats spent less time immobile when the

light/dark schedule was reversed (Ma, Xu, Wang, & Li, 2019). This factor of light could be explored for its effects in reducing stress or delaying the emergence of depressive-like behaviors.

Based solely on the results of the present study, more research needs to be done during the adolescent time period to determine at what point depressive-like behaviors begin to emerge in acute and chronic ELS conditions. By performing the sucrose preference, FST, or other measures of depressive-like behavior at progressively later PND time periods, or by scaling back a replication of another study which found significant results in adults, researchers may be able to find these answers.

References

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Molet, J., Heins, K., Zhuo, X., Mei, Y.T., Regev, L., Baram, T.Z., and Stern, H. (2016). Fragmentation and high entropy of neonatal experience predict adolescent emotional outcome. *Translational Psychiatry*, 6, e702.

Figures

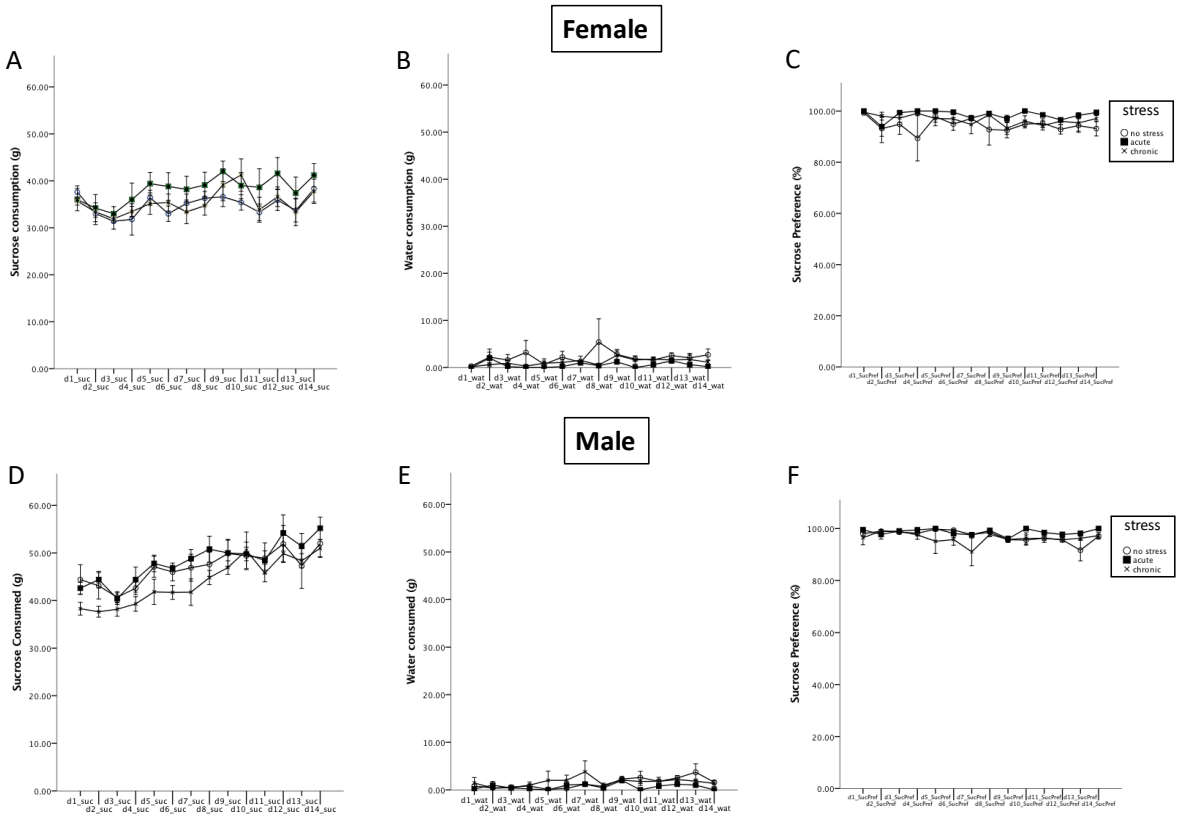

Figure 1: Displays the trends in drinking consumption across 14 days of testing in adolescent Long Evans rats. Sucrose preference was a percentage calculated by the sucrose consumed compared to total consumption.

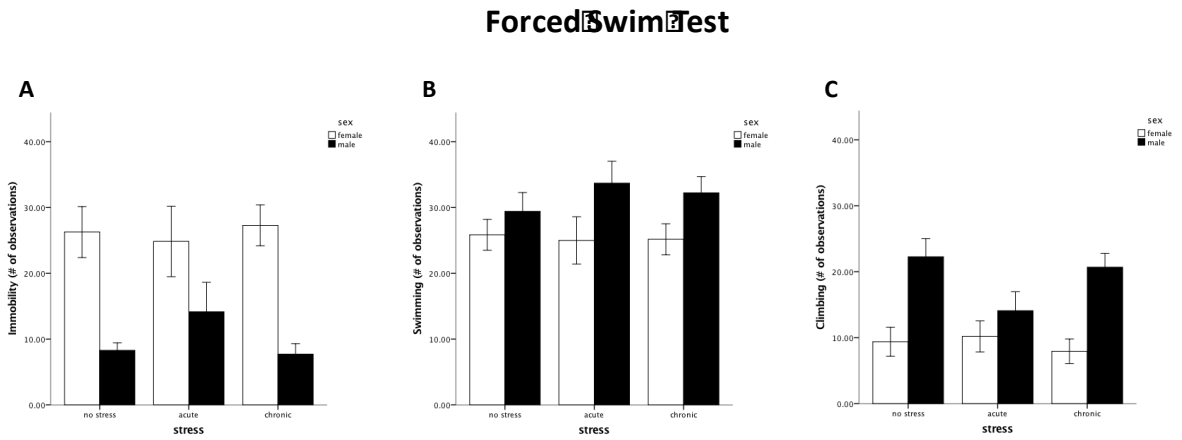

Figure 2: Displays the behaviors exhibited by adolescent Long Evans rats during five-minute Forced Swim Tests, separated by each of the three categories of behavior. Immobility is defined as movement necessary only to keep the nose above water, swimming is a paddling fashion of alternating limb movement, and climbing/struggling is more erratic upward motion with front paws moving in sync. The first independent variable, displayed on the x-axis, is the stress condition and the second independent variable is the sex of the rats.