

Effect of socially induced early life stress in juvenile rats on stress responsivity to intermittent swim stress in adulthood

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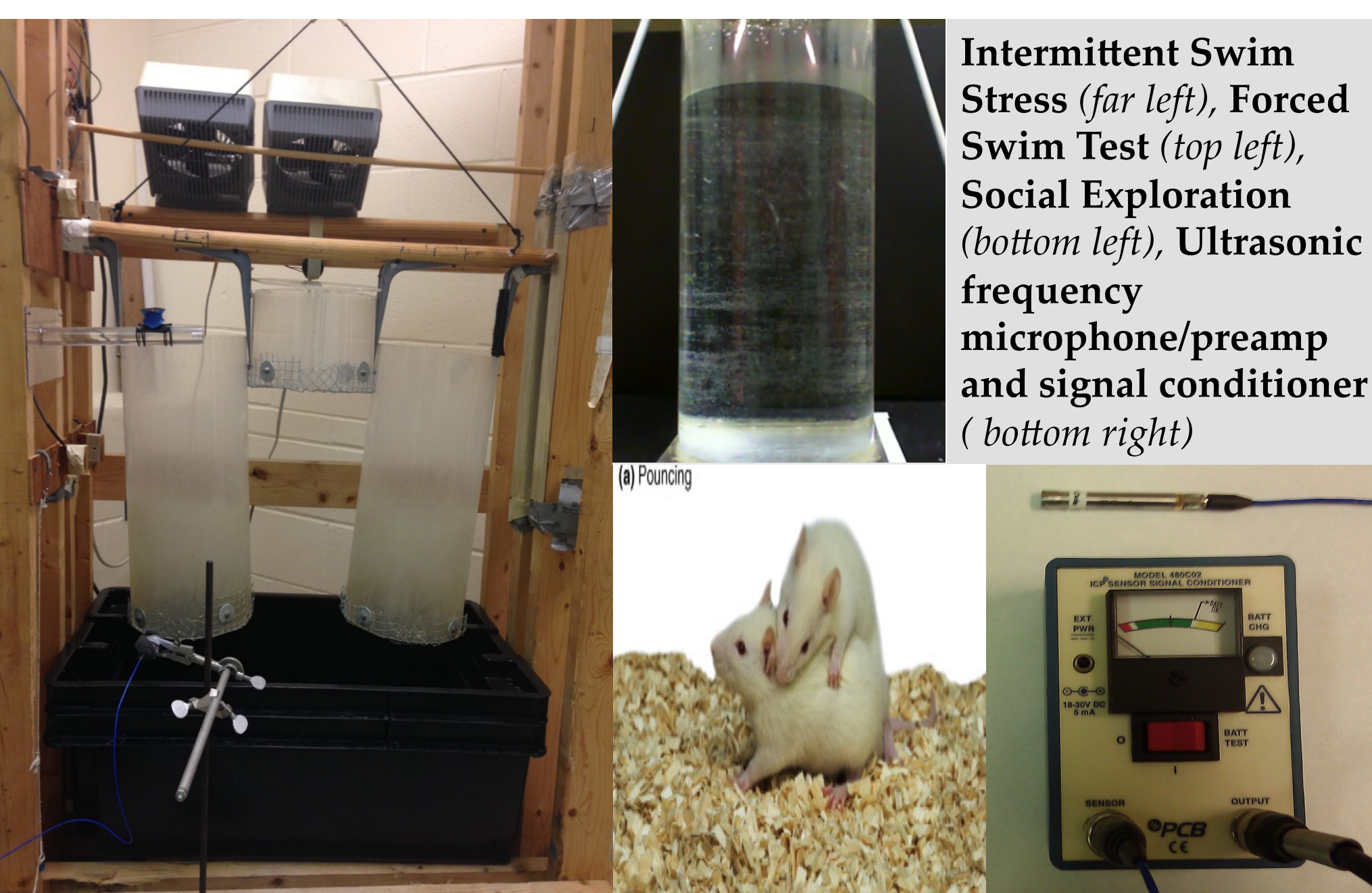
Introduction

Early life stress (ELS), such as abuse and neglect, is linked with major depressive disorder (MDD) and post-traumatic stress disorder (PTSD). The changes that occur within the brain during childhood and adolescence are pronounced and easily affected by outside factors making the brain vulnerable (7). This vulnerability contributes to many of the negative effects and deficits in patients with MDD or PTSD and plays a role in effects seen in pre-clinical models.

Rat models are often used to study the effects of ELS because adolescent humans and juvenile rats experience similar changes in brain development (4). A variety of juvenile stressful stimuli are correlated with increased depressive and anxious behavior following subsequent stress in adulthood compared to rats who only experience adult stress (5,6). Current literature does not explore the effects of stress transmission, or stress induced by social interactions with another individual (3), on subsequent stress responsivity. Rats, like humans, are social animals. Understanding the effects of social interactions is important in determining how stress may be passed on to juveniles and how stress affects future stress responses.

The ability to use ELS as a predictor for future stress responses is important as well. In the intermittent swim stress (ISS) paradigm, ultrasonic vocalizations (USVs) have been shown as a predictor of stress resilience (2). Determining how ELS affects USVs will help increase the ability to accurately predict behavior.

This current study investigates the effects of socially transmitted juvenile stress on USV during and behavior following subsequent stress in adulthood.



Methods

Animals

Subjects were 24 male Sprague-Dawley rats. Rats were randomly assigned to either the social exploration (SE) or the confined control (CC) group. The SE group was further divided into SE baseline (SE/B) or SE treatment (SE/T) groups.

Social Exploration (SE)

As juveniles, all SE subjects were placed in a cage with an adult rat for three minutes and allowed to freely interact. Each SE subject was paired with a total of four adults. SE/B subjects were paired with four adults that had undergone no stress (baseline adults). SE/T subjects were paired with two control adults and two stressed adults (treatment adults). CC rats remained in the home cage during exploration sessions.

Intermittent Swim Stress (ISS)

ISS was administered in Plexiglas cylinders with wire mesh floors, suspended over a tank of 15°C water. All SE subjects experienced 80 5-sec swim trials where the cylinder was lowered into the water. CC subjects were in a shorter cylinder that experienced the same procedure without reaching the water. Space heaters blew warm air into the cylinders during variable length inter-trial-intervals.

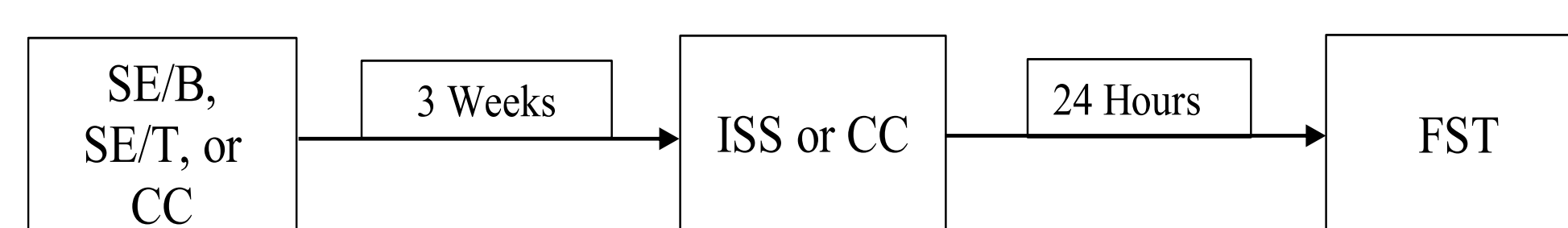
Ultrasonic Vocalization (USV) Detection and Analysis

USVs were recorded during all ISS procedures and detected using a prepolarized ¼ inch free-field precision condenser microphone and preamplifier connected to an ICP signal conditioner. The signal was converted via analog-to-digital acquisition device, refined via band-pass filters set to 18kHz and 32kHz, and quantified (duration, frequency, time) with a custom Lab View program.

Forced Swim Test (FST)

The FST was conducted in Plexiglas cylinders (20 cm dia.) containing 29cm of 24±1°C water. Twenty-four hours after ISS or CC, one at a time all rats were placed in FST for 5 min. Climbing, swimming, and immobility behaviors were analyzed using a 5-sec sampling procedure (5).

Timeline



Analysis

Treatment means were compared via one-way ANOVA. Comparisons among means were conducted by post-hoc LSD test.

Results

Figure 1: Immobility during FST of rats exposed to ISS or CC 24 hours prior. SE/T significantly differed from SE/B ($p=0.010$), while only marginally different from the CC ($p=0.053$).

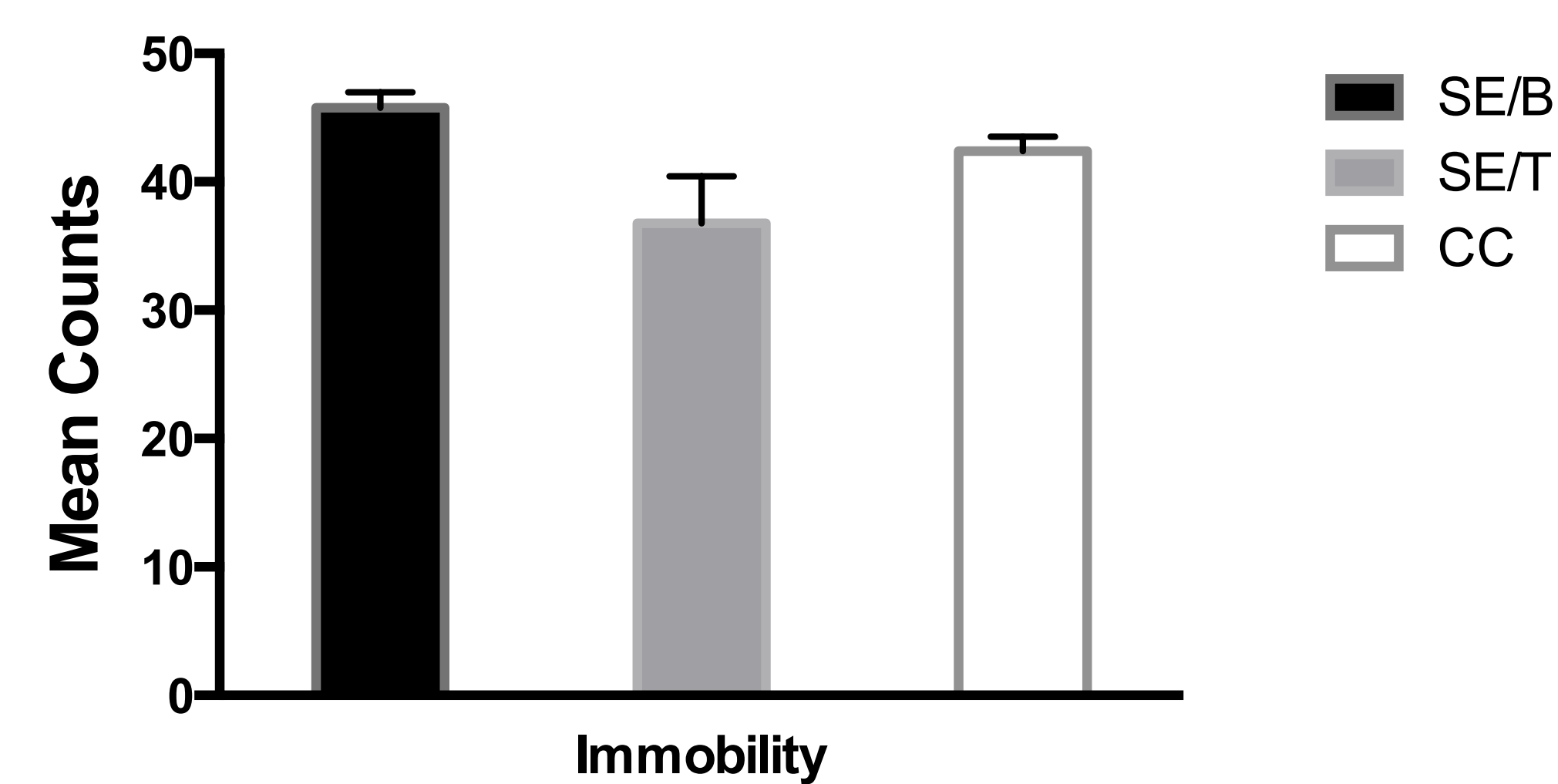


Figure 2: Climbing behavior during FST. SE/T significantly differed from SE/B ($p=0.019$), while only marginally different from CC ($p=0.059$).

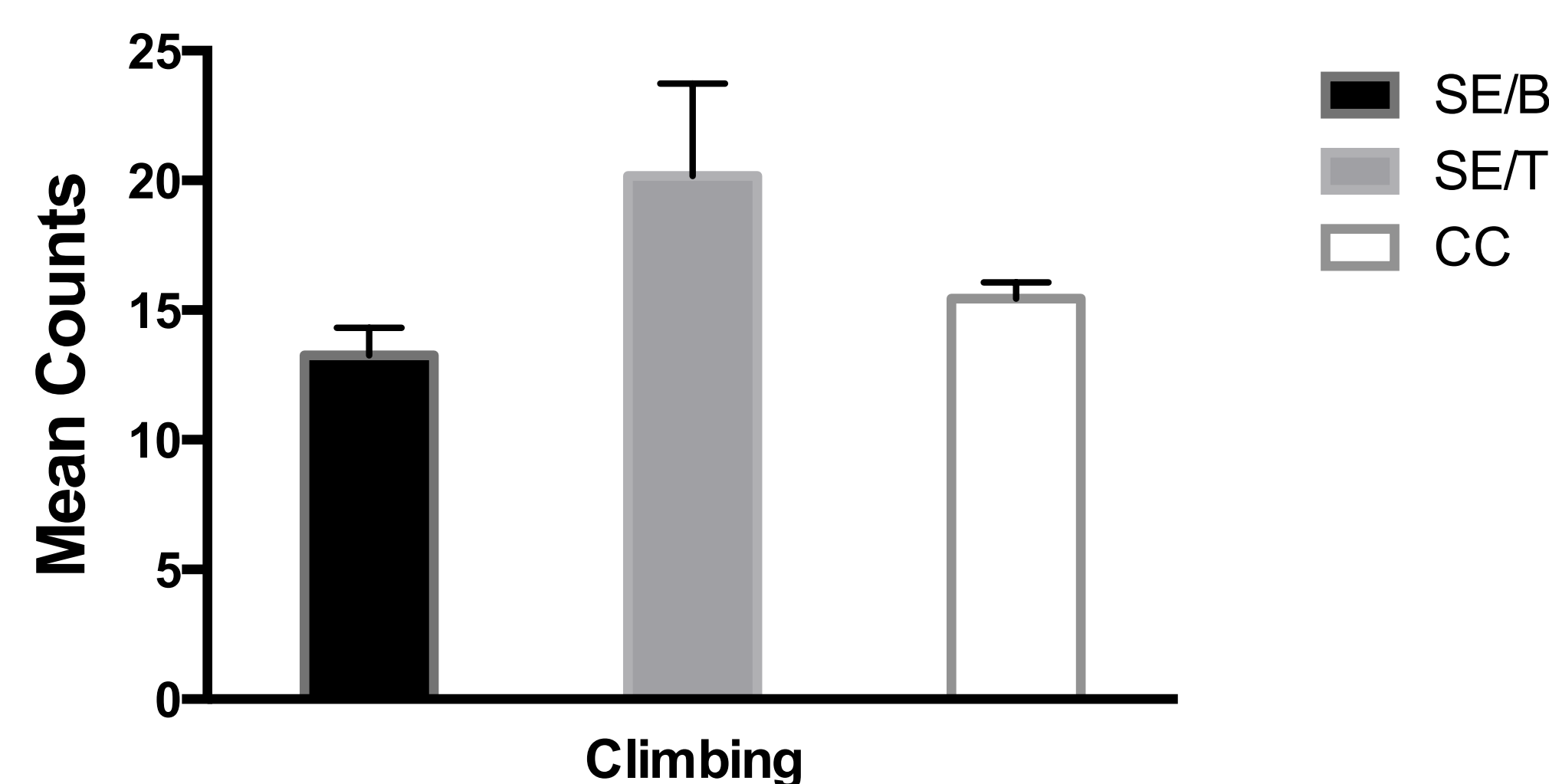
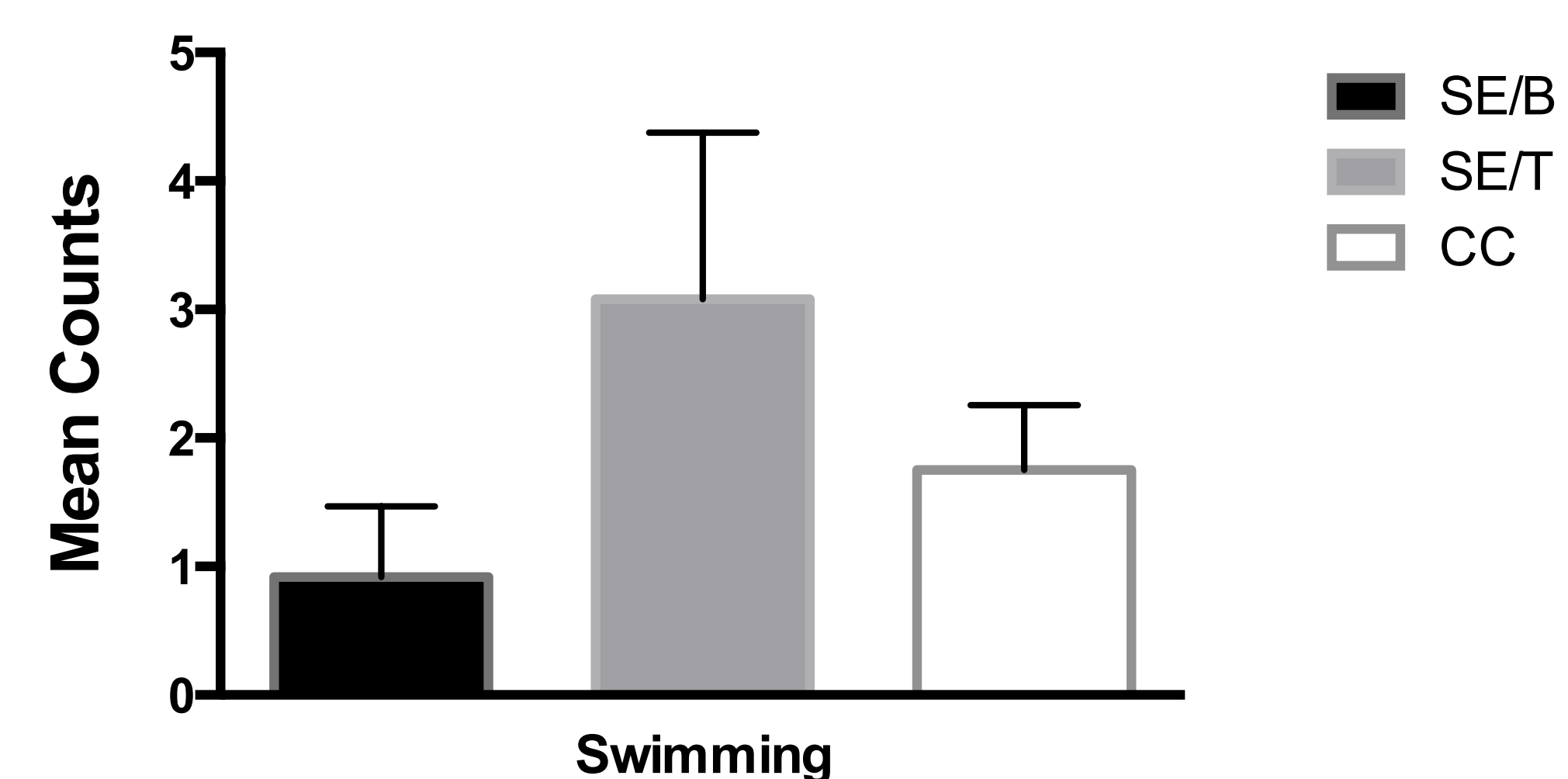


Figure 3: Swimming behavior during FST. There were no significant difference between groups.



Conclusions

- The SE/B group had overall higher immobility and lower climbing behaviors compared to the SE/T group.
- The SE/T group has increased climbing and decreased immobility compared to CC, though the significance was marginal.
- SE/B and CC groups did not show any significant different in climbing or immobility behaviors and swimming behavior did not differ for any of the three conditions.
- These results shows that prior exposure to a combination of stressed and control adults alters the reactivity to a subsequent stress (ISS).
- No USVs were emitted, this may be due to the early life experiences.
- We also observe that the CC group has higher immobility than other CC groups in previous experiments done in the lab. This may be due to uncontrollable factors during the 3 week waiting period that affected both CC and SE/B but not SE/T groups.

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