

Effects of chronic reboxetine administration on intermittent swim stress-induced ultrasonic vocalizations and subsequent performance on the forced swim test

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Introduction

- Depression is a serious mental illness that is estimated to plague 12-17% of the population at some point during their lifetime [4]. A significant proportion of patients suffering from depression are treatment resistant. In order to spur novel drug discovery and assist those that are treatment resistant the focus must be switched from the vulnerable brain to the resilient brain.
- The Intermittent Swim Stress (ISS) is a hybrid of the learned helplessness and behavioral despair models as it exposes a rat to intermittent inescapable forced cold-water swims [1,2]
- During ISS, some rats emit ultrasonic vocalizations (USVs), and this seems to predict subsequent resilient or stress-resistant behaviors [3].
- If this resiliency is working through the same pathway as antidepressants then antidepressant administration should potentiate USVs.

Method

Animals

24 male Sprague-Dawley rats served as subject and were randomly assigned to either ISS/reboxetine, ISS/saline, CC/reboxetine, or CC/saline.

Drug

Reboxetine methanesulfate was administered by intraperitoneal injections at a dose of 20 mg/kg. Control subjects received equal volume of 0.9% saline as vehicle. Injections were administered twice a day for 21 days prior to ISS.

Intermittent Swim Stress (ISS) Apparatus

ISS treatments were administered in Plexiglas cylinders with wire mesh floors, suspended over a tank of 15°C water. On a swim trial, the cylinders were lowered into the water. The apparatus was controlled by a computer with Med-PC hardware and software.

Ultrasonic Detection and Analysis

During ISS, a prepolarized ¼ inch free-field precision condenser microphone model 377101 (PCB Piezotronics) recorded Ultrasonic Vocalizations (USVs) from the animals. The microphone was placed beneath the Plexiglas cylinder containing the stress rat.

Forced Swim Test (FST)

The forced swim test was conducted in Plexiglas cylinders (20 cm dia.) containing 29cm of 24±1°C water.

Procedure

Day 1-21: Drug Administration

- All subjects were injected intraperitoneally twice daily for 21 days with either saline (n=12) or reboxetine (n=12) prior to ISS.

Day 22: Intermittent Swim Stress

- Half of the rats (n=12) were put into the ISS for 80 5-second cold water swims.
- The other half of the rats (n=12) were put into confined control (CC) in which they were lowered and raised intermittently with the ISS rats but in the absence of water.
- USVs were recorded from ISS subjects during the procedure.

Day 23: Forced Swim Test

- 24h after ISS or CC the rats were placed into the FST for five minutes.
- The procedure was recorded for later analysis in which the rats are scored for time spent immobile, climbing, or swimming.



Results

Figure 1: No significant differences between groups for mean counts of time spent immobile in the FST [$F(3,20)=0.469$, $p=0.707$].

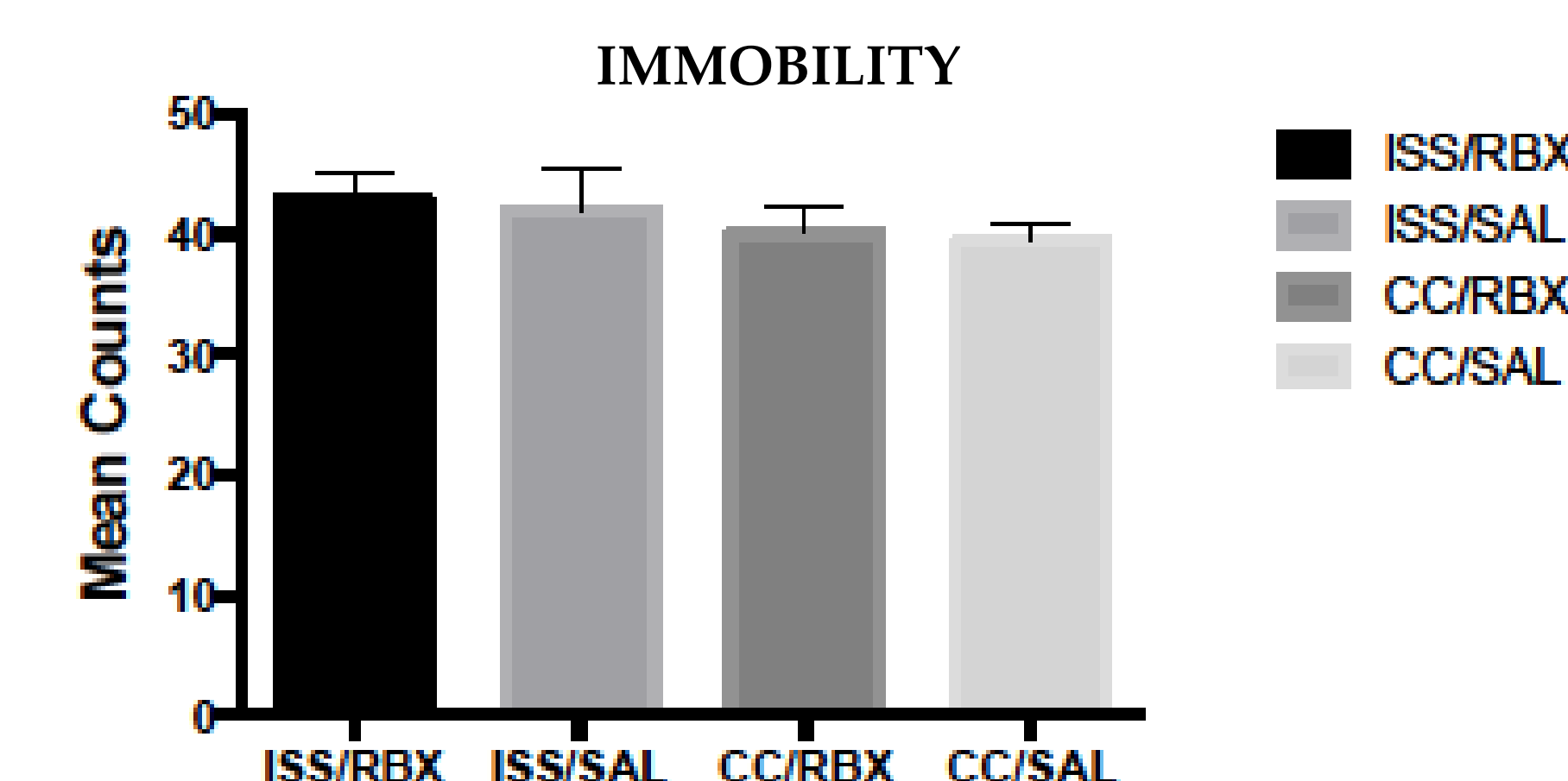


Figure 2: No significant differences between groups for mean counts of time spent climbing in the FST [$F(3,20)=0.328$, $p=0.289$].

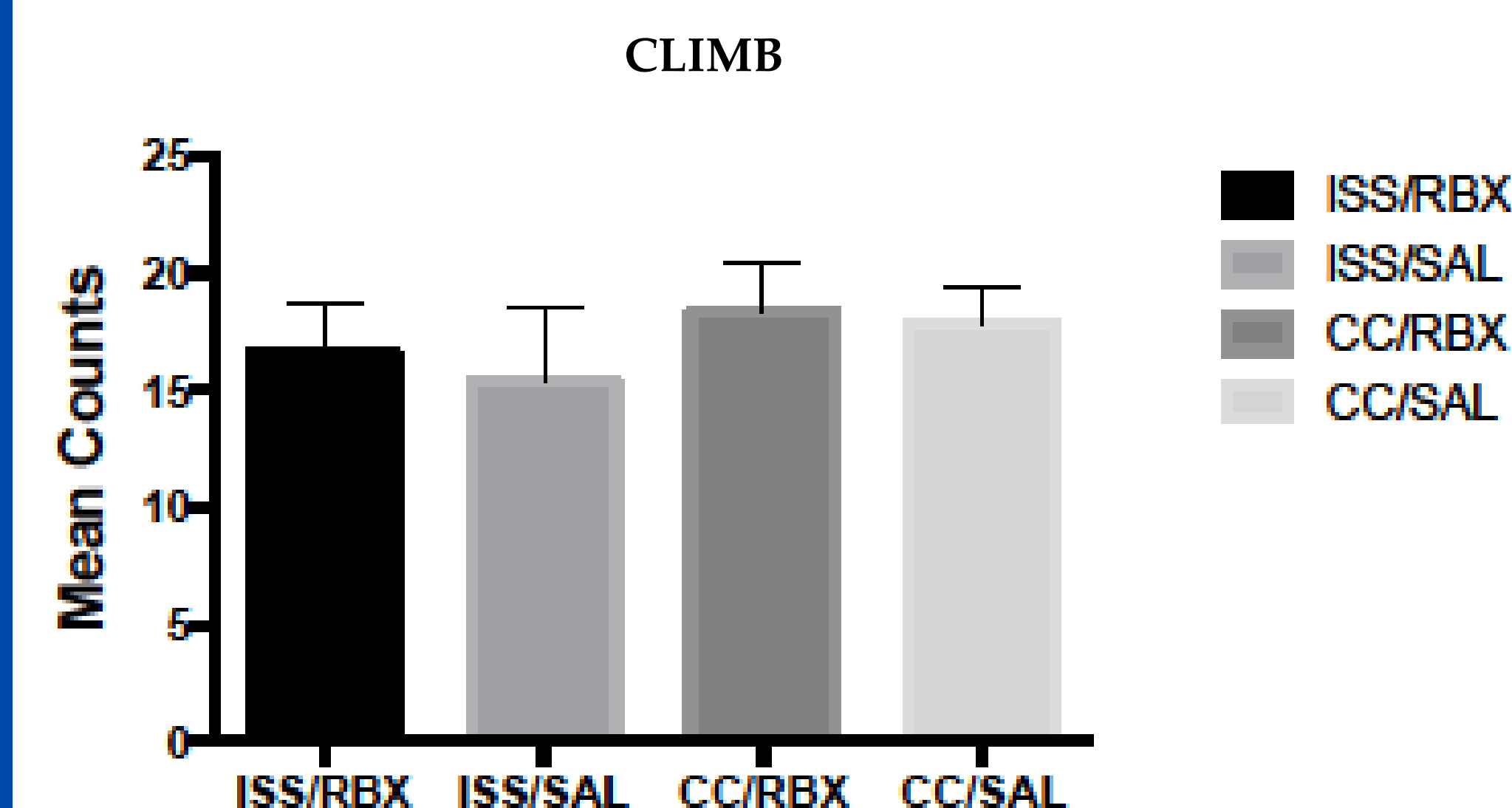
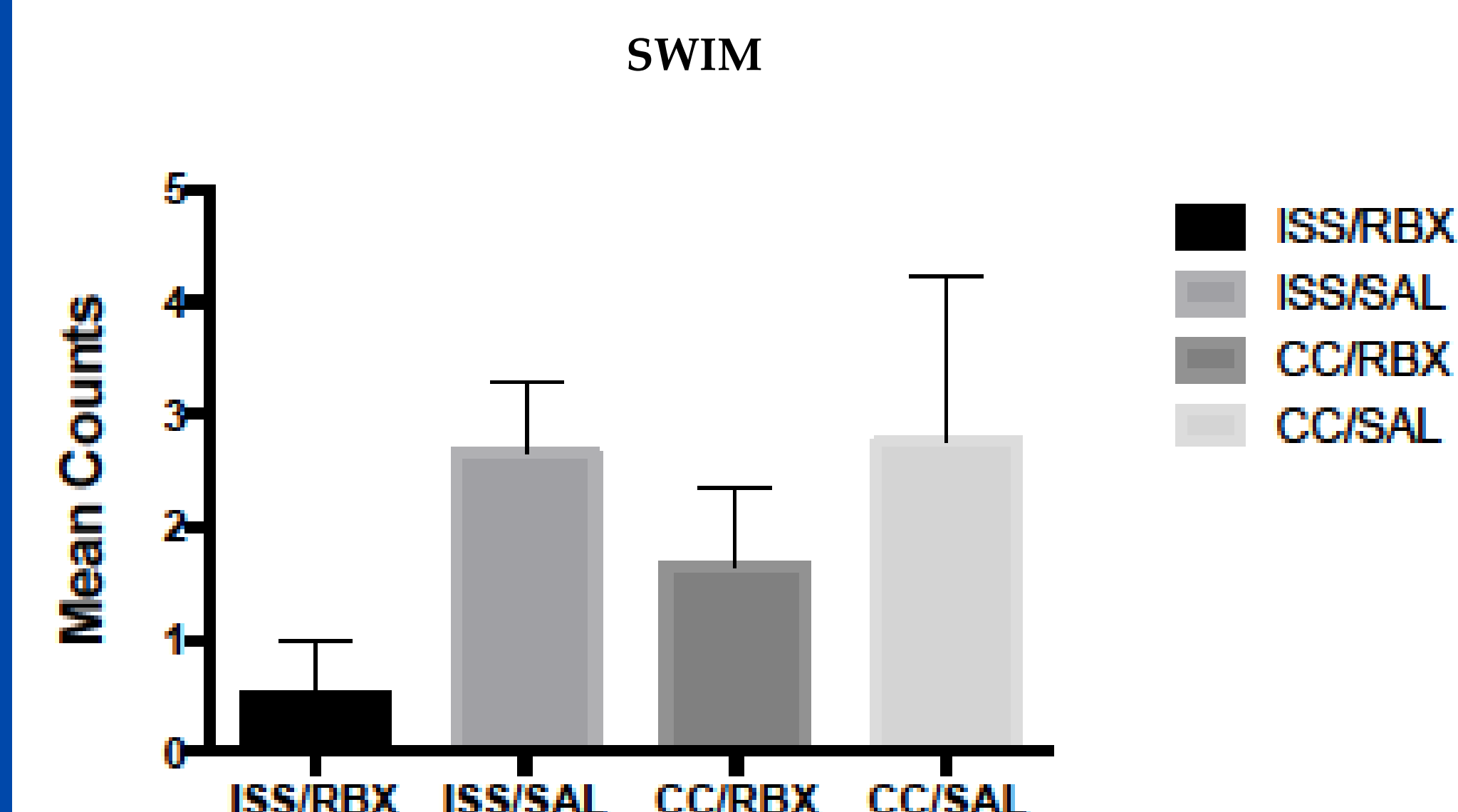


Figure 3: No significant differences between groups for mean counts of time spent swimming in the FST. [$F(3,20)=0.328$, $p=0.805$].



Conclusions

- ❑ No significant differences were observed between ISS/reboxetine, ISS/saline, CC/reboxetine, or CC/saline.
- ❑ The results show that there was no drug main effect or a stress main effect.
- ❑ There were two rats, one in each drug group (reboxetine and saline), that produced USVs but their performance in the FST did not demonstrate resiliency to stress.
- ❑ These results indicate that USV mediated resilience does not appear to work in the same neural pathway as the antidepressant, reboxetine.

References

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