The chronic, recurring nature of addiction remains a worldwide problem. Even after apparently successful clinical treatment and long-term abstinence, individuals may still relapse many months or years later. Although many individual differences exist among substance abusers, relapse tends to occur during periods of high stress (Sinha et al., 2006). Behavioral training and therapy can help cope during these high stress times, but pharmacological interventions have not been shown to be effective (Ross & Pieselow, 2009). Although some therapeutic options decrease relapse rates, more effective treatments for relapse need further investigation.

The effect of stress on use of and relapse to drugs of abuse likely stems from coupled stress and reward circuits in the brain. Stress leads to increased release of stress-related hormones including 3α, 5α tetrahydroprogesterone or, allopregnanolone (Purdy et al., 1991). Allopregnanolone is a neurosteroid tied to several brain circuits involved with stress and reward. Elevated levels of this neurosteroid occur throughout the mammalian brain and periphery after cocaine administration, and rats show enhanced dopamine release in the nucleus accumbens after an injection of finasteride, which inhibits the enzyme (5α-reductase I) responsible for allopregnanolone synthesis (Dazzi et al., 2002). Finally, acutely stressed rats exhibit increased dopamine release in the prefrontal cortex after an injection of finasteride, further indicating allopregnanolone’s involvement with brain reward systems (Devoto, 2012). Based on this information, we hypothesized that administration of finasteride would result in increased stress induced amphetamine locomotor sensitization.

**METHODS**

**Subjects:** Fifty adult male Long-Evans rats (sibling pairs) were pair-housed on a 12:12 h light-dark cycle with lights on at 0700. Rats were randomly assigned to one of three pretreatment conditions (saline, 100 mg/kg finasteride, or 25 mg/kg finasteride) followed by pseudo-random assignment to control or restraint stress conditions.

**Drugs:** Finasteride (RBS-Research, Inc., New York, NY) was dissolved until dissolved in 30% 2-Octylglycopyrrolate in a concentration of 1.6 g/ml (5.0 mg/ml). Allopregnanolone (2mg/ml) was dissolved in saline in a concentration of 1.0mg/ml.

**Pretreatment:** Rats received i.p. injections of either vehicle, 10 mg/kg finasteride, or 25 mg/kg finasteride both 48-hours and 24-hours before stress procedure.

**Acute stress:** Twenty-four hours after the last pretreatment injection rats received control or restraint stress procedure (no injections were administered on this day). During both 90-120 minutes after behavioral training in the stress group, rats were placed in restraints for 30 minutes. After 30 minutes, rats were injected with 0.1mg/kg allopregnanolone and placed back in the chamber for 120 minutes. Distance traveled was collected using a Tri-Trak photobeam tracking system (Waterston, Inc.), and Premo recorded the recording for later scoring of stereotypy behavior. Stereotypy was rated using a 1 to 10 scale for each behavior.

**RESULTS**

**Allopregnanolone concentrations follow finasteride pre-treatment.** A 2 x 3 (condition x drug) ANOVA (vehicle, 100 mg/kg finasteride, or 25 mg/kg finasteride) was performed on all samples for each condition for each sample, the mean concentration for the samples was run in duplicates. 30 μl of standard, and samples were pipetted into appropriate wells. Detection fluorogen A was added to each well prior to one hour incubation. Following incubation, wells were aspirated and washed. Detection fluorogen A was added by following 80 minute incubation. Aspiration/wash process was repeated. Substrate solution was added to the well followed by incubation for 15 minute incubation. Stop solution was added and plate was read through microplate reader at 450 nm to assess absorbance.

**Corticosterone concentrations measured during stress exposure.** Time to bouts of activity (i.e. self-stimulation) was performed on all samples for each condition for each sample, the mean concentration for the samples was run in duplicates. 30 μl of standard, and samples were pipetted into appropriate wells. Additional 4 ul of assay buffer were pipetted into N96 wells. Blue fluorogen was pipetted into ass wells, except blank T9 and N96 wells. The plate was incubated for 3 hours at room temperature on a plate shaker. Following incubation, wells were washed/aspirated. Blue fluorogen was added to all wells. Magenta substrate solution was added to all wells, followed by one hour incubation. Stop solution was added to all wells and plate was read through microplate reader at 590 nm for absorbance.

**REFERENCES**


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