**Methods**

**according to the ARRIVE Guidelines (**<https://doi.org/10.1371/journal.pbio.1000412>**)**

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| Ethical statement | All live animal procedures were approved in advance by the University of Prince Edward Island Animal Care Committee that functions in compliance with the guidelines of the Canadian Council on Animal Care |
| Study design | Three (3) treatment groups plus a vehicle control group were included, namely, (1) sucrose vehicle, (2) G115, (3) Fluoxetine and (4) Fluoxetine + G115. Rats were randomly assigned to treatment group and coded by a technician not involved in the study on arrival in the animal facility. Rats were housed in pairs with each pair being assigned to the same group. The experimental unit in all analyses was single animal. An experimental timeline is depicted in Figure 1 |
| Experimental procedures | Rats were acclimated to voluntarily consume a small amount of the drug vehicle (10% sucrose solution) within a predetermined amount of time (2 minutes) by removing the water bottle and inserting a temporary cage divider and presenting the sucrose solution in a small plastic culture dish attached to a broad-based immovable stand. Rats that failed to meet criterion were excluded. Remaining rats were weighed daily and fed vehicle, 20 mg/kg G115, 5 mg/kg fluoxetine or G115+fluoxetine twice daily (0800 and 1600) for 14 days and 4 test days in their home cage with a temporary divider to separate the rats. Voluntary consumption was considered the least stressful method of drug administration and rats were continually observed during feeding to confirm consumption of the entire solution. All behavioural testing took place between 1000 and 1400 during the light phase of the cycle in an environment controlled test room adjacent to the housing area. Euthanasia was performed by decapitation under deep isoflurane anesthesia |
| Experimental animals | All experiments used male Sprague-Dawley (CD subtype) weighing 225-250g at the time of arrival in the animal facility which corresponds to approximately 7-8 weeks of age. Rats were purchased from Charles River laboratories in St Constant, Quebec, Canada. Rats were housed in pairs and left undisturbed for a minimum of 7 days after arrival.  |
| Housing and husbandry | Housing was in an SPF certified facility. Rats were housed in pairs in Plexiglas cages fitted with filter tops and on wood chip bedding changed every third day. Lights in the colony room were on at 0600 and off at 1800 daily. The colony room was illuminated with overhead fluorescent lighting at 300-400 lux although this was reduced to approximately 150 lux when the animals were in the housing rack. Mean room temperature was 24 +/- 2 C at 30-52% humidity. Room air was subject to 18-20 changes/hour. Food was standard Purina rat chow and food and water were available ad libitum with the exception of drug solution feeding |
| Sample size | A total of 51 rats divided over 4 groups were used. Group sizes were uneven at the time of experimentation because some rats failed to achieve criterion. Final group sizes were vehicle (n=13), G115 (n=14), fluoxetine (n=12), G115+fluoxetine (n=12). Group sizes were based on previous work in our lab using these behavioural tests as well as relevant literature. Rats were tested in 4 cohorts with all 4 treatment groups represented in each cohort. |
| Allocating animals to experimental groups | Rats were randomly allocated to each group by a technician not otherwise involved in the project on arrival in the facility  |
| Experimental outcomes | The primary experimental outcomes were behaviours scored experimenter blind using either behavioural analysis software (AnyMaze) or from video recordings in the case of the forced swim test. Secondary outcomes were expression of BDNF and TrKB protein in the hippocampus and prefrontal cortex as measured by Western Blot and quantified by automated image analysis |
| Statistical methods | Data based on individual animals for each behavioural parameter were analysed by one-way ANOVA after confirmation of homogeneity of variance (Levene’s test). When a significant main effect was detected post-hoc comparisons using Tukey’s Multiple Comparison Test. Western Blot samples were run in duplicate and band density was normalized to total protein. Comparisons between groups were done using one-way ANOVA and Tukeys MCT. All analyses were performed in SPSS (v.23) and P<0.05 was established a priori as the level of significance |