Fragile x syndrome is the most common single gene cause of autism. It is caused by a mutation in the fmr1 gene that produces fmrp—a protein. We utilize a mouse model of FXS that contains a deletion in the fmr1 gene. This mouse model demonstrates learning and motor abnormalities comparable to human patients that suffer from FXS. We believe that these abnormalities are due to the abnormal regulation of dopamine in FXS caused by the decreased number of D2 autoreceptors. D2 autoreceptors normally regulate the release of dopamine in the brain; in fxs patients the decrease in d2 autoreceptors causes increased tonic and decreased phasic dopamine release.

We specifically wanted to look at whether these d2 abnormalities mediated other behaviors, such as sucrose conditioned flavor preference. We have previously found that the D2 autoreceptor agonist quinpirole inhibits SCFP expression in mice derived from WT mothers, but not KO mothers. We then attempted to study whether quinpirole is able to inhibit SCFP acquisition in heterozygous mice.

We conducted three different experiments in order to test this. In the first experiment we injected mice with either quinpirole (the d2 autoreceptor agonist) or saline, and then presented them with a bottle with either cherry or grape kool-aid flavoring, as well as a 10% sucrose additive. The next day we injected them once again and then presented mice with the other flavor and no sucrose additive. On the third day we tested them to see if they showed a preference for the flavor reinforced by sucrose by providing them with both flavors, neither of which were reinforced with sucrose. We then repeated this training and testing procedure a few more times. Mice failed to acquire a sucrose preference through this procedure. We realized that this occurred because mice were only on a 50% reinforcement schedule; only half of the time they were receiving the CS+ was it actually being reinforced. From this we realized that we had to increase our reinforcement schedule, so we moved to a 75% reinforcement schedule. We presented the CS+ and CS- 3 times each before testing the mice on their preference. In this procedure mice displayed a preference for the CS+. However, they failed to display a learning curve—they all learned by the first day. We then reduced our reinforcement schedule to 67% by presenting the CS+ and CS- twice each before testing. These mice also displayed a CS+ preference by the first day, so we were once again unable to establish a learning curve.

After these multiple failures we were worried that the materials we were using were faulty, so we conducted a few control experiments to make sure that our baseline thinking was accurate. First we wanted to ensure that there was no baseline genotypic difference in sucrose preference between heterozygous and wild type mice. We found that all mice preferred sucrose over water equally. This confirms findings by smith, L. et al. (2014)

We then wanted to ensure that our quinpirole was effectively suppressing dopamine release. In order to study this we used a locomotor assay—a tried and true method for determining the effectiveness of quinpirole. In mice treated qith quinpirole, they usually show a serious decrease in movement 20-40 minutes after injection. This is what we found in our control experiment.

Once we realized that our materials were accurate, we turned to focusing on other ways to obtain an accurate learning curve in mice. In our sucrose preference control experiment we presented mice with only a 1.5% concentration of sucrose, while in our SCFP experiment we presented them with a 10% concentration. Researchers have found a 100% preference at an 8% concentration of sucrose, so our sucrose concentration may have simply been too high. However, in our sucrose preference control experiment mice failed to display a learning curve at all—their preference stayed relatively low. Therefore in future experiments we would attempt to find the correct level of sucrose concentration to present mice with in order to obtain a learning curve.