Session/Poster# Presenter

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Sex differences in motor learning flexibility in post-pubertal mice are related to mushroom spine density

Human studies report that females have more flexibility in motor learning than males. One factor that may impact this ability is the density of mushroom spines in layer 5 (L5) of the primary motor cortex (M1), which is intrinsic to motor learning. Our lab has shown that pruning of mushroom spines in CA1 hippocampus at puberty is necessary for optimal spatial learning flexibility post-pubertally. My current work shows that pruning of L5 M1 mushroom spines in the proximal, basilar dendrites only occurs in the female mouse, an effect prevented by knock-out of Î±4-containing GABA-A receptors. Thus, we tested the hypothesis that post-pubertal female mice would have better motor learning flexibility than groups with higher mushroom spine density, male wild-type (WT) and female Î±4-/-. To assess this, we performed a rotarod test: mice were first trained at constant speed (4 RPM) for 4 (5min) trials (â€œlearningâ€). The next day, each group was trained at an accelerated speed (4 to 40 RPM) for 4 trials (â€œlearning flexibilityâ€). The latency to fall off the rotarod was assessed for each trial. A linear regression was performed on each learning curve (latency to fall/trial number) for each animal, and a one-way ANOVA used to compare groups, with a post-hoc Tukey's test. On the constant speed test there were no significant differences in the learning curve slopes (female WT = 52.3-15.4 sec/trial, N=5, female Î±4 -/- = 89.2-7.7 sec/trial, N=4, male WT = 62.2-12.4 sec/trial, N=4). (F (2,10)=2.16, P=0.17) On the accelerated speed test, the female WT learning slope was significantly higher than that of the female Î±4 -/- and male WT (female WT = 17.4-4.98 sec/trial, N=5, female Î±4 -/- = -2.58-4.59 sec/trial, N=5, male WT = -0.08-2.09 sec/trial, N=5). (F(2,12)=7.18, P=0.009). These findings suggest that a lower mushroom spine density in female adolescent mice improves motor learning flexibility and may underlie the reported sex differences in motor learning flexibility in humans.