Presentation: Lithium ameliorates behavioral deficits in mouse model of fragile X syndrome-550.12

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Fragile X syndrome (FrX) is the most common inherited cause of mental retardation resulting from the silencing of the *FMR1* gene and the consequent loss of its protein product, the fragile X mental retardation protein. Features of FrX include cognitive disability, hyperactivity, autistic behavior, seizures and learning deficits. Lithium is used clinically to treat bipolar disorder, and it has been used to treat mood dysregulation in individuals with FrX. Lithium has also been shown to reverse learning deficits and improve viability in a *Drosophila* model of FrX (Chang et al, Nat Chem Biol. 4: 256, 2008; McBride et al, Neuron 45:753, 2005). In the present study, we examined whether dietary lithium would alter behavioral abnormalities in *fmr1* knockout mice (KO). Four groups of mice were studied: 1) wild type (WT) controls; 2) KO controls; 3) WT lithium-treated; 4) KO lithium-treated. Lithium treatment commenced at weaning; mice were fed 0.3% lithium carbonate-containing chow or control chow throughout the experiment. Between 8 and 12 weeks of age mice were subjected to the following behavioral tests: open field, social interaction, elevated plus maze, elevated zero maze and passive avoidance. We found that compared with WT controls KO controls were hyperactive and had lower anxiety-related behavior as suggested by relatively less time in closed arms in elevated plus and zero mazes. The control KO mice also showed impaired social interactions and learning deficits on a passive avoidance test. Lithium treatment ameliorated the impaired social interaction and learning deficits on passive avoidance. Lithium treatment tended to reverse the reduced anxiety-related behavior, but it had no effect on hyperactivity. These findings have important implications for lithium treatment of FrX patients.

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