Regional alteration of cholinergic function in central neurons of trisomy 16 mouse fetuses, an animal model of human trisomy 21 (Down syndrome)

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The trisomy-16 (TS16) mouse is considered to be a model of human trisomy 21 (Down syndrome) because of genetic homology between mouse chromosome 16 and human chromosome 21. We examined cholinergic function of brain and spinal cord tissue and in cultured neurons from TS16 mouse compared with that of age matched controls. Mean acetylcholinesterase activity in both tissue types did not differ between trisomic and control conditions. Acetylcholine (ACh) synthesis, measured as choline O-acetyltratransferase (acetyl-CoA) activity, was reduced to 67% of control in TS16 brain but not in TS16 spinal cord. Steady-state accumulation of ACh precursor, [3H]choline, was measured in primary cell cultures. Steady-state choline uptake was reduced to 35% and to 61% in neurons of TS16 brain and spinal cord, respectively, when compared with controls. Kinetics experiments in TS16 brain cells showed a 50% reduction of the maximal velocity of choline uptake when compared to controls. Further, the ACh release