Can Epigallocatechin gallate (EGCG) Treatment Rescue Hippocampal-Dependent Cognitive Function in a Down Syndrome Mouse Model?

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Down Syndrome (DS) is caused by the trisomy of human chromosome 21 (Hsa21). Trisomy 21 can cause various behavioral, cognitive, learning and memory deficits. Deficits in hippocampal structure and function have been identified in mouse models of DS and are implicated in cognitive and learning impairments. Mouse models have suggested that deficits in cognitive function are associated with overexpression of *Dyrk1a*, a gene on Hsa21 found in three copies of individuals with DS. *Dyrk1a* is a gene that is involved in brain development and function. Ts65Dn DS model mice exhibit trisomy for approximately half of the genes on Hsa21 including *Dyrk1a* and exhibit cognitive and learning impairments. We are using Ts65Dn mice to test the effects of Epigallocatechin gallate (EGCG), a Dyrk1a inhibitor, on Dyrk1a activity and cognitive function. We hypothesize that EGCG will reduce Dyrk1a activity in the hippocampus and improve hippocampal-dependent spatial learning and memory in the Morris water maze place learning task in Ts65Dn mice. The mice were given daily EGCG treatment (200 mg/kg per day) by means of oral gavage beginning on postnatal day 54 and continuing throughout water maze testing (postnatal days 67-74). Measures of spatial learning included latency and path length to find a submerged platform during acquisition trials (postnatal days 67-73). Memory for the previously learned location of the platform was assessed on a probe trial (postnatal day 74) in which the platform was removed and the amount of time spent swimming in the area of the tank previously containing the platform was measured. These measures allowed us to analyze the mice's ability to learn and remember the position of the platform and to spatially orient themselves. Preliminary data indicates that EGCG treatment may not be an effective treatment for the spatial learning and memory deficits evident in this mouse model of DS.