Effects of EGCG treatment on deficits in a radial-arm maze spatial pattern separation task in a Down syndrome mouse model

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Down syndrome (DS) is caused by three copies of human chromosome 21 (Hsa 21) and results in a constellation of phenotypes that include intellectual disability. Ts65Dn mice, the most extensively studied model of DS, have three copies of approximately half the genes on Hsa 21 and display many of the phenotypes associated with DS, including cognitive deficits. DYRK1A is found in three copies in humans with Trisomy 21 and has increased expression in a number of tissues. Dyrk1a is also found in three copies in Ts65Dn mice, and has been shown to be involved in a number of critical pathways including CNS development and osteoclastogenesis. Epigallocatechin-3-gallate (EGCG), the main polyphenol found in green tea, is an inhibitor of Dyrk1a activity. We have previously shown that a three week treatment with EGCG normalizes skeletal abnormalities in Ts65Dn mice. Previous work has found that Ts65Dn mice are significantly impaired in several hippocampal-dependent tasks, including the Morris water maze and novel object recognition. Another hippocampal-dependent process, pattern separation, is the ability to differentiate between similar memories acquired during learning. Distinctive encoding of these similar memories in hippocampal formation is thought to be necessary to distinguish between them. Experimental reductions in adult neurogenesis have produced impairments in pattern separation performance. Given that recent studies in Ts65Dn mice have reported significant reductions in adult hippocampal neurogenesis, we hypothesize that Ts65Dn mice will be impaired in the pattern separation task. Furthermore, we hypothesize that treating Ts65Dn mice with EGCG throughout task learning would improve performance to control levels. A radial arm maze-delayed non-matching-to-place pattern separation task with three different degrees of spatial separation is used. Preliminary data suggests that, in contrast to control mice, Ts65Dn mice do not improve their performance over training.

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