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Mice expressing the A53T mutant form of human alpha-synuclein exhibit unexpected improvements of spatial learning and memory abilities

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Parkinson's Disease (PD) pathology is characterized by the formation of intra-neuronal inclusions called Lewy bodies which are comprised of alpha-synuclein (α-syn). PD is primarily a movement disorder but patients are known to experience memory deficit and mood disorders. In the present study, we examined the effect of hA53T mutation during development on the locomotor, anxiety-like behavior and spatial learning and memory abilities. We used the open-field test, elevated plus maze, Morris water maze and rotarod tests to evaluate hA53T transgenic mice and wild-type littermate at 3, 6 and 9 months of age. Results from open field and elevated plus maze tests show A53T mice develop age-dependent changes in locomotor activity and reduced anxiety-like behavior. Results from Morris water maze task showed no obvious differences between A53T transgenic mice and the wild type in the latency to escape on the hidden platform. In the probe test, A53T mice exhibit unexpected improvements of learning and spatial memory abilities at 3 and 9 months as demonstrated by a significant increase in spending more time in target quadrant on 5th and 7th days. Further studies by a reverse learning test also showed that 3 and 9-month-old transgenic mice spent more time in target quadrant compared with wild-type controls. No motor coordination impairments were observed by rotarod tests in the transgenic mice at 3, 6 and 9 months. These results indicate a possible role of the A53T α-syn mutation in enhancing spatial learning and memory abilities suggesting that these behaviors might be disturbed in hA53T mutation PD mouse model.

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