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Nitrinergic and cholinergic system in the tegmental nuclei of a murine model (Ts65Dn mice) for Down syndrome

S.Gotti; E.Caricati; C.Viglietti–Panzica; G.Panzica*

Dept Anat Pharm & For Med, Univ. of Torino, Torino, Italy

Ts65Dn mice, bearing a partial triplication of mouse chromosome 16, have been largely used as animal model for the study of Down Syndrome. These mice show several behavioral alterations (i.e., learning and memory, altered sexual and aggressive behaviors) that, in humans, are related to Down Syndrome. Previous studies demonstrated a precocious (3 month-old) reduction of the nitrinergic system in the basal forebrain (Gotti et al, 2004) followed by that of cholinergic system (age 4–6 months; Granholm et al., 2000). These alterations have been observed in the medial septum and the nucleus of the diagonal band, where the two systems are largely co-existent. We have here investigated the nitrinergic and cholinergic systems in both basal forebrain and pontine tegmental nuclei, in male Ts65Dn mice at the age of 3 months. Our results indicate that co-localization of the two markers is extensive only at the level of pontine nuclei, whereas in the forebrain, they largely co-exist in the same regions, but rarely co-localize in the same cells. By means of quantitative analysis we demonstrated a significant reduction of the nitrinergic system only in the forebrain with no effect of mutation on the cholinergic system. On the contrary, both cholinergic and nitrinergic systems are unaffected at the pontine level. This is an intriguing feature, due to the fact that tegmental nuclei send and receive connections from the basal forebrain. It appears therefore that precocious alterations of the nitrinergic systems are very selective and circumscribed to the basal forebrain.

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