BEHAVIOURAL CHARACTERIZATION OF ENGRAILED MUTANT MICE AS MODEL OF PARKINSON'S DISEASE

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The most difficult feature to be reproduced in an animal model of Parkinson's disease (PD) is the gradual degeneration of dopamine (DA) neurons. Indeed, contrary to the acute degeneration of DA neurons produced by MPTP and 6-hydroxydopamine, the degeneration of DA neurons in humans occurs over a long period of time.
Recently, it has been demonstrated that Engrailed genes (En-1 and En-2) have a prominent role in specification and survival of midbrain DAergic neurons. Heterozygous null for En-1/ homozygous null for En-2 (En-1+/-;En-2-/-) mice have an adult phenotype showing neuropathological hallmark of PD. These mice exhibit a slow progressive degeneration of nigral DAergic neurons starting at birth, progressing until third month of live and reaching a maximal loss of DA neurons of about 60%.
In order to investigated in these mutant mice whether the loss of DA neurons produces changes in motor behaviour similar to PD symptoms, we have conducted a battery of tests evaluating spontaneous motor activity, strength, motor performance and coordination.
Male (En-1+/-;En-2-/-) mice of 4 and 8 months old were tested in the following behavioural test: 1) *inverted grid test* (used to evaluate motor performance and strength); 2) *beam-walking test* (used to assess motor performance and motor coordination); 3) *pole test* (used to identify coordination deficits). Male (En-1+/+;En-2-/-) mice were utilised as control.
Mutant (En-1+/-;En-2-/-) mice showed fine motor skills and strength altered at 4 months and worsened at 8 months respect to the control mice, assessed by the inverted grid test; whereas they at both age did not show deficits in motor performance during the beam-walking test. Moreover, in the pole test we observed significant deficits in motor coordination in mutant mice respect to control mice that became progressive worse with age.
These results suggest that although these mutant mice did not show motor deficits in motor performance, they demonstrated deficits in motor coordination in particular during performance that required sophisticates movements of coordination. Together, these results suggest that En-1+/-; En2-/- have an adult behavioural phenotype that might be used as a model of PD.