## Environmental enrichment and brain repair: the therapeutic effects of cognitive training in neurological diseases

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Cognitive dysfunctions, depression and anxiety, poor movement control are common symptoms of central neurodegenerative diseases as well as of ageing. Life experience, sensory stimulation, cognitive activity and spontaneous physical exercise reinforce the "brain reserve", the synaptic plasticity which permits to cope brain damage and are proposed as complementary to drugs for therapeutic approaches aimed to the cure of central diseases. Environmental enrichment (EE) refers to the addition of objects to the animal's environment to increase levels of novelty and complexity. It partially reproduces the physical-social activity experienced by aged patients participating to rehabilitative programs. In recent years our study was dedicated to assess whether EE training can affect chemical transmission in the CNS of young and aged mice.

To this aim, six and twenty months old male and female mice were housed in enriched environment three months before sacrifice. Animals were housed in large cages containing a variety of objects such as plastic tunnels, climbing ladders, running wheels, toys in wood and plastic suspended from the ceiling, paper, cardboard boxes, and nesting material that are renewed every 2 days. Control animals (i.e. those exposed to standard environment) were housed in normal cage containing nests. The weight of animals was controlled before during and after the environmental training. The anxiety and curiosity of both trained and non-trained animals were also analysed in the "light-dark box". At the end of the training period animals were sacrificed and the spontaneous and the evoked release of preloaded [3H]noradrenaline ([3H]NA) as well as of endogenous glutamate and GABA monitored from cortical and hippocampal nerve endings. Inasmuch, the efficiency of NMDA and AMPA receptors in controlling glutamate exocytosis was investigated. Finally, we monitored the efficacy of EE in delaying the course of experimental autoimmune encephalomyelitis (EAE) and to recover the glutamate defects that became detectable in the cortex staring from the early stage of disease.

Our results clearly indicate amelioration of curiosity and reduced anxiety in trained animals when compared to control. [3H]NA exocytosis was significantly reduced in aged mice when compared to young ones but significantly recovered in trained aged mice. GABA exocytosis also was significantly reduced in aged mice but significantly recovered to physiological level in trained old animals, while glutamate exocytosis was largely unaffected. Relevant changes in NMDA and AMPA receptors expression and efficiency was also highlighted. Data will be also provided concerning the gender dependency of the EE training impact in young and aged mice as well as the impact of training in EAE mice.

Our data seem to support the notion the environmental training is beneficial to central transmission in aged mice as well as in animals suffering from EAE.