ENVIRONMENTAL TRAINING AMELIORATES THE COURSE OF DEMYELINATING DISEASE IN MICE: A GLUTAMATERGIC HYPOTHESIS

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Environmental enrichment (EE) refers to the addition of objects to the animal's cage to increase the levels of novelty and complexity. It potentiates the endogenous mechanisms to cope brain damage. Remodelling of neurones and glial cells are thought to have a role in the EE-induced amelioration of disease symptoms.

EE training was shown to promote adult neuronal progenitor cell mobilization into demyelinating lesions in mice suffering from Experimental Autoimmune Encephalomyelitis (EAE). In these mice the oligodendrocyte fate of the stem cells from the subventricular zone was favoured. Our recent data demonstrated that in EAE mice trained in EE, clinical symptoms were significantly less pronounced than that observed in EAE mice reared in standard environment(1.57 ± 0.28 in SE-EAE mice; 0.52 ± 0.16 in EE-EAE mice; n=7, $p<0.05$). Inasmuch, EE significantly recovered the spontaneous motor activity in the open field maze as well as the anxiety behaviour in the light-dark box in the EAE mice. In order to propose a molecular mechanism accounting for the positive effect, we found that EE can restore the chemical transmission at cortical glutamatergic synapses. Actually, the release of endogenous glutamate from cortical terminals from EAE was significantly lower than that observed in control, non-immunized mice (control mice 293 ± 26; 137 ± 11 in EAE mice; n=6, $p<0.05$, data expressed as pmoles/mg prot). EE failed to modify the exocytosis of endogenous glutamate elicited by high KCl in control mice, but it significantly recovered it in mice suffering from EAE (EE mice 251 ± 26; 238 ± 18 in EE-EAE mice; n=6, n.s, data expressed as pmoles/mg prot.). Amelioration of glutamate release was accompanied by the restoration of the production of endogenous cAMP and of the expression of synaptic proteins. Immunocitochemical analysis confirmed the positive role of training on disease progression.