Intensity-dependent Immune-modulatory Effects of Exercise Training in Experimental Multiple Sclerosis

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Abstract

Background: Exercise training (ET) has beneficial effects on multiple sclerosis (MS) and its animal model experimental autoimmune encephalomyelitis (EAE). However, the intensity-dependent effects of ET on the systemic immune system in EAE remain undefined.

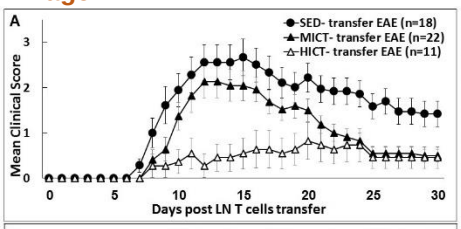
Objective: (1) To compare the systemic immune-modulatory effects of moderate vs. high intensity ET protocols in EAE; (2) To investigate whether ET affects autoimmunity selectively, or causes general immunosuppression.

Methods: Healthy mice were subjected to moderate or high intensity treadmill running programs. Proteolipid protein (PLP) -induced transfer EAE was utilized to examine ET effects specifically on the systemic immune system. To examine effects of ET on systemic autoimmunity, lymph-node (LN)-T cells from trained- vs. sedentary donor mice were transferred to naïve recipients and EAE severity was assessed. LN-T cells derived from donor trained vs. sedentary PLP-immunized mice were analyzed *in vitro* for proliferation assays and cytokine and chemokine receptor genes expression. T cell-dependent immune responses of trained- vs. sedentary mice to the non-autoantigen ovalbumin and susceptibility to *Escherichia coli* - induced acute peritonitis were examined.

Results: High intensity training in donor mice induced stronger inhibitory effect than moderate intensity training on disease development and PLP-reactivity of LN- T cells derived from PLP-immunized mice. High intensity training also inhibited LN- T cell proliferation in response to ovalbumin immunization. *E-coli* bacteria counts and dissemination were similar in trained and sedentary mice.

Conclusion: High intensity training possesses superior modulatory effects on autoimmunity in EAE, while also inhibiting T cell responses to ovalbumin, but sustains immune defenses against *E-coli* bacteria.

Image



B	SED- transfer EAE (n=18)	MICT- transfer EAE (n=22)	HICT- transfer EAE (n=11)
Day Of Onset	8.7 ± 0.4	11.3 ± 0.7 *	13.0 ± 1.9 *
Maximal Clinical Score	2.9 ± 0.4	2.8 ± 0.3	1.2 ± 0.5 *
Burden of Disease	45.3 ± 6.8	29.7 ± 4.0 *	12.0 ± 6.0 **

Figure 1: Superior inhibitory effect of high intensity training on the encephalitogenicity of lymph node (LN) T cell-derived from proteolipid (PLP) - immunized mice in transfer model of experimental autoimmune encephalomyelitis (EAE).
Clinical course (A) and clinical parameters (B) of transfer EAE in mice that received PLP- reactive LN T cells from moderate intensity continuous trained (MICT- transfer EAE, n=22), high intensity continuous trained (HICT- transfer EAE, n=11) or sedentary (SED- transfer EAE, n=18) mice. The severity of EAE was scored on a 0–6 scale. Transfer of LN- T cells derived from HICT, PLP-immunized mice to naïve recipients induced the most significant attenuation of EAE development. Data are mean ± SE. *p<0.05, **p<0.01, as compared to SED- transfer EAE.

Recent Publications

1. Einstein O, Grigoriadis N, Mizrachi-Kol R., Reinhartz E, Polyzoidou E, Lavon I, Milonas I, Karussis D, Abramsky O, Ben-Hur T. Transplanted neural precursor cells reduce brain inflammation to attenuate chronic experimental autoimmune encephalomyelitis. Exp Neurol. 2006;205(1):294.
2. Einstein O, Fainstein N., Vaknin I., Mizrachi-Kol R., Reihartz. E., Grigoriadis N., Lavon I., Baniyash, M., Lassmann H., and Ben-Hur T. Neural Precursors Attenuate Autoimmune Encephalomyelitis by Peripheral Immunosuppression. Ann Neurol. 2007;61(3):209-18.
3. Einstein O, Ben-Hur T. The changing face of neural stem cell therapy in neurologic diseases. (Review). Arch Neurol. 2008;65(4):452-6.
4. Einstein O, Friedman-Levi Y., Grigoriadis N. and Ben-Hur T. Transplanted Neural Precursors Enhance Host Brain- Derived Myelin Regeneration. The J. of Neuroscience. 2009;29(50):15694-702.
5. Einstein O, Fainstein N, Touloumi O, Lagoudaki R, Hanya E, Grigoriadis N, Katz A, Ben-Hur T. Exercise Training Attenuates Experimental Autoimmune Encephalomyelitis by Peripheral Immunomodulation rather than Direct Neuroprotection. Exp. Neurol. 2018;299(Pt A):56-64.



Biography

Prof. Einstein's area of specialization is neuro-immunology and neuro-regeneration in neurodegenerative diseases, specifically on animal models of human Multiple Sclerosis (MS). Her major studies concern on the neurobiology of neural stem cells and cell therapy in neurodegenerative diseases. Her work published in 2003 was the first to show that transplanted neural stem cells have anti-inflammatory effects on the rodent brain. This finding was a breakthrough for further research of her group, as well as other research groups around the world. Her current research focuses mainly on neuro-immunological, neuro-protective and neuro-regenerative effects of exercise training on neurodegenerative diseases, particularly on experimental autoimmune encephalomyelitis (EAE) the animal model of MS. The studies involve animal training, clinical evaluations, histopathological analyses, cell cultures and molecular biology techniques.

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