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# Muscle carnosine in Experimental Autoimmune Encephalomyelitis and Multiple Sclerosis: effects of exercise

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Short title: Muscle carnosine in EAE and MS.

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**Introduction.** Part of the neuromuscular dysfunction in Multiple Sclerosis (MS) may reside within the muscle (impaired cross-bridging, impaired  $\text{Ca}^{2+}$  handling, altered exercise-induced lactate response). Muscle carnosine may affect this. The impact of MS on muscle carnosine however was never investigated before.

**Methods.** First, muscle carnosine levels of m. tibialis anterior were measured in control rats (CON, n=40) and in an animal MS model (EAE, Experimental Autoimmune Encephalomyelitis, n=40) before and after exercise therapy (EAE<sub>EX</sub>, CON<sub>EX</sub>, 10d, 1h/d, 24m/min treadmill running) and sedentary conditions (EAE<sub>SED</sub>, CON<sub>SED</sub>, n=20). Furthermore, m. vastus lateralis carnosine levels of healthy controls (HC) and MS patients were measured (HC, n=22; MS: n=24). Hereafter and in a subgroup of MS patients only, the effect of high intense exercise therapy (MS<sub>EX</sub>, n=11, 12w, 5sessions/2w, 80-100% HR<sub>max</sub>) versus sedentary conditions (MS<sub>SED</sub>, n=6) on muscle carnosine levels were evaluated.

**Results.** EAE decreased ( $p<0.05$ ) muscle carnosine levels by -40% to -64% in EAE<sub>SED</sub> 10d to 17d following EAE induction. This was not restored/prevented by exercise therapy (-37% to -64%). MS decreases ( $p<0.05$ ) muscle carnosine levels by ~25% compared to HC. Exercise did not appear to remediate this.

**Conclusion.** EAE and MS decrease muscle carnosine levels substantially. Exercise therapy does not appear to restore this.

