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High-Speed Treadmill Running Reduces Systemic Inflammation But Fails as Secondary Intervention For Peripheral Musculoskeletal Discomfort

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It has been shown that performance of highly repetitive tasks increases serum cytokines, nerve inflammation and sensorimotor declines in a rat model. **Purpose:** Investigate the effectiveness of flat treadmill running in preventing these responses. **Methods:** Thirteen young adult female Sprague-Dawley rats were trained to perform a high force task for 5 weeks (15 min/day, 5 days/week). All trained rats went on to perform a high repetition, high force reaching and lever-pulling task for 10 weeks (10-week HRHF; 2 hrs/day in four 30 min sessions, 3 days/week). Five task rats were randomly chosen to run on a flat treadmill (TM) for the last 6 weeks of task performance (10-week HRHF+TM; ramping up to 23 m/min, 1hr/day, 5 days/week). Results were compared to 10 control rats. Voluntary task and reflexive sensorimotor behavioral outcomes were assessed and compared. Serum was assayed for inflammatory cytokines, median nerves were assayed for CD68+ macrophages and extraneuronal thickening, flexor tendons were assayed for any pathological changes. **Results:** Treadmill running attenuated HRHF task-induced increases in serum TNF-alpha (HRHF+TM 7.720 ± 11.89 vs HRHF 146.7 ± 228.1 pg cytokine/mL serum), IL-1beta (HRHF+TM 0.00 ± 0.00 vs HRHF 42.47 ± 56.15 pg cytokine/mL serum) CXCL2/MIP2 (HRHF+TM 1.320 ± 0.3633 vs HRHF 12.32 ± 3.800 pg cytokine/mL serum) and IL-10 levels (HRHF+TM 1.600 ± 3.578 vs HRHF 23.58 ± 21.97 pg cytokine/mL serum). However, voluntary task performance outcomes such as percent successful reaches (HRHF+TM 9.4 ± 5.8 vs HRHF $45 \pm 12\%$) worsened with treadmill running. The treadmill intervention failed to rescue HRHF task-induced declines in reflexive grip strength (HRHF+TM 349.9 ± 84.79 vs HRHF 300.8 ± 149.5 g) and forepaw mechanical sensitivity (HRHF+TM 1.764 ± 2.351 vs HRHF 4.364 ± 0.8090 g of withdrawal threshold), and increases in CD68+ macrophages and extraneuronal fibrosis (HRHF+TM 86.34 ± 5.907 vs HRHF $56.43 \pm 17.16\%$ Dense CT Surrounding Nerve) within and around median nerves. **Conclusions:** The treadmill intervention attenuated systemic inflammation and moderate tendinosis, but did not improve task performance or sensorimotor behaviors most likely because this exercise intervention continued to load involved injured forelimbs and worsened median nerve inflammation and fibrosis.

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