Exercise selectively mobilises skin-homing effector CD8+ T cells and natural killer cells into peripheral blood.

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ABSTRACT

Introduction: Acute exercise induces a transient mobilisation of lymphocyes into peripheral blood that is largely comprised of CD8+ T cells and natural killer (NK) cells. The magnitude of this response is dependent on the differentiation status of these lymphocyte subsets, thus cells with a capacity to initiate rapid effector function (i.e., cytokine secretion and target killing) exhibit the largest changes in response to exercise. It is hypothesised that the effector cells preferentially mobilised into the bloodstream have high tissue-migrating potential, however, the origin of these cells, and their potential homing destination(s) following exercise has not been established in humans. Accordingly, this study investigated whether CD8+ and NK cell subsets expressing the cutaneous lymphocte antigen (CLA) – a molecule expressed on skin-associated memory lymphocytes (≤ 20% CD8+ T cells and ≤ 50%NK cells) that binds to endothelial cell leukocyte adhesion molecule 1 (ELAM-1) – were selectively mobilised in response to acute exercise. **Methods:** Ten healthy males (mean ± SD age: 22 ± 3 yrs) completed two different exercise sessions: high-intensity continuous cycling (CC; 85% at HR^{Peak} for 30 mins) and high-intensity interval training (HIIT; 90% of HR^{peak} 10 x 1 min repetitions with 1 min rest intervals). Blood was taken before, immediately- and 30 min post-exercise for cryo-preservation of peripheral blood mononuclear cells. CD8+ subsets were classified into naive (NA; CD45RA+CCR7+), central memory (CM; CD45RA−CCR7+), effector-memory (EM; CD45RA−CCR7−) and CD45RA-expressing effector-memory cells (EMRA; CD45RA+CCR7−). In parallel, $CD56^{bright}$ 'regulatory' and $CD56^{dim}$ 'cytotoxic' NK subsets were identified using CD56 and CD16. Lymphocyte subpopulations were examined for CLA expression. **Results:** The number of CLA+CD8+ cells increased in response to both exercise modes. This observation was driven by a preferential mobilisation of effector-memory CLA+CD8+ T cells, as shown by the percentage change in cell number from baseline to exercise: EMRA (CC 244%, HIIT 86%) > EM (CC 142%, HIIT 75%) > CM (CC 104%, HIIT 51%) > naive (CC 82%, HIIT 34%). Within the NK cell pool, $CLA+CD56^{dim}$ cells (CC 520%, HIIT 326%) were mobilised to a greater extent than $CLA+CD56^{bright}$ cells (CC 180%, HIIT 129%). 30-min post-exercise, there was a reduction in the number of CLA+ cells compared to pre-exercise values. **Conclusion:** This is the first study to demonstrate a selective mobilisation of skin-homing lymphocytes during exercise, suggesting that exercise redistributes effector cells to peripheral tissue, contributing to immune-surveillance.