The Current State of Exercise-Induced Lymphocyte Apoptosis

James W. Navalta* and Jonato Prestes

1Department of Kinesiology and Nutrition Sciences, University of Nevada, Las Vegas, Nevada
2Graduate Program on Physical Education, Catholic University of Brasilia, Águas Claras, Brasilia - DF, 71966-700, Brazil

Abstract

Research into the area of exercise-induced lymphocyte apoptosis is a relatively new field of interest. The number of published manuscripts in PubMed peaked in the year 2005 and has been declining in recent years. Possible reasons for this decrease may be a lack of perceived relevance and some investigations that have questioned whether the phenomenon occurs. We proposed that continued study should be focused toward this issue as improvement in technology may allow for more sensitive measurement in the future. Finally, it is possible that this line of research may provide a mechanistic link between the benefits of exercise and a reduction in many chronic diseases that have been observed.

Keywords: Physical activity; Programmed cell death; Immune cells

Short Commentary

Research into exercise and the immune system is a relatively new field within the discipline of exercise physiology. Within this sub discipline, investigations specifically on the ability of exercise to induce lymphocyte apoptosis began with a report from Mars et al. in 1998 [1]. In that initial paper, evidence was provided that a single bout of exhaustive treadmill running in humans was sufficient to induce the cell death process termed apoptosis in the circulating lymphocyte population [1]. Since then various laboratories have reported that other modalities of exercise were also capable of inducing apoptosis in lymphocytes including cycling [2], tennis [3], and resistance training [4, 5].

However, as more researchers began to investigate the ability of exercise to serve as a stimulus to induce apoptosis in lymphocytes, some authors began to question these findings, particularly in terms of its role in the post-exercise decrease in immune cell volume, termed lymphocytopenia [6, 7]. In fact, two opposing views began to form: that exercise is capable of inducing lymphocyte apoptosis and does contribute to lymphocytopenia; and that exercise does not induce apoptosis and therefore plays no role in the decrease in circulating lymphocyte concentration observed following exercise. We have detailed potential reasons for the discrepancy between these two views [8] including differences in sampling time, no standardized methodology, and not accounting for various lymphocyte subsets.

A recent PubMed search through the US National Library of Medicine revealed that 96 articles have been published since 1998, peaking with 10 manuscripts in 2005 and showing a general trend to decline each successive year (Figure 1). The question that arises is whether or not research into exercise-induced lymphocyte apoptosis is still relevant, or was it a passing fad that has run its course. Only time will be able to provide the answer to this question, but we would like to provide an argument for continued investigation.

Lymphocyte cell death induced by exercise represents a relatively rare event when analyzed by flow cytometry, where percentages ranging from 1.3% [6] to 2.5% [9] are the standard. We have begun a paradigm shift in our analysis such that our recent investigations have reported absolute changes from rest and employ χ2 testing against expected results [10, 11]. This has allowed us to draw inferences that would have been missed through traditional forms of analysis. It is likely that as instrumentation advances progress, researchers will have a greater ability to measure rare events (such as exercise-induced lymphocyte apoptosis) through more sensitive equipment.

It is well established that exercise reduces the incidence of certain types of cancer including breast [12], and colorectal [13]. While no clear mechanism exists to explain this phenomenon, we would like to suggest that increased removal of potentially pre-oncogenic cells through a cell death mechanism induced by exercise should be considered. Obviously more research is needed to establish this connection, but is unlikely to occur if exercise-induced apoptosis studies continue to decline. In addition to the potential link between exercise and reductions in cancer incidence, it is possible that the benefits of exercise on other chronic diseases are also impacted by an apoptotic mechanism.
In conclusion, while the research on exercise-induced lymphocyte apoptosis appears to be on the decline, we would like to express our view that it is a phenomenon with ample scientific evidence. As instrumentation and statistical techniques progress, these may allow for measurements that are specific and sensitive to the exercise and immunology arena. We propose that continued focus be placed in this area of inquiry as it has the potential to provide the link between the benefits of exercise and a reduction in various chronic diseases.

References
1. Mars M, Govender S, Weston A, Naicker V, Chuturgoon A (1998) High intensity exercise: a cause of lymphocyte apoptosis? Biochemical and Biophysical Research Communications 249: 366-370.
2. Navalta JW, McFarlin BK, Lyons TS, Faircloth JC, Bacon NT, et al. (2009) Exercise-induced lymphocyte apoptosis attributable to cycle ergometer exercise in endurance-trained individuals. Applied Physiology, Nutrition, and Metabolism 34: 603-608.
3. Schaefer M, Kell H, Navalta J, Tibana R, Lyons S, et al. (2014) Effects of a simulated tennis match on lymphocyte subset measurements. Research Quarterly in Exercise and Sport 85: 90-96.
4. Prestes J, Pereira GB, Tibana RA, Navalta JW (2014) The acute response of apoptosis and migration to resistance exercise is protocol-dependent. International Journal of Sports Medicine 35: 1051-1056.
5. Kruger K, Agrinischock S, Lechtermann A, Tiwari S, Mishra M, et al. (2011) Intensive resistance exercise induced lymphocyte apoptosis via cortisol and glucocorticoid receptor-dependent pathways. Journal of Applied Physiology 110: 1226-1232.
6. Simpson RJ, Florida-James GD, Whyte GP, Black JR, Ross JA, et al. (2007) Apoptosis does not contribute to the blood lymphocytopenia observed after intensive and downhill treadmill running in humans. Research in Sports Medicine 15: 157-174.
7. Peters EM, Van Eden M, Tyler N, Ramautar A, Chuturgoon AA (2006) Prolonged exercise does not cause lymphocyte DNA damage or increased apoptosis in well-trained endurance athletes. European Journal of Applied Physiology 98: 124-131.
8. Navalta JW, McFarlin BK, Lyons TS (2010) Does exercise really induce lymphocyte apoptosis? Frontiers in Bioscience (Elite Edition) 2: 478-486.
9. Mooren FC, Blomling D, Lechtermann A, Lerch MM, Volker K (2002) Lymphocyte apoptosis after exhaustive and moderate exercise. Journal of Applied Physiology 93: 147-153.
10. Navalta JW, Lyons S, Prestes J, Arnett SW, Schaefer MA, et al. (2013) Exercise intensity and lymphocyte subset apoptosis. International Journal of Sports Medicine 34: 268-273.
11. Navalta JW, Tibana RA, Fedor EA, Vieira A, Prestes J (2014) Three consecutive days of interval runs to exhaustion affects lymphocyte subset apoptosis and migration. Biomedical Research International 2014: 694801.
12. Goncalves AK, Dantas Florencio GL, Maisonneuve de Atayde Silva MJ, Cobucci RN, Giraldo PC, et al. (2014) Effects of physical activity on breast cancer prevention: a systematic review. Journal of Physical Activity and Health 11: 445-454.
13. Sanchez NF, Stelman B, Saab S, Mahajan D, Yeung H, et al. (2012) Physical activity reduces risk for colon polyps in a multiethnic colorectal cancer screening population. BMC Research Notes 5: 312.