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Title: Time course effects of exercise training on pulmonary injury induced by exposure to cigarette smoke in mice

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Body: Rationale: Experimental study recently developed by our group showed that the regular physical training attenuated the pulmonary injury in an experimental model of chronic exposure to cigarette smoke (CS). Objective: The goal of this study was to evaluate the time course effects of the mechanisms related to the exercise protection. Methods: Male C57BL/6 mice were divided into four groups: control, exercise, smoke and smoke+exercise. Exposure to CS and treadmill training were carried out: 5 days/week for 4, 8 and 12 weeks. We evaluated lung mechanics by using a FlexiVent ventilator (Scireq, Montreal, Canada); the number of total and differentials cells in bronchoalveolar lavage fluid (BALF); mean linear intercept (LM); TNF α , IL-1 β , IL6, IL10, TBARS, antioxidant enzymes (SOD, Gpx and TRAP) in the lung tissue. Results: Exercise protected mice exposed to CS from the: reduction on tissue damping and tissue elastance (p<0.01) after 12 weeks; increase in total inflammatory cells in BALF preferably due to recruitment of neutrophils and lymphocytes after 8 weeks and lymphocytes and macrophages after 12 weeks (p<0.001) and increase in LM after 12 weeks. The protection conferred by exercise in mice exposed to CS was induced by an increase in IL6, IL10 and antioxidants enzymes (SOD, GSH/GSSG, TRAP) and a decrease in TNF α and TBARS levels. Conclusion: Exercise protection in mice exposed to CS is more pronounced after 12 weeks and the mechanisms involved include anti-inflammatory mediators and antioxidants enzymes that have an important role in COPD development. .