High-Intensity Interval Training Decreases Circulating HMGB1 in Individuals with Insulin Resistance; Plasma Lipidomics Identifies Associated Cardiometabolic Benefits

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Background: Bodyweight high-intensity Interval Training (BW-HIIT) is an effective, time-efficient exercise method that reduces cardiovascular risk factors and improves muscle endurance without needing external equipment. HMGB1 is a proinflammatory protein involved in insulin resistance. Our earlier study revealed that HMGB1 knockout mice show improved insulin sensitivity. This study investigates whether BW-HIIT exercise will reduce proinflammatory markers like HMGB1 in individuals with insulin resistance. **Method:** Fourteen adults (2 male/12 female) aged 18 to 55 were used. Adult male mice (5 per group) were used at 10 weeks of age under 2 groups. Human and mouse pre- and post-exercise serum/plasma samples were analyzed for Lipidomics, metabolic, and Cytokine Multiplex assays. Standard of care, as well as cardiometabolic parameters, were also performed in human subjects. Results: After six weeks, BW-HIIT exercise changes Metabolic hormones like Amylin, Glucagon, and Insulin increased in post-exercise human and mouse models. Also,8 weeks of treadmill exercise of the animal model showed anti-inflammatory cytokines IL-10, IL-12p40, and IL-12p70 increased, and the proinflammatory cytokines Eotaxin, Il-2, and MIP-2 or CXCL2 reduced in the post-exercise mouse model. Post-exercise decreased systolic blood pressure, cholesterol, triglycerides, HDL, and Chol/HDL ratio in individuals with insulin resistance. Reduced circulating HMBG1 levels in insulin-resistant individuals and exercised mice. **Conclusion:** Six weeks of BW-HIIT exercise improves cardiometabolic health, anti-inflammatory markers, metabolic hormones, and insulin sensitivity in the human and exercised mice model. Changes in circulating HMBG1 levels using BW-HIIT exercise make HMGB1 a suitable marker for metabolic disease, potentiating its role beyond an alarmin. Further studies are needed to confirm these effects and to elucidate the underlying physiological mechanisms.

Author Contributions

GMB, PP: Writing – review & editing, Writing – original draft, Software, Methodology, Investigation, Formal analysis, Data curation. QJ, GFB, HZ: Validation, Resources, Methodology, Formal analysis, Data curation. FA: Visualization, Validation, Supervision, Resources, Methodology, Funding acquisition, Conceptualization. RIMA: Writing – review & editing,

Writing – original draft, Visualization, Validation, Supervision, Software, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Data curation, Conceptualization. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

The Ethics Committee of The University of New Mexico (UNM) Institutional Review Board (IRB) Main Campus approved the research protocol with reference number 21-319. All individuals provided signed informed consent. All animal experiments were approved by the ethics committee of the University of New Mexico (UNM) Institutional Animal Care and Use Committee (IACUC) and Animal Welfare Committee. All live animal studies were carried out ethically, following relevant guidelines and regulations at the University of New Mexico under protocol number 23-201405-HSC.

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Conflict of Interest

The authors declare no conflict of interest.