Published in final edited form as:

Exerc Sport Sci Rev. 2019 April ; 47(2): 64–65. doi:10.1249/JES.0000000000000187.

Insulin at the Crossroads of Metabolic, Neurologic, and Vasculature Disease

Steven K. Malin

Department of Kinesiology University of Virginia, Charlottesville, VA

Insulin is an established hormone that regulates blood glucose. The inability of body tissues to respond to insulin, that is insulin resistance, is considered a primary feature in the development of several obesity-related diseases, including metabolic syndrome and type 2 diabetes. The exact tissue involved in the pathology of these chronic diseases is difficult to identify, but skeletal muscle, liver, adipose, small intestines, beta- and alpha-cells of the pancreas, kidney, and brain have been suggested (1). Although skeletal muscle metabolism has been at the forefront of understanding glucose regulation in exercise science, an article in this issue of *Exercise and Sport Sciences Reviews* presents novel work examining the impact of insulin on the vasculature (2).

In the review, Dylan *et al.* (2) provide the novel idea that insulin is at the crossroads of metabolic and neurologic disease through links in the vasculature. The authors suggest that human movement is key for improving insulin signaling within endothelial cells, thereby allowing maintenance and enhanced cardiometabolic health. Indeed, work discussed suggests that metabolic dysfunction often is preceded by limitations in blood vessel function that, in turn, impair adequate oxygen and nutrient delivery for subsequent use. However, the effectiveness of any physical activity or exercise intervention to recover from such from disturbances depends on the dose (*i.e.*, frequency, intensity, time, or type) as this will alter skeletal muscle and neurologic recruitment patterns that induce unique cellular responses for adaptation. Although there is evidence that resistance exercise contributes to glycemic control and “metabolic” insulin sensitivity of skeletal muscle in the hours following the last bout, the effectiveness of this exercise modality on endothelial function, microcirculatory blood flow, and arterial compliance has mixed results, if any. In contrast, aerobic exercise appears to raise insulin-stimulated glucose uptake as well as to increase macro- and micro-vasculature insulin sensitivity.

Given these exercise modality observations, the authors hypothesize (2) that shear stress from aerobic exercise is critical for the promotion of increased vascular insulin sensitivity within skeletal muscle and the brain. To that end, the tissue- and region-specific response to exercise is also important to acknowledge. Through classic one-legged training models, it has been demonstrated that exercise promotes adaptations specific to the region taxed. However, to date several studies examining the protective roles of exercise on the vasculature have been conducted using flow-mediated dilation approaches in the arm. While this measure predicts future cardiovascular disease, it is focused on large conduit arteries. Whether the endothelium of these arteries is reflective of resistance arterioles and microcirculation warrants additional attention, as is the need to examine vessels in different

regions of the body. Without this information, it is difficult to prescribe an appropriate training dose with the specific vascular adaptations required to combat chronic disease.

Future work should also consider the context in which the measurements are performed. Many exercise studies report benefits to the endothelium in the fasting state, but few examine the impact of nutrients, meals, or hormones per se on the vasculature despite our understanding that the post-prandial state (*e.g.*, insulin, GLP-1) modulates vasodilation. For example, we recently examined the influence of interval versus continuous exercise training for 2 wk on fasted and post-prandial arterial stiffness in obese adults with prediabetes (3). Interestingly, neither exercise treatment impacted fasting arterial stiffness, yet we noted significant reductions in the post-prandial state that were independent of exercise intensity. Thus, discerning fasting versus fed or movement states may provide better understanding of not only if, but also when, exercise confers benefits. Importantly, the work summarized by the authors of the review (2) reminds us that physical activity has dose-regional-specific responses, and attention to these are needed to align treatment with the desired goal for optimal clinical and public health care.

Acknowledgments:

SKM is supported by National Institutes of Health RO1-HL130296.

REFERENCES

1. DeFronzo RA. Banting Lecture. From the triumvirate to the ominous octet: a new paradigm for the treatment of type 2 diabetes mellitus. *Diabetes* 2009;58(4):773–95. [PubMed: 19336687]
2. Dylan TD, Laughlin MH, Padilla J. Exercise and Vascular Insulin Sensitivity in Skeletal Muscle and Brain. *Exercise Science & Sports Reviews*. 2019; [Epub ahead of print].
3. Eichner NZM, Gaitan JM, Gilbertson NM, et al. Postprandial augmentation index is reduced in adults with prediabetes following continuous and interval exercise training. *Exp Physiol* 2018; [Epub ahead of print].