Comment on: Lazo et al. NH_2-Terminal Pro–Brain Natriuretic Peptide and Risk of Diabetes. Diabetes 2013;62:3189–3193

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Lazo et al. (1) reported that plasma NH_2-terminal pro–brain natriuretic peptide (NT-proBNP) levels, a cleavage product of brain natriuretic peptide (BNP), are inversely associated with diabetes risk in ~7,800 healthy patients over a period of 12 years. In line with this, genetic evidence suggests a protective effect of BNP on diabetes risk (2). So far, mechanistic insight is lacking on how natriuretic peptides (NPs) reduce the risk of diabetes. Lazo et al. speculate that improvements in energy expenditure through mitochondrial respiration and biogenesis through BNP mediate this protective outcome, referring to data derived from transgenic mouse models (3). In fact, we have previously demonstrated that NPs prompt lipid oxidation, energy expenditure, and mitochondrial respiration in human subjects (4–6), in a manner akin to physical activity (6).

We would also like to add another silhouette to the picture. NPs have been shown to modulate expression and secretion of several hormones (7–9), including the insulin-sensitizing adipokine adiponectin (9). Moreover, infusion of atrial NP in healthy subjects increased circulating total and high molecular weight adiponectin, the most effective isoform of adiponectin to improve insulin sensitivity (8). Adiponectin enhances insulin sensitivity through mechanisms dependent and independent of mitochondrial metabolism. Thus, the observation of Lazo et al. (1) might at least in part be explained by the effect of BNP on adiponectin levels, which then mediate their effect on glucose metabolism, protecting from insulin resistance and ultimately diabetes. Therefore, we should also consider that the antidiabetic role of NPs could be mediated by promoting adiponectin secretion together with lipid oxidation and energy expenditure in humans. Further studies need to address this important issue.

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