

Letters to the Editor

Hypovolemia-induced obesity and diabetes

To the Editor:

The article by Saiki and colleagues [1] published in the *Metabolism* entitled “Circulating angiotensin II is associated with body fat accumulation and insulin resistance in obese subjects with type 2 diabetes mellitus” is very interesting in that it points out clearly the association between circulating angiotensin levels and the pathophysiology of obesity and diabetes. At first glance, this is rather unusual, as why would a hormone intimately implicated in cardiovascular and water balance functions be involved with fat accumulation and insulin resistance. However, these “unusual” associations have given rise to a series of reports, all independent at the time, which now taken together make sense [2–4]. It would appear that the common feature in the origin not only of hypertension but also of obesity and diabetes is hypovolemia. This is a physiologic state that comes about through reduced fluid intake and has as primary signal the release of renin that generates angiotensin II in the blood. Interestingly, neurochemical changes characteristic of extracellular dehydration have been found in the brain of obese Zucker rats, a model of obesity and type 2 diabetes [5]. Moreover, in animal studies on obesity, inhibition of the renin-angiotensin system produces an increased fluid intake that has been suggested to lead to lipolysis and subsequent weight loss [3].

In other studies, it has been noted that inhibition of the renin-angiotensin system allows cells to restore membrane glucose transport and to increase insulin sensitivity [4]. It was thus proposed that this would restore to normal cellular carbohydrate and fat metabolism [4]. However, insulin signaling is linked also to cell volume regulation [6]; and cell volume regulation would be dependent on body hydration state. We thus come back to the regulation of hypovolemia.

It is thus not surprising to find that circulating angiotensin levels are elevated in conditions of obese subjects with type 2 diabetes mellitus [1], and it would be interesting to

propose that increased water intake be encouraged along with renin-angiotensin system blockade in cases of obesity and diabetes.

Serguei O. Fetissov
*Digestive System and Nutrition
Laboratory (ADEN EA3234)
Institute of Biomedical Research
Rouen University
IFR23, Rouen, France*

Simon N. Thornton
*INSERM, U684
Vandoeuvre les Nancy, France
Université Henri Poincaré
Nancy Université, Nancy, France*
E-mail address: Simon.Thornton@scbiol.uhp-nancy.fr

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