Suppressed insulin secretion and fat content of weight loss: association and causal direction


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In a recent article, Wong et al. (1) commendably used regression instead of analysis of variance to compare their experiment’s outcomes between levels of another variable. A regression line having a slope reliably different from zero is consistent with causal connection of some sort. However, it is surprising that the paper claims support for one causal direction over the other, especially with authorial insistence elsewhere that association be distinguished from causation. The view that high insulin secretion in response to dietary carbohydrate disposes to weight regain through increased fat deposition faces the broadly evidenced interpretation in the opposite direction that high BMI is associated with both insulin resistance and greater weight loss on a low-calorie diet (2), which leaves room for greater regain as the initially stronger compliance lapses.

Even more to the point, the scatterplots of % weight loss as fat against insulin concentration at 30 minutes after an oral glucose load (Figure 1, panels C and F) indicate that the association is generated by participants who lose a lower proportion of fat -- opposite to the paper’s interpretation. There are very few data points for Insulin-30 above 300 μIU/mL; moreover, these include potential outliers. Most of the data are clustered below about 200 μIU/mL in what appears to be near-normal distributions in both variables. Hence, low insulin secretion contributes more to the association than high, and more reliably. Indeed, the lower β value in participants from the FS(3) trial goes with a numerically lower proportion of fat at the low insulin end of the scatter, which has the much more precise estimate of the mean.

These low insulin secretory responses may have nothing to do with the carbohydrate content of the low-calorie diet. Insulin secretion in the reported experiment could be suppressed by sympathetic activation (3) generated by osmotic stress from the free glucose in the oral load, which is easily avoided by use of food glucose polymers (4). Individual differences in autonomic response to the stresses of treatment could also affect the fat content of weight loss (5).


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