Should insulin resistance degree be taken into account for assessment of glycemic index?

Dear Sir:

We read with great interest the insightful article published by Eelderink et al (1). Their highly relevant findings encourage further analysis and add complexity to the assessment and interpretation of the role of glycemic index in energy homeostasis. Such novel results contribute to explain why a beneficial effect of glycemic index on human metabolism has been difficult to prove under the conventional way of classifying carbohydrates, ie, by determining blood glucose concentration (2, 3). We here highlight some aspects that may deserve discussion.

Eelderink et al’s article confirmed previous studies that showed that glycemic response to nutrients results from the combination of glucose absorption, endogenous glucose production, and tissue glucose uptake (4). In this regard, ingestion of slowly digested compared with rapidly digested starches (pasta and bread meals, respectively) led to expected differences in glucose absorption. However, this difference was not accompanied by a corresponding change in glycemic response because the extent to which endogenous glucose production was suppressed and tissue glucose uptake promoted also differed between meals.

Interestingly, the reduced glucose disposal was the main factor counterbalancing the slow glucose absorption from the pasta meal. Indeed, endogenous glucose production was suppressed at an even higher extent than anticipated from the lower insulinemia achieved after pasta compared with bread meal. This observation suggests that hepatic insulin sensitivity was enhanced after pasta relative to bread meal, highlighting the need for understanding the mechanisms involved. Taken together, these findings challenge the common assumption that ingestion of starches with differential digestion and absorption rates will necessarily lead to contrasting glycemic responses.

Although blood glucose response was similar between meals, relevant differences were observed at the intracellular level. Thus, postprandial exogenous glucose oxidation over the first 2 h was lower for pasta relative to bread. Considering that insulin-stimulated glucose disposal rate is a critical determinant of glucose oxidation (5), and tissue glucose uptake was nearly half of the amount observed after bread consumption, one could anticipate such a finding. However, it appears that the reduction in exogenous glucose oxidation was not proportional to the decrease in tissue glucose uptake, because the amount of exogenous glucose oxidized per unit of glucose taken up by tissues was greater after pasta consumption compared with after bread meal consumption (based on data from Eelderink et al’s Table 1). Thus, the reduction in glucose clearance rate only partially explained the lower exogenous glucose oxidation observed after the pasta meal.

A proportionally higher glucose oxidation relative to its uptake may form the basis to understand glycemic index–dependent outcomes. For instance, a lower proportion of glucose would be expected to be incorporated into glycogen after pasta consumption. In this regard, a diminished whole-body carbohydrate balance (size of glycogen depot) has been associated with increased ad libitum food intake and greater prospective weight gain (6–8). We based such speculation on the exogenous glucose oxidation estimated over the first 2 h after meal consumption. However, exogenous glucose oxidation after pasta consumption compared with after bread consumption was higher at the end of the assessment period. Thus, those differences in oxidative and nonoxidative glucose disposal may be compensated throughout the whole postprandial period. This scenario is consistent with a previous study by Sparti et al (3), which showed that transitory metabolic differences found after meals were compensated throughout the day, resulting in a similar macronutrient balance at the end of the 24-h period.

We would finally like to consider the potential influence of insulin resistance on the assessment of glycemic index and its metabolic consequences. The authors pointed out that blood insulin response was highly dependent on the type of carbohydrate consumed. Then, it is proposed that blood insulin response may be a better predictor of the type of carbohydrate consumed. Because the blood insulin response is also a consequence of the degree of insulin resistance, we estimate that the influence of insulin resistance on glycemic index–dependent metabolic effects should be explored. Indeed, we recently reported that whole-body glycolytic and oxidative glucose disposal between insulin-sensitive and insulin-resistant individuals remained similar after the consumption of a 75-g glucose solution (9). Thus, highly contrasting differences in postprandial insulinemia were not associated with changes in whole-body glucose metabolism.

Therefore, appropriate comparison of glucose metabolism in response to carbohydrates differing in their digestion and absorption rates may require matching individuals for their degree of insulin resistance, particularly in studies with a parallel design. This task may be relatively feasible before initiating the intervention. However, such a goal may be unlikely to be achieved once the intervention has begun, particularly if changes in insulin resistance are expected to occur (10).

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Reply to JE Galgani and G Valentino

Dear Sir:

We thank Galgani and Valentino for their appreciation of our work and their thoughtful discussion of some aspects of our results.

In our study (1) we found that starchy products with slowly and rapidly digestible starch (pasta and bread, respectively) can elicit the same postprandial glucose response. The rate of digestion of starch was highly correlated with the concentration of carbohydrate-dependent insulinotropic polypeptide (GIP), a gastrointestinal hormone known to potentiate the insulin response. As a consequence, insulin concentrations were lower after the pasta meal, resulting in decreased glucose uptake into tissue. Thus, the decreased glucose uptake into tissue could explain the similar glucose concentrations after both meals despite the slower starch digestion after pasta consumption.

On the basis of these results we proposed that the GIP or the insulin response may be a more relevant parameter to consider in classifying starchy foods than the total blood glucose response, which is standardly used to determine the glycemic index (GI) of foods.

Galgani and Valentino agree with our conclusion that the existing assumption that ingestion of starches with different digestion and absorption rates will always lead to different glycemic responses does not hold anymore. They also point out that glucose oxidation relative to its uptake into tissue is an important issue to consider in understanding outcomes related to the glycemic response. We agree that this is a highly relevant issue because this might affect long-term energy storage and the associated compensatory mechanisms are not yet well understood. Thus, the oxidation and storage of glucose are other parameters that should be assessed in understanding long-term health effects of different carbohydrate-rich foods in addition to, for instance, the glycemic response, the insulin/incretin response, and protein glycation.

Galgani and Valentino recommend taking the degree of insulin resistance into account when assessing the GI and its metabolic consequences.

In our opinion, there are 2 different conditions in which this aspect should be considered: 1) with the classification of carbohydrate-rich foods on the basis of the insulin response instead of the glycemic response and 2) with investigation of postprandial metabolic consequences of carbohydrate-rich foods.

With regard to the first condition, in dietary intervention studies exploring the health effects of carbohydrate-rich foods, the GI is often used to define the intervention and control diet (low- compared with high-GI foods). The same accounts for epidemiologic studies assessing the association between a high- and a low-GI diet and the development of disease. However, these studies have reported inconsistent results (2, 3). Because carbohydrate-rich foods with a high GI apparently can elicit different GIP and insulin responses (1), this food group seems to be quite heterogeneous with regard to its metabolic response, which perhaps could explain these inconsistencies. Classifying carbohydrate-rich foods on the basis of the insulin response would of course have to be performed in a homogeneous group of persons with a normal degree of insulin sensitivity to exclude individual-specific influences on insulin concentrations after ingestion of the foods.

As we proposed, the GIP response would also be a good candidate because it is even better correlated with the rate of starch digestion and not substantially altered in the insulin-resistant state (4, 5).

However, we have now tested 2 products and, in our opinion, it is necessary to determine the metabolic response of a greater variety of starchy foods while simultaneously assessing postprandial glucose kinetics before giving a final recommendation.

With regard to the second condition, we agree with Galgani and Valentino that it is important that in intervention studies exploring the effect of different carbohydrate-rich foods on postprandial metabolic consequences the degree of insulin resistance has to be taken into account to be able to interpret the study results correctly.

In our study, healthy, lean, young volunteers [mean ± SEM age: 21 ± 0.5 y; BMI (in kg/m²): 23 ± 0.6] took part in a crossover manner. We therefore can assume that their degrees of insulin sensitivity were normal and could not have affected the insulin response to our test meals. In this setting, the main determinant of the insulin response was the digestive characteristic of the test meals.

However, in studies with older volunteers and/or with volunteers with a high BMI, assessing insulin resistance seems necessary. It would also be preferable if these studies were conducted in a cross-over manner to account for other differences in individual characteristics in postprandial metabolism.

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