Metabolic and Inflammatory Responses to Different Caloric Loads of a High-Fat Meal Are Distinct between Normal-Weight and Obese Individuals

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The prevalence of obesity and of its metabolic and clinical consequences has been increasing over the past few decades (1,2). Although the origin of obesity and related metabolic disorders is multifactorial, the quantity and the quality of dietary macronutrients are 2 of the main factors that can be modified to diminish obesity risk and to lessen its comorbidities. It has long been recognized that obese, insulin-resistant, and diabetic individuals show exaggerated responses to an oral fat load, as demonstrated by higher concentrations of circulating TGs over the postprandial period (3–5). This reflects diminished ability to efficiently handle the incoming fat of dietary origin and is analogous to the exaggerated glucose response to an oral-glucose load seen in the same individuals. Fat and glucose loads are also associated with alterations in circulating concentrations of a range of gut-derived hormones called incretins (6,7) and of inflammatory markers (8,9). Meal-induced changes in the concentrations of metabolic, hormonal, and inflammatory markers are influenced by the nature of the meal itself and by the phenotypic characteristics of the individual. Thus, the use of such meal challenges in research requires standardized procedures to be adopted and an improved understanding of the between-individual and between-group variation in response and the reasons for such variation. This is important because recent considerations of the use of biomarkers in human nutrition research recommended the use of challenge tests to determine the robustness of biologic systems (10,11,12). Because meal challenges are still relatively rarely used to probe metabolic, hormonal, and inflammatory robustness, little is known about the responsivity of these systems to different doses of the challenge. This could be an important approach in human nutrition research, because dose-response studies (e.g., to an oral fat challenge) could reveal differences in sensitivity to the challenge between different subgroups that may not be apparent from using just 1 dose of the challenge. In an article published in this issue of The Journal of Nutrition, Schwander et al. (13) evaluated the postprandial metabolic, hormonal, and inflammatory responses of normal-weight and obese participants to high-fat meals with 3 different caloric contents (500, 1000, and 1500 kcal). Importantly, the relative macronutrient composition was the same across the 3 meals, comprising 61% of energy from fat, 21% of energy from carbohydrates, and 18% of energy from protein. The amounts of fat provided in the 3 meals were 34, 68, and 102 g, respectively. By adopting this novel design, the study aimed to identify the effect of increasing meal energy content on postprandial responses while keeping the (relative) macronutrient content of the meals unchanged. This design is technically and clinically interesting and unique.

In the study, normal-weight (n = 19) and obese (n = 18) men consumed the 3 meals in random order at least 1 wk apart. After an overnight fast, blood was collected at 5 time points (0, 1, 2, 4, and 6 h) and was analyzed for markers of metabolic (glucose, TGs, and total and HDL cholesterol), hormonal [insulin, glucacon-like peptide-1 (GLP-1)], and inflammatory [C-reactive protein (CRP), IL-6] responses. In addition, the inflammatory trigger, endotoxin, was measured. Both normal-weight and obese participants were well defined according to anthropometric measurements and metabolic variables, which were quite different between the 2 groups. In the obese participants, there were dose-response relations to the meals for all variables except for CRP, with the clearest relations seen for insulin and TGs. In the normal-weight participants, there were dose-response relations to the meals for all variables except for cholesterol, CRP, and GLP-1. Insulin was the only variable that could differentiate the postprandial response of the normal-weight and obese men at all 3 caloric doses.

With regard to inflammatory markers, IL-6 was higher in response to the 1500-kcal meal than with the 500-kcal meal in both groups of participants, whereas CRP was not affected over the time frame studied. This may be because CRP is produced hepatically secondary to an elevation in certain cytokines, including IL-6, and 6 h may simply be not enough time to see an effect on CRP concentration. Alternatively, CRP production and circulating concentration may not be sensitive to this type of meal challenge. Previous studies on the postprandial inflammatory response to a high-fat meal providing ~1000 kcal showed inconsistent effects (14,15,16). Masson and Mensink (14) observed an increase in IL-6 and CRP concentrations in obese individuals after the consumption of a high-fat diet rich in SFAs compared with a diet rich in PUFAs, whereas Phillips et al. (15)
observed an increase in IL-6 in normal-weight individuals and an increase in CRP in obese individuals with a decrease in normal-weight individuals; Blackburn et al. (16) observed an increase in IL-6 but no change in CRP in both normal-weight and obese individuals. These differences may reflect genuine differences between the participant groups but may also reflect differences in experimental procedures, highlighting the need to establish a clear methodology to allow for the reliable assessment of the impact of meal macronutrients on postprandial inflammatory responses. The work of Schwander et al. (13) goes some way toward this. One refinement of this approach could be to normalize the energy content of the meal to an individual’s BMI, lean body mass, or body surface area and to take into account the physical activity of the participants because it might influence the levels of some variables and their responsiveness to the meal challenge. Schwander et al. (13) did not control either habitual diet or physical activity of the individuals studied and this might relate to some of the variable responses seen. Once a dose-response model is firmly established and is shown to be reproducible within certain groups of interest, it would become possible to then modify the quality of the fat component of the meal, to generate much needed data on the importance of fat quality in driving or modulating the postprandial responses reported by Schwander et al. (13).

In summary, this article by Schwander et al. (13) demonstrates 2 different and complementary aspects. First, the caloric dose-response method is an interesting approach to evaluate the robustness of metabolic, hormonal, and inflammatory responses to a high-fat diet. Second, the method offers the possibility to observe and evaluate differences in the responses of relevant biomarkers according to the phenotypic status of the individuals studied, in this case normal-weight and obese men, which makes this methodology even more interesting. More studies are needed to further refine and evaluate this approach, which in our view appears to be very promising.

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References