LETTER TO THE EDITOR

The art of quantifying glucose metabolism

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TO THE EDITOR: With great interest we have read the article by Wang and colleagues recently published in this journal (26). Wang et al. describe a method to assess glucose production rates in rodents from the kinetics of an IP injected glucose tracer, i.e., U-13C-glucose. The authors compared IV and IP injection protocols in rats and mice and demonstrated anticipated outcomes after treatment of IZDDF rats and ob/ob mice with PPARγ agonists. Their method compared satisfactorily with the “gold standard” approach to assess insulin sensitivity of glucose production, i.e., the euglycemic hyperinsulinemic clamp. It is concluded that “...it is possible to (i) quantify glucose production using an intraperitoneal injection of tracer and (ii) derive a “glucose production index” by coupling estimates of basal glucose production with measurements of fasting insulin concentration; this yields a proxy for clamp-derivered assessments of insulin sensitivity of endogenous production.”

We were particularly interested in this work since our laboratory has gone through a similar sequence of experimental developments during the past 15 years. For quantification of relevant fluxes of glucose metabolism in unanesthetized rodents we have adapted the mass isotopomer distribution analysis (MIDA) approach developed by Hellerstein et al. (e.g., Refs. 7–9, 14, and 15) using permanent jugular vein catheters for continuous infusion of tracers. Studies were performed in rats (25) and, after adjustments to allow for bloodspot and urine collections on filter paper, also in mice (24). We have successfully demonstrated effects of feeding state (3, 4, 18, 24), enzyme deficiencies (5, 10, 11), metabolic manipulations (1, 2, 17), and drugs (13, 16, 25) on the various pathways of glucose metabolism. By applying a double-inlet catheter, we also performed euglycemic hyperinsulinemic clamp studies in unanesthetized mice (6, 13, 21). Although highly informative, procedures are labor-intensive and multiple tests in individual animals and hence contributes to the societal quest to reduce numbers of experimental animals in biomedical research. Importantly, the concept appears to be translatable to humans upon oral intake of a small amount of [6,6-2H2]glucose (van Dijk TH, Jalving H. Kuipers F, unpublished observations): initial experiments in healthy volunteers showed that kinetic parameters derived from both venous blood draws and fingertip bleeding were highly similar to those obtained by invasive techniques (20, 27). Thus this method is promising for use in longitudinal studies in humans.

DISCLOSURES
No conflicts of interest, financial or otherwise, are declared by the authors.

AUTHOR CONTRIBUTIONS

REFERENCES


