Take my breath away: measuring sugar intake in exhaled air

Article

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People who eat more sugar are less likely to be overweight or obese than people who eat more sugar - at least when we rely on what those people tell us they eat. Alas, for those of us with a sweet tooth, this is no longer true when using an objective measure of intake (1). Unfortunately, this is not restricted to sugar intake, but many other foods: self-reported dietary measures are often biased and neither precise nor accurate. This is well known, and there have been many approaches to improve these measurements: for individual compounds such as sugars however, nutritional biomarkers are among the most reliable instruments (2) as they neither rely on self-reported dietary data nor on food composition tables which introduce further uncertainty.

Stable isotope ratios are commonly used in many research areas to investigate diet, but they are remarkably absent from research into human nutrition. O'Brien and colleagues have provided some outstanding data to demonstrate how useful stable isotope ratios can be to nutrition research and made a very good case for a much wider use. They have been used in observational studies (3), but their potential has still not been realised. This is in particular surprising when considering that they can provide information on long-term dietary intake when measured in hair or nails, specimens that are easily accessible (4). A further advantage of stable isotope ratios is that they can provide information about the origin of a compound – for example whether dietary protein has been derived from plant or animal sources.

There is currently a considerable interest in the impact of sugar intake on health, especially of added sugar or from sugar sweetened beverages. Research into long-term associations between sugar intake and health are impeded by the difficulties of estimating actual sugar intake accurately. In populations where added sugars are mainly from C4 plants such as corn and sugar cane, stable carbon isotope ratios (CIR, $\delta^{13}C$) are ideally suitable as biomarkers of added sugar. C3 plants use ribulose-1,5-bisphosphate carboxylase/oxygenase (RuBisCo) for carbon fixation, and this enzyme discriminates against heavier carbon isotopes in CO_2. C4 plants however use a different metabolic strategy which does not result in the same discrimination, and thus C4 plants contain a higher amount of ^{13}C and consequently sugar derived from these plants has a higher $\delta^{13}C$. Previously, Cook and colleagues have shown that $\delta^{13}C$ of blood glucose has a strong relationship with sugar intake in a US population (5), where sugar is mainly derived from C4 plants.

A key obstacle for the use of nutritional biomarkers is sample collection, processing and analysis. In order to analyse $\delta^{13}C$-glucose in blood, extensive sample processing is necessary which is time consuming and laboursome. In this issue of the *Journal of Nutrition*, O'Brien and colleagues (6) investigate a very different approach: instead of collecting blood samples with all the associated difficulties, they use breath samples and analyse CIR of exhaled CO_2 using cavity ring-down spectroscopy and found a strong association with added sugar intake. The advantage of the method is that breath can be easily – and non-invasively – sampled and quickly analysed without the need for laborious sample preparation. Like 24h dietary recalls, a breath sample can only provide a dietary snapshot – but with repeat analyses, it can provide useful information on long term diet.

The big question is: how can these results be interpreted? In contrast to blood glucose, which is mainly derived from dietary carbohydrates and glucogenic amino acids, exhaled CO_2 can also be derived from fat metabolism. The $\delta^{13}C$ of lipids is lower than that of non-lipid molecules as lipid synthesis discriminates against the heavier carbon isotope. A shift to carbohydrate metabolism therefore increases $\delta^{13}C$-CO_2, independent of the dietary source of carbohydrates (6). A combination with the respiratory quotient could therefore help to interpret the results better.

The results of O'Brien and colleagues found the acute change in breath CIR to be strongest, which shows the rapid metabolism of added sugars. The study design did not allow to investigate whether breath CIR could be used to estimate long-term, habitual added sugar and sugar-sweetened beverage consumption, which would make this more useful for long-term dietary assessment. It is important that future research explores this approach and evaluates this biomarker in a larger population.

The approach described here has unfortunately one crucial limitation: it relies on a food system where the main sources of added sugar and sugar in SSBs are C4 plants, i.e. corn and sugar cane. While this is the case for the USA, the marker would not work in Europe where sugar is mainly produced from sugar beet, a C3 plant.

Using stable isotope ratios to estimate dietary intake in humans is still very much a rough diamond (7), but studies like this help polishing it. There are sufficient data to justify a much wider use in nutritional research, and it is important that such an important technique gets the recognition it deserves. It is time for those working in this field to collaborate more closely with each other and make this technique better known among nutrition researchers and help it realise its potential.

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