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**Letter to the Editor: RE: Excessive Sugar Consumption May Be a Difficult Habit to Break: A View From the Brain and Body**

**Fergal M. Grace, Lawrence D. Hayes, and Nicholas Sculthorpe**

**The Journal of Clinical Endocrinology & Metabolism Volume 100, Issue 7**

We read with great interest the recent article by Tryon et al (1) who set out to test their “glucocorticoid-metabolic-brain model” in 19 women consuming beverages sweetened with either aspartame or an undefined amount of 25% sucrose thrice daily for 2 weeks. We compliment the authors on an interesting, timely, and potentially progressive research study. However, we wish to highlight some important limitations in relation to the primary outcome measures used to determine stress response that were not sufficiently addressed within the manuscript.

The first relates to the variability in daytime cortisol measurement. In clinical practice, saliva cortisol sampling is normally reserved as a convenient initial test for Cushing's syndrome, whereby the collection of duplicate late-night samples over two separate evenings (2) allows systemic cortisol concentrations to reach their nadir. Further to diurnal oscillation, multiple other factors are known to affect salivary cortisol such as the use of oral contraceptives, smoking, diet, and nontraditional supplements that impact the biological variability of salivary cortisol and contrive to increase measurement error.

To achieve meaningful data, it should be an a priori aim of such applied research to control preanalytical and analytical variability, thus allowing the biological component to be the one true variable. In this respect, we draw the authors' attention to the original work of Fraser and Fogarty (3) and would urge the authors to determine the critical difference (clinically relevant difference) should they wish to employ saliva cortisol measurement in future work. The absence of complete control for biological variants, coupled with what appears to be single sample measurements, in a small sample population, the potential for having fallen victim to classic type 1 error, cannot be eliminated.

The study of Tryon et al (1) also employed the Montreal Imaging Stress Task as used by Pruessner et al (4) to induce a psychological stress response, although Pruessner et al employed a time-resolved fluorescence immunoassay using the method described by Dressendorfer et al (5); even then, due to significant heterogeneity in individual salivary cortisol responses, Dressendorfer and colleagues split their entire cohort into subjects where salivary cortisol had either increased or decreased during the course of their experiment.

With these aspects in mind, we perceive that the authors remarks relating to their manuscript being among the first evidence that consumption of beverages sweetened with sugar, but not the artificial sweetener aspartame, inhibits stress-induced cortisol secretion in humans, to be preliminary until such time as the critical difference is established and clinically meaningful changes to salivary cortisol can be validated.

## References

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