Credit: Peter Dazeley/Getty

reduced central sensitivity to sweet taste. The researchers suggest that the consumption of low-calorie sweeteners in combination with carbohydrates could therefore have a negative effect on metabolic health. However, they note that more research is needed as their study had a small sample size, a short period of exposure and no washout period to assess the reversibility of the changes.

Claire Greenhill

> A new paper suggests that when sucralose is consumed with carbohydrates, insulin sensitivity is impaired in healthy humans

ORIGINAL ARTICLE Dalenberg, J. R. et al. Short-term consumption of sucralose with, but not without, carbohydrate impairs neural and metabolic sensitivity to sugar in humans. *Cell Metab.* **31**, 493–502 (2020)

> CaSR forms heteromeric complexes with γ-aminobutyric acid B_1 receptor

is the rate limiting enzyme for GABA synthesis.

"Key and unexpected findings included an increased formation of CaSR–$GABA_{B1}$R heteromers in hyperparathyroid states, as well as PTH hypersecretion due to the negative allosteric action of $GABA_{B1}$R on CaSR signalling via heterotrimeric G proteins," describe Chang and Vilardaga. "In addition, we saw synthesis of GABA in PTGs, which might act via an autocrine pathway where the release of GABA binds directly to $GABA_{B1}$R–CaSR heteromers, thus promoting the PTH hypersecretion encountered in HPT."

The present study describes new molecular mechanisms for PTH hypersecretion in HPT. These findings could have implications for physiological processes other than mineral and skeletal homeostasis, given that CaSR and $GABA_{B1}$R are expressed in neurons and many other peripheral tissues.

Shimona Starling

ORIGINAL ARTICLE Chang, W. et al. PTH hypersecretion triggered by a $GABA_{B1}$ and Ca^{2+}-sensing receptor heterocomplex in hyperparathyroidism. *Nat. Metab.* https://doi.org/10.1038/s42255-020-0175-z (2020)

ENDOCRINE DISRUPTORS

Maternal paraben exposure and childhood weight gain

Parabens are alkyl esters with antimicrobial activity that are widely used as preservatives in cosmetics, food, toiletries and medications. Irina Lehmann, Tobias Polte and colleagues have published a new study in *Nature Communications* showing that maternal exposure to parabens triggers childhood overweight development.

"Parabens are considered to be endocrine disrupting chemicals just like phthalates or bisphenol A; however, whether low-dose paraben exposure could cause adverse health effects has been a controversial topic in the past few years," explain Lehmann and Polte. "The prenatal period is a sensitive time window for chemical exposure, therefore we decided to focus in the present study on maternal exposure to parabens and its effect on children's body weight development."

The researchers examined epidemiological evidence of the effects of paraben exposure from the LINA prospective cohort of 629 mother–child pairs. Mothers reported their use of 'leave-on' and 'rinse-off' cosmetic products during pregnancy by questionnaire and maternal paraben exposure was assessed by measurements of urine. Notably, mothers reporting use of paraben-containing leave-on products had threefold higher levels of urinary parabens than mothers using paraben-free products. Adjusted logistic regression models were applied to data from LINA to examine associations between prenatal paraben exposure, child birth weight and weight gain in childhood. High prenatal maternal exposure to long-chain butylparabens (BuPs) increased the risk of overweight in early to mid-childhood.

To investigate potential mechanisms, the researchers conducted in vivo studies of BuP exposure in mice. Female offspring from perinatally nBuP-exposed dams showed 20–45% increased weight gain over the study, compared with 10% gain in control animals. Moreover, female offspring in the nBuP group had increased food intake. No weight differences were seen in male offspring. Importantly, urinary nBuP concentrations from exposed dams were measured and found to be in the same range as the LINA cohort.

Further analyses of female offspring from nBuP-exposed dams showed reduced hypothalamic expression of leptin receptor (*Lepr*) and pro-opiomelanocortin (*Pomc*) mRNA along with hypermethylation of a regulatory region of *Pomc* (nPE1). These findings suggest that BuP might affect central regulation of hunger.

"We are currently lacking mechanistic explanations for the initial molecular events at the placental–fetal interface and how prenatal exposure to BuP or other oestrogenic compounds might lead, for example, to an altered epigenetic profile and an increased risk of childhood overweight," conclude Lehmann and Polte. "Thus, further studies are needed to reproduce our epidemiological findings and bring more light into the very early mechanisms behind this association."

Shimona Starling

Credit: Brian Hagiwara/Getty

ORIGINAL ARTICLE Leppert, B. et al. Maternal paraben exposure triggers childhood overweight development. *Nat. Commun.* **11**, 561 (2020)