THE INVESTIGATION OF SUGAR SUBSTITUTE COMPOUNDS ON NEUROENDOCRINE FUNCTIONS - IN ENVIRONMENTAL LOAD MODEL

István Varga, Zsolt Molnár, Anna Gutási, Ildikó Trója, Péter Hausinger, Marianna Radács, Márta Gálfi

Institute of Applied Natural Science, Faculty of Education, University of Szeged Hungary
Department of Environmental Biology and Education, JuhászGyula Faculty of Education, University of Szeged
e-mail: vargaistvan551@gmail.com

Abstract
Nowadays in the society sugar substitutes are gaining high importance. These substitues can enter the human body through nutrition and may alter metabolic pathways through potential related mechanisms. The neuroendocrine system plays a key role in maintaining homeostasis, including sugar balance. The aim of this present work was to develop a model system in which the effects of certain sugar substitutes on endocrine function can be traced and presented with a well-understood data system.

Introduction
Psycho-immuno-neuroendocrine activity is essential in the homeostasis, which enables human potential to maintain social, biological equilibrium. The viability of psychogenic activity (eg. learning, cognitive function, behaviour, etc.) is embedded in the complex biogenic activity (neuroendocrine immune functions). It is a very interesting question how much the psychic activity elements of social life (e.g. cognition) can change when neuroendocrine communication is interrupted when it is necessarily altered by chemical environmental influences (e.g. nutritional biological agents) through actual technosphere exposures [1, 2]. Nowadays, sugar substitutes are widely used, are nutritionally important, and can thus act as potential external agents to activate internal biological metabolic pathways; e.g. modulating sugar metabolism. Adaptation is achieved in human activities (such as social, learning, emotional, intellectual, etc.) through social engagement. We investigated this by studying regulation of the hypothalamic-pituitary axis by *in vivo* and *in vitro* model systems as neuroendocrine regulation, in which the neurohypophysis (NH) hormones oxytocin (OT) and arginine-vasopressin (AVP) were prominent [3, 4]. Due to its antidiuretic role, AVP is essential in osmoregulation, volume regulation, and is also known as an effector neuropeptide of behavior, learning (implicit), memory functions, attachment, trust, cognitive function, properties) mediation (creative) element [5, 6]. These endocrine hormones are involved in neuronal processes via monoamine (MA) signalling [7], which is confirmed by the mechanisms of action of dopamine (DA), norepinephrine (NE), and serotonin (5-HT). Events regulated through the cellular energy cascade will be detected, which can be strongly modulated by the presence of nutritional biological conditions (sugar substitues).

Aims
Our aim is to investigate the effects of changes in environmental conditions in cognitive processes mediated by neuroendocrine communication, in which we study the (chemical) changes in the environmental conditions of neuroendocrine cycles in a standardized model system; and how they may affect homeostatic complexity (which we also want to follow through cognitive function, learning).

Methods

In our experimental model, male Wistar rats were used to prepare primary neurohypophysis cell cultures. The rats were treated in vivo with sugar replacement compounds for 16 weeks: erythriol 4 g / day, saccharin 0.2 mg / day, xylitol 40 mg / day and stevia at 40 mg / day. After anesthesia with pentobarbital (4.5 mg / kg kg, Nembutal, Abott, USA), the rats were decapitated and then subjected to a preparative microscope to separate the neurohypophysis and adenohypophysis. Primary, monolayer neurohypophysis cell cultures were prepared by enzymatic and mechanical dissociation. The tissues were digested enzymatically (trypsin: 0.2 % /Sigma, Germany/ for 30 min; collagenase /Sigma, Germany/: 30 µg/ml for 40 min; dispase /Sigma, Germany/: 50 µg/ml for 40 min in phosphate-buffered saline /PBS-A/; temperature: 37°C). After viability and functional standardization, the starting cell density was $2x10^5/cm^3$. cell cultures were treated with 10^{-6}M of NA. The AVP content of supernatant media was determined by RIA method.

Results and discussion

According to our results, discrete modulation has occurred as a result of the effects of these sugar-substituting compounds on cell cultures, it is demonstrated that the discrete differences in the sugar substitutes used were modulated in the activation-driven model system The assay protocol shown may be suitable for environmental exposures, in particular for nutritional biologically important sugar substitutes.

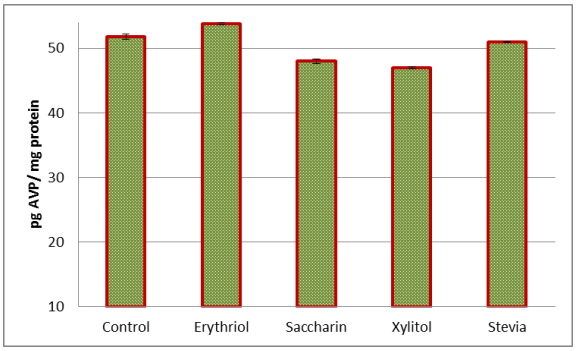

Figure 1. Effect of sugar substitutes on AVP secretion of NH cell cultures (means±SEM, n=6)

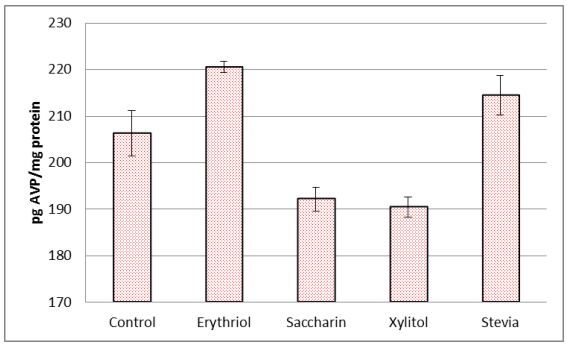

Figure 2. Effect of NA activated and sugar replacement compounds on AVP secretion in NH cell cultures (means±SEM, n=6)

Conclusion

In order to meet basic needs in society, many substances which have a significant effect on the endocrine system and / or its system of contacts are warranted, and therefore endocrine-related compounds of nutritional importance should be investigated.

Acknowledgements
EFOP-3.4.3-16-2016-00014, EFOP-3.6.1-16-2016-00008, TÁMOP-4.2.4.A/2-11/1-2012-0001

References
[1] S. D. Anton, C. K. Martin, H. Han, S. Coulon, W.T. Cefalu, P. Geiselman, D. A. Williamson, Effects of stevia, aspartame, and sucrose on food intake, satiety, and postprandial glucose and insulin levels. Appetite, 2010, 55, 37-43.
[2] Z. Molnár, R. Pálföldi, A. László, M. Radács, K. Sepp, P. Hausinger, L. Tiszlavicz, Z. Valkusz, M. Gálfi, Effects of chronic and subtoxic chlorobenzenes on adrenocorticotrophic hormone release. Journal of Environmental Sciences, 2015, 34, 165-70.
[3] Gálfi, M., Radács, M., Molnár, Z., Budai, I., Tóth, G., Pósa, A., Kupai, K., Szalai, Z., Szabó, R., Molnár, H.A. 2016. Ghrelin-induced enhancement of vasopressin and oxytocin secretion in rat neurohypophyseal cell cultures. Journal of Molecular Neuroscience 60 ,525-530.
[4] H. F. Clarke, S. C. Walker, H. S. Crofts, J. W. Dalley, T. W. Robbins, A. C Roberts,. Prefrontal serotonin depletion affects recersasl learning but not attentional set shifting. The Journal of Neuroscience, 2005, 25, 532-538.
[5] R. Hurlemann, A. Patin, O. A. Onur, M. X. Cohen, T. Baumgartner, S. Metzler, I. Dziobek, J. Gallinat, M. Wagner, W. Maire, K. M. Kendrick, Oxytocin enhances amygdala-dependent, socially reinforced learning and emotional empathy in humans. Journal of Neuroscience, 2010, 30, 4999-5007.
[6] C. W. Harley, Norepinephrine and dopamine as learning signals. Neural Plasticity, 2004, 11, 191-204.
[7] de D. Wied, Neuropeptides in learning and memory processes. Behavioural Brain Research, 1997, 83, 83-90.
[8] B. Alescio-Lautier, B. Soumireu-Mourat, Role of vasopressin in learning and memory in the hippocampus. Prog. Brain. Res., 1998, 119, 501-521.