Journal of the Endocrine Society

AN OPEN ACCESS PUBLICATION

ENDO 2021 ABSTRACTS

ANNUAL MEETING OF THE ENDOCRINE SOCIETY
VOLUME 5, ISSUE SUPPLEMENT_1, APRIL-MAY 2021

ENDOCRINE SOCIETY

on fasting serum levels of appetite-regulating hormones (leptin, insulin, adiponectin, GIP, PP, PYY, CCK, FGF21) were available. Hormone levels were correlated to BMI at baseline (T0) and compared across three time points: T0, T1 (after 10 weeks; initial weight loss) and T2 (after 75 weeks; weight loss maintenance). T0-T1 hormone changes were correlated to BMI changes between T1 and T2 to investigate whether hormonal alterations during initial weight loss are associated with weight regain. At T0, hormone levels were not associated with BMI. BMI decreased significantly from T0 (40.13 kg/m^2 ± 5.7) to T1 (38.2 ± 5.4, p < .001) which was maintained at T2 (38.2 kg/m^2 ± 5.9, p < .001). There were no significant changes in GIP, PP, PYY, CCK and FGF21. Leptin decreased from T0 (44.9 ng/nl ± 15.3) to T1 (33 ng/nl ± 14.8, p < .001) and T2 (38.6 ng/nl ± 16.0, p < .01), just like insulin which was significantly decreased at T1 (123 pmol/l ± 65, p < .05) and T2 (128 pmol/l ± 64, p < .05) compared to T0 (160 pmol/l ± 80). Adiponectin did not change between T0 (3.36 ug/ml ± 2.1) and T1 (3.2 ug/ml ± 2.1), but was increased at T2 (3.7 ug/ml ± 2.9, p < .01) compared to T1. T0-T2 BMI decrease correlated positively with T0-T2 decreases in leptin (r = .667, p < .001), insulin (rho = .535, p < .001) and increases of adiponectin (r = .412, p < .01), but no other hormone. T0-T1 hormone changes did not predict T1-T2 BMI changes. Thus, a 75-week CLI was associated with beneficial changes in the long-term energy regulators adiponectin, leptin and insulin, but no changes in short-term appetite-regulating hormones were observed despite significant weight loss. Initial changes in appetite-regulating hormones were not associated with subsequent weight regain. Overall, our data suggest that a CLI does not lead to adverse changes in appetite regulation, but rather long-term improvements such as e.g. increased leptin and insulin sensitivity.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

In-Vitro Exposure to Endocrine Disruptors Alters Inflammatory Markers in Whole Hypothalami and Immortalized GnRH Neurons

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Bisphenol A (BPA), a monomer of polycarbonate plastics, and Benzophenones (BPs), used as UV-filters, are endocrine disrupting chemicals (EDC) found in everyday products. Previously, we showed that the in-vitro exposure to BPA decreased Kiss-induced GnRH expression in GN11 cells (donated by Dr. Susan Wray, NIH), immature GnRH neurons, and that exposure to all the EDC decreased Kiss-induced GnRH gene expression in GT1-7 cells (donated by Dr. Pamela Mellon, UCSD), mature GnRH neurons. In this study, we analyzed the effect of in-vitro exposure to the same EDC (BPA, BP2 or BP3, Sigma, 1x10^{-9} M) or medium as control (C) in mature GnRH neurons (GT1-7 cells), and isolated hypothalami from adult Balb/c males on Glial fibrillary acidic protein (GFAP) and cytokine gene expression. Cells were exposed to the compounds for 12 or 24 h, in DMEM (high glucose) with charcoal-stripped FBS, and the hypothalami for 6 h to the EDC, in Krebs-Ringer buffer. After the incubations, RNA was extracted using Tri-Reagent (Molecular Research Center, OH, USA), 1-2 µg RNA was reverse transcribed and Real-Time PCR performed using specific primers. Results were expressed as Mean±SE and analyzed by T-test or ANOVA using Statistica v12 (StatSoft Inc, USA) Twenty-four hour BPA exposure increased *il18* in GT1-7 cells (C=1.0±0.04, BPA=1.2±0.1, T-test p<0.05, n=7), whereas neither BP2 nor BP3 had an effect on *il18* expression (ANOVA: ns, n=7). When *il6* was analyzed, 24-hour BPA decreased its expression relative to C and to 12-hour BPA, whereas BP3 had a dual effect depending on the time-point analyzed, increasing the expression at 12-hour stimulation and decreasing it after 24-hour stimulation (DMSO-12h=0.82±0.08, DMSO-24h=1.01±0.13, BPA-12h=1.00±0.11, BPA-24h=0.68±0.06, BP2-12h=0.75±0.12, BP2-24h=0.82±0.18, BP3-12h=1.20±0.10, BP3-24h=0.83±0.05; Repeated Measures Two-way ANOVA: BPA-24h different from DMSO-24h and BPA-12h p<0.05, BP3-12h different from DMSO-12h and from BP3-24h p<0.05, n=4). In the hypothalami, 6-hour BPA exposure increased *gfap* gene expression (C=0.8±0.2, BPA=1.7±0.4; T-test p<0.05, n=9), whereas neither BP2 nor BP3 had any significant effect (C=0.8±0.2, BP2=1.4±0.3, BP3=1.0±0.3, ANOVA ns, n=9). There was no significant change in *il18, il6 or il1b* gene expression in whole hypothalami with any of the EDC tested (ANOVA ns). Our results show that the EDC herein studied have the potential to alter the inflammatory state of mature GnRH neurons and to activate astrocytes in the hypothalamus. The pattern for cytokine expression in the whole tissue could be different from the one observed in GnRH neurons, as the hypothalamus contain multiple cell types, and effects can be different in the different cells. More experiments are needed to dissect the mechanisms involved in the effects observed.
Funding: CONICET, ANPCyT, UBA, International Society for Neurochemistry, Asoc. ORT Arg., Fund. R. Barón, Fund. Williams.

Endocrine Disruption

ENDOCRINE DISRUPTING COMPOUNDS: MECHANISMS OF ACTION AND CLINICAL IMPLICATIONS

PFOA Exposure Prior to Hepatocyte Differentiation Leads to Gene Expression Changes Implicated in Non-Alcoholic Fatty Liver Disease

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Background: Perfluorooctanoic acid (PFOA), is a persistent fluorinated compound with oil and water repelling