Impact of environmental enrichment on individual food intake and hypothalamic genes related to energy balance

Emily E Noble1,4, Alix Dieuleveult1,4, Cayla Duffy1, Rachel Lee1, Heather Bainter, Joshua Nixon1,5, Tammy Butterick1,5, Charles J. Billington1,5, Catherine M. Kotz1,2,4,5, and ChuanFeng Wang1,4,5

Department of 1Food Science and Nutrition, 2Department of Neuroscience, 3Department of Medicine, and 4Minnesota Obesity Center, University of Minnesota, St. Paul, MN USA 55108, 5Minneapolis VA Health Care System, Minneapolis, MN USA 55417

Background

An enriched environment (EE) may protect against obesity by influencing hypothalamic genes related to energy balance. The rodent EE incorporates both social and inanimate (toys) components and sometimes physical exercise. We hypothesize that an EE protects against obesity by reducing individual food intake and affecting hypothalamic signaling factors related to energy balance.

Methods

Animals: Sprague Dawley rats (n=52) weighing ~300 g were randomized into 2 groups of equal body composition, and placed into either EE or control housing (C). All animals were maintained on Purina D12450B chow.

Housing: EE cages (17x17x12 inch, plexiglass) included toys and crinkle bedding and housed 4 animals per cage. Rats in the C group were individually housed in standard shoebox cages with a single nipple. Toys were removed during scheduled meal times, and order was rotated upon replacement. Once a week cages were cleaned and toys were switched between cages, such that each group of animals interacted with each set of toys during two separate weeks.

Experimental Protocol: For both EE and C, feeding took place during scheduled meal times. Food intake measurements were recorded every 4 hours and body composition was measured every 2 weeks. After 8 weeks animals were sacrificed at the end of the dark cycle, and hypothalamic tissue was dissected and stored at -80°C.

qRT-PCR: Total mRNA from cultured cells was isolated using a commercial kit (Qiagen). Primers for the following genes were designed using MacVector 12.0: OX1R (NM_198959), OX2R (NM_198962), BDNF (NM_012871.2), TrkB (NM_001163168.2) and GAPDH (NM_017008). PCR reactions were performed in a Roche LightCycler. Relative mRNA levels were normalized to GAPDH using the 2ΔΔCT method.

Results

1) EE including social housing reduces individual food intake and protects against weight gain.

2) Anorexigenic signaling pathway genes in the PVN, (BDNF, trkB, CRH) were elevated.

- BDNF injections in PVN decrease food intake, body weight, and elevate energy expenditure [1].
- BDNF regulates expression of CRH in the PVN [2]; activation of CRH receptor slows gastric emptying and reduces feeding [3, 4].
- Blocking CRH receptors abolishes BDNF effects on food intake and body weight.
- These data suggest existence of a common pathway whereby EE elevates PVN BDNF, increasing expression of CRH and reducing food intake.

3) EE elevates OXA expression in the LH and increased OX1R in the PVN as well as increased levels of CRH.

- Activation of OX1R by OXA in PVN elevates CRH-mediated pathways [6].
- BDNF/trkB receptor signaling may mediate this effect, as BDNF/trkB have known plasticity functions and regulate expression of CRH.

4) OXT was reduced in the PVN, but its receptor was elevated.

- In VMN, OXT [7] and BDNF [8, 9] both reduce feeding and elevate energy expenditure.
- We did not observe differences in expression of these peptides between EE and C housed animals in the VMN (data not shown).

5) Animals housed in an EE had elevated levels of OXA in the caudal LH as well as increased receptors OX1R and OX2R suggesting enhanced orexinergic tone.

- Lateral hypothalamic increases in orexin expression and signaling promote resistance to obesity via elevating spontaneous physical activity [10].

Acknowledgments

This work was supported by the Department of Veterans Affairs BLR&D BX001686, NIH grant 1R01DK080782, and NIDDK 1214548. We would like to thank Lauren Wisdorf, Vincent Truong and Spencer Printen for their contributions.