Int. J. Devl Neuroscience 49 (2016) 50–59

Contents lists available at ScienceDirect

International Journal of Developmental Neuroscience

journal homepage: www.elsevier.com/locate/ijdevneu

Low protein diet during gestation and lactation increases food reward seeking but does not modify sucrose taste reactivity in adult female rats

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ARTICLE INFO

Article history:
Received 22 May 2015
Received in revised form
25 December 2015
Accepted 12 January 2016
Available online 22 January 2016

Keywords:
Low protein diet
Motivation
Taste
c-Fos
Female
Rats

ABSTRACT

Introduction: Nutritional deficiencies during neural development may lead to irreversible changes, even after nutritional rehabilitation, promoting morphological and functional adaptations of structures involved with various behaviours including feeding behaviour. However, the ability of the exposure low protein diet during gestation and lactation to affect the hedonic component of food intake is still poorly understood, especially in females.

Methods: Wistar rats were divided into two groups according to the diet offered to the dams during pregnancy and lactation: control female (CF; diet with 17% protein, $n = 7$) and low protein female (LPF; diet with 8% protein, $n = 7$). The following parameters were evaluated: (a) body weight during weaning, 30, 45, 60, 75, 90 days of life; (b) standard diet intake from 110 to 132 days of life; (c) fat diet and consumption of simple carbohydrates (HFHS) for 1 h at 145 days of life; (d) incentive runway task 60 days after 82 days of life; (e) taste reactivity at 90 days of life; and (f) neuronal activation in the caudate putamen, amygdala, paraventricular nucleus of the hypothalamus under stimulus HFHS at 145 days of life.

Results: The exposure, a low protein diet during gestation and lactation, decreased the body weight throughout the study period from weaning to 90 days of life. However, there was no significant change in the body weight of low protein females from 110 to 132 days of life compared with the control females. There was an increase in the rate of the search for reward and reduced the latency of the perception of bitter taste. The exposure, a low protein diet during gestation and lactation, also promoted hypophagy in adult females compared with control animals. The low protein female had increased HFHS diet consumption compared with the control. Undernutrition increased neuronal activation in response to HFHS diet consumption compared with female controls in the amygdala and in the caudate putamen.

Conclusion: Females subjected to the exposure, a low protein diet during gestation and lactation, exhibit hypophagy on a standard diet but a higher consumption of a diet rich in lipids and simple carbohydrates. And also were more motivated by the pursuit of reward and reduced latency of the bitter taste reactivity, and increased the number of immunoreactive cells c-fos protein activated in the caudate putamen, amygdala and paraventricular nucleus.

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http://dx.doi.org/10.1016/j.ijdevneu.2016.01.004
0736-5748/

1. Introduction

During pregnancy and lactation, the offspring's developing nervous system undergoes diverse formation and maturation of its physiological and morphological patterns. These periods are considered "critical" because they comprise a sequence of well-defined ontogenetic events that are subject to external agents. This period may occur "set points" (adaptations) that influence later events (Morgane et al., 2002). These adjustments occur in response to environmental demands; in other words, the individual modifies its morphological and functional patterns in response to a stimulus or insult to maintain its survival in its environment (Hales and Barker, 2001).

Early exposure to a low protein diet can induce such adaptations because exposure to poor nutrition can result in metabolic changes that encourage the economic and efficient use of scarce energy substrates (Bellinger and Langley-Evans, 2005). Overall, these adaptations are beneficial to organisms that remain in the same metabolic environment they were exposed to in the perinatal period (Bellinger et al., 2006), but long-term damage may occur if there is an excess of nutrients (Bouret and Simerly, 2006). Epidemiological studies and animal model studies have shown that maternal health and nutritional status during pregnancy and lactation affect the offspring's development of the central and peripheral systems that regulate energy balance and body weight (Desai et al., 2005; Hales and Barker, 1992, 2001).

Effects of undernutrition have been implicated in feeding behaviour. The expression of peptides like neuropeptide Y and agouti-related peptide (NPY/AgRP) that stimulate food intake is increased, and levels of peptides like pro-opium-melanocortin and cocaine- and amphetamine-regulated transcript (POMC/CART) that inhibit food intake are decreased, especially in the hypothalamus, which integrates hunger and satiation stimuli (Bouret and Simerly, 2006). In addition, the anorexic actions of leptin and insulin (Fernandez-Twinn et al., 2005) are reduced in animals exposed to malnutrition in early development, resulting in increased food consumption (Vickers et al., 2000). Palatable foods can stimulate food consumption, resulting in a positive energy balance (Erlanson-Albertsson, 2005). Diets high in simple sugars and fat are very palatable and can promote metabolic disorders by stimulating fat synthesis, mainly triglycerides, which are stored in adipose tissue (Estadella et al., 2004). Increased adipose tissue may stimulate the release of adiposity signals such as leptin and insulin (Ashino et al., 2012; Fam et al., 2007). Greater release of these peptides may result in resistance to their cellular actions; thus, their effects are reduced (Kirk et al., 2009; Srinivasan et al., 2006). Another consequence is the increased food intake, as these two factors work together to stimulate satiety (Belgardt and Bruning, 2010). Palatable foods also have organoleptic properties, capable of stimulating food reward pathways and generating a feeling of pleasure (Lowe and Butryn, 2007).

The hedonic control components of food intake are translated and integrated through the cortico-mesolimbic system formed by the nucleus accumbens, ventral striatum, ventral tegmental area, prefrontal cortex, hippocampus, and amygdala (Berridge et al., 2009). The perception of palatable information is more complex because it depends on the nutritional value (high in carbohydrates or fat) and sensory properties (sight, smell, taste, texture) (Rolls, 2006). Food information that stimulates sensory receptors is processed in different brain regions depending on the sense (Rolls, 2006). Therefore, sensory receptor stimulation can occur in the temporal cortex (vision), olfactory bulb (smell), thalamus (texture), and nucleus of the solitary tract (taste) (Rolls, 2006). This information will be shaped by the nucleus accumbens and ventral tegmental area (Rolls, 2006). The amygdala transforms the information received from other reward system regions into emotional stimuli (pleasure), while the hippocampus records the "pleasurable experience" in memory (Kelley and Berridge, 2002). Increased palatability might involve the stimulation of endogenous opioid activity (Tsujii et al., 1986); in addition, dopaminergic signalling within the reward areas is also influenced by energy-dense food intake (Vucetic et al., 2012).

There are few studies of motivation in animals fed a low protein diet. Recently, it was observed that perinatal malnutrition increases motivation for the search of food reward in adulthood (da Silva et al., 2013). This motivation was related to increased neuronal activation in reward system brain regions (da Silva et al., 2013). Therefore, our objective was to study the effect of low protein diet exposure during gestation and lactation periods on food motivation and responsiveness in adult rats. We hypothesized that the low protein diet condition would promote increased food motivation and that taste reactivity changes would be detectable in reward regions of the adult rat brain.

2. Materials and methods

2.1. Animals

All experiments were approved by the Ethics Committee on Animal Experiments of UFPE (no process 23076.037409/2011-64) following the rules of CONCEA (National Council for Animal Experiments Control). Wistar albino rats (200–250 g body weight) were reared in the Nutrition Department of the Federal University of Pernambuco. The rats were mated at a ratio of two females to one male. Pregnancy was diagnosed based on the presence of sperm in the vaginal smear and confirmed by body weight gain. After the diagnosis of the pregnancy, the rats were transferred to individual cages, and during pregnancy and lactation, the rats received isocaloric diets (Table 1) with two different protein concentrations: control diet with 17% protein, ($n = 7$) or low protein diet with 8% protein, $n = 7$). Sexing was performed to form litters with eight pups of both sexes per dam (four males, four females). Throughout the experiment, the animals were kept in standard vivarium conditions (temperature of $22 \pm 1\,^{\circ}C$ under light/dark inverted 12 h, the light on 18:00, with ad libitum access to food and water. After weaning at 22 postnatal days, pups from both groups were fed the vivarium's standard diet (Labina Presence®, Paulinia, São Paulo, Brazil).

The experimental groups were formed by randomly collecting two female pups from each dam. After the manipulation diet, two perinatal experimental groups were obtained. Control female (CF, $n = 14$) from dams who received a normal protein diet during the perinatal period and low protein female (LPF, $n = 14$) from dams who received a low protein diet during the perinatal period.

Table 1
Composition of the experimental diets offered during the period of pregnancy and lactation.

Components	Low protein (8%)	Normoprotein (17%)
G%	100.00	100.0
Protein	8.20	17.05
Carbohydrate	74.75	65.90
Lipidis	7.00	7.00
Fiber	5.00	5.00
Vitamin	1.00	1.00
Minerals	3.50	3.50
Metionin	0.30	0.30
Coline	0.25	0.25
% Kcal	394.8	394.8