Neuropeptides 48 (2014) 213–220

Contents lists available at ScienceDirect

Neuropeptides

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

Expression profile of hypothalamic neuropeptides in chicken lines selected for high or low residual feed intake

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ARTICLE INFO

Article history:
Received 14 December 2013
Accepted 15 April 2014
Available online 9 May 2014

Keywords:
Hypothalamus
Neuropeptides
Feed intake
Food deprivation
Chickens
Hyperphagia

ABSTRACT

The R^+ and R^- chicken lines have been divergently selected for high (R^+) or low (R^-) residual feed intake. For the same body weight and egg production, the R^+ chickens consume 40% more food than their counterparts R^- lines. In the present study we sought to determine the hypothalamic expression profile of feeding-related neuropeptides in these lines maintained under fed or food-deprived conditions.

In the fed condition, the suppressor of cytokine signaling 3 (SOCS3) was 17-fold lower ($P < 0.05$) and the ghrelin receptor was 7-fold higher ($P < 0.05$) in R^+ compared to R^- chicken lines. The hypothalamic expression of the other studied genes remained unchanged between the two lines. In the fasted state, orexigenic neuropeptide Y and agouti-related peptide were more responsive, with higher significant levels in the R^+ compared to R^- chickens, while no significant differences were seen for the anorexigenic neuropeptides pro-opiomelanocortin and corticotropin releasing hormone. Interestingly, C-reactive protein, adiponectin receptor 1 and ghrelin receptor gene expression were significantly higher (12-, 2- and 3-folds, respectively), however ghrelin and melanocortin 5 receptor mRNA levels were lower (4- and 2-folds, $P = 0.05$ and $P = 0.03$, respectively) in R^+ compared to R^- animals.

We identified several key feeding-related genes that are differently expressed in the hypothalamus of R^+ and R^- chickens and that might explain the difference in feed intake observed between the two lines.

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1. Introduction

The physiological regulation of energy homeostasis is critical to animal long term survival and is relevant to their welfare. Energy homeostasis regulation is a complex, yet poorly understood, system involving peripheral and central mechanisms. In avian species, these mechanisms can be altered by genetic selection which has resulted in marked change in body composition (Leclercq et al., 1994), growth rate (Burkhart et al., 1983) and reproductive performance (Flock et al., 1991). R^+ and R^- chicken lines have been divergently selected from a base Rhode Island Red egg-laying chickens for high (R^+) or low (R^-) residual feed intake (Bordas and Merat, 1981; Bordas et al., 1992). After 30 generations of selection for the same body weight and egg production, the R^+ animals consume 50% more food but they are leaner than their counterpart R^- animals (El-Kazzi et al., 1995). The difference in leanness between the two lines has been extensively studied and has been attributed, at least partly, to higher diet-induced thermogenesis (Gabarrou et al., 1997, 1998; Swennen et al., 2007), higher expression of uncoupling protein (Raimbault et al., 2001), and lower hepatic fatty acid synthesis in R^+ compared to R^- lines (Lagarrigue et al., 2000). Still, the signaling mediators of the difference in energy intake between the two lines remain to be fully defined.

The hypothalamus, which contains the satiety and feeding centers, plays a crucial role in the regulation of body energy balance

Abbreviations: Adip-R1/2, adiponectin receptor 1 and 2; AgRP, agouti related peptide; ANOVA, analysis of variance; cAMP, cyclic adenosine monophosphate; CART, cocaine and amphetamine regulated transcript; CRH, corticotropin releasing hormone; CRP, C-reactive protein; Ghr, ghrelin; Ghr-R, ghrelin receptor; JAK, Janus Kinase; MAPK, mitogen activated protein kinase; MCH, melanin concentrating hormone; MCR, melanocortin receptor; NF-κB, nuclear factor κB; NPY, neuropeptide Y; Ob-R, leptin receptor; ORX, orexin; ORXR, orexin receptor; PKA, protein kinase A; POMC, pro-opiomelanocortin; SOCS3, suppressor of cytokine signaling 3; STAT3, Signal Transducer and Activator of Transcription 3.

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http://dx.doi.org/10.1016/j.npep.2014.04.007
0143-4179/Published by Elsevier Ltd.

(Kuenzel et al., 1999; Sawchenko, 1998). It contains two separate populations of neuronal cell types. One synthesizes orexigenic neuropeptide Y (NPY) and agouti-related peptide (AgRP) (Kuenzel et al., 1987; Phillips-Singh et al., 2003), while the other produces anorexigenic pro-opiomelanocortin (POMC) and cocaine- and amphetamine-regulated transcript (CART) (Gerets et al., 2000; Tachibana et al., 2003). These neuropeptides interact with the central melanocortin system (MCRs), melanin-concentrating hormone (MCH) and orexin to regulate feeding behavior in mammals (for review see, Schwartz et al., 2000).

Although the high conserved neuronal signaling network governing feeding behavior between avian and mammalian species, some peptides do not always exhibit similar function. For instance, ghrelin stimulates feed intake in mammals but it has been found to inhibit feeding in chickens (Furuse et al., 2001; Geelissen et al., 2006; Kaiya et al., 2002; Saito et al., 2002, 2005). On the other hand, orexin (A and B) also referred to as hypocretin 1 and 2, MCH, galanin and motilin are orexigenic peptides in mammals but are without apparent effect on feed intake in birds (Ando et al., 2000; Furuse et al., 1999). Peptide YY and pancreatic polypeptide suppress feed intake in mammals whereas they are orexigenic peptides in birds (Ando et al., 2001; Kuenzel et al., 1987). Several G protein coupled receptors, that are linked to the regulation of feeding behavior, including NPY receptors (Bromee et al., 2006; Holmberg et al., 2002; Lundell et al., 2002; Salaneck et al., 2000), melanocortin receptors (Boswell and Takeuchi, 2005; Takeuchi and Takahashi, 1998), adiponectin receptors (Ramachandran et al., 2007), ghrelin receptor (Tanaka et al., 2003), orexin receptor (Ohkubo et al., 2003) and the leptin receptor (Horev et al., 2000; Liu et al., 2007; Ohkubo et al., 2000; Richards and Poch, 2003) which belongs to the cytokine-class 1 single membrane-spanning receptor have been identified in birds.

In a search for molecular markers of the differences observed in energy intake between the R^+ and R^- chickens, the feeding-related hypothalamic neuropeptide profiling was investigated in the present study.

2. Results

2.1. Feed intake

Feed intake was higher in R^+ compared to R^- males and females (Fig. 1a and b) and this difference increased from one generation to the next in both male and female chickens. Indeed, the magnitude of the difference in feed intake passed from 3% for both sexes in the first generation to reach 50% and 57% in the 30th generation in male and female respectively (Fig. 1a and b).

Since the effect of some neuropeptides in chicken is not fully understood and established, we classified them in the following section based on their effects in mammals.

2.2. Orexigenic neuropeptide gene expression in R^+ and R^- chicken lines

NPY mRNA abundance did not differ between the two lines at fed state, however it was increased by fasting ($P < 0.05$) and this effect was more pronounced in R^+ than in R^- line (Fig. 2a). AgRP gene expression was affected by genotype ($P < 0.05$), although this effect was only apparent in the fasted state as reflected in the

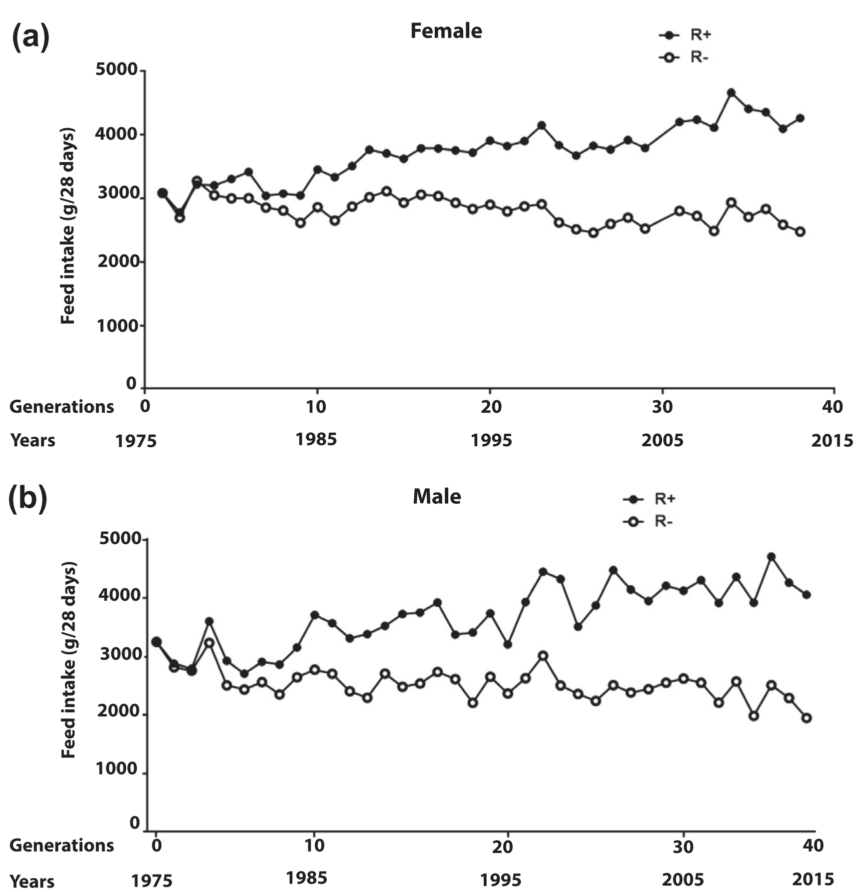

Fig. 1. Average feed intake change in successive generations of R^+ and R^- chickens. (a) Females and (b) male chickens. Footnote: the feed intake for female in the year 2004 has not been recorded.