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下丘脑－垂体－肾上腺轴参与动物采食调控的研究进展

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摘 要: 采食是动物维持生命活动的基本生理过程,是动物生长发育的基础。畜禽采食量的高低直接影响到营养物质的摄入量及生产性能的发挥。在畜牧业生产中,影响采食的因素很多,而应激是其中一个非常重要的影响因素。动物机体的应激反应主要由下丘脑－垂体－肾上腺(HPA)轴来调控。下丘脑、垂体和肾上腺皮质通过释放促肾上腺皮质激素释放激素(CRH)、促肾上腺皮质激素(ACTH)和糖皮质激素(GC)这 3 种应激激素来协同调控动物的应激反应。应激激素对采食行为的调节是一个非常复杂的过程,主要通过稳态和非稳态途径来调节采食,可以双向调控食物的摄入量。稳态途径指的是通过调控机体能量稳态而调控采食。CRH 和 ACTH 通过抑制下丘脑促食欲肽的表达而抑制采食;而 GC 在中枢和外周发挥着完全相反的作用。非稳态途径指的是通过影响中脑奖赏系统调控采食的愉悦感,是近年来食欲调控研究的热点,越来越多的研究证明了应激激素与奖赏系统的联系。作者针对应激激素调控采食的最新研究报道进行综述,以期为生产实践中新型的采食调控技术研发提供一定的参考。

关键词: 下丘脑－垂体－肾上腺轴;应激;采食
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Research Advances on Effects of Hypothalamic-pituitary-adrenal Axis in Animal Feeding Regulation

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Abstract: Feeding is the basic physiological process of animal survival, growth and development. Food intake of livestock and poultry directly affects the absorption of nutrients and production performance. In animal production, feeding is affected by many factors, and stress is one of the most important factors. The stress response of animal is mainly regulated by the hypothalamic-pituitary-adrenal (HPA) axis. The hypothalamus, pituitary and adrenal cortex regulate the stress response of the animals by releasing three stress hormones such as corticotropin releasing hormone (CRH), adrenocorticotropic hormone (ACTH) and glucocorticoid (GC). The regulation of feeding by stress hormones is a very complex process where it can regulates feed intake in both positive and negative way. Specifically, stress hormones may participate in both homeostatic and non-homeostatic pathways to regulate eating behavior. Homeostatic pathways refer to the regulation of food intake by sensing energy status of the body. In this case, CRH and ACTH inhibit feed

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intake by inhibiting the expression of the appetite peptide in the hypothalamus; GC plays a completely opposite role in the central and peripheral regions. The non-homeostatic pathways refer to the regulation of hedonic eating by modulating the midbrain reward system. It is a hotspot in the study of appetite regulation in recent years. More and more studies have focused on the crosstalk between stress hormone and reward system. In this review, the latest researches on regulation of feeding by stress hormone will be summarized. It will provide some theoretic basis for the development of new techniques on feeding regulation in animal production.

Key words: hypothalamus-pituitary-adrenal axis; stress; feeding

采食是动物维持生命活动的基本生理过程，也是畜牧业生产中至关重要的一环。畜禽采食量的高低直接影响营养物质的摄入量及生产性能的发挥。而应激根据应激源的不同，可分为热应激、冷应激、运输应激、断奶应激、去势、断尾等。已经有研究表明，热应激会显著降低畜禽的采食量，且温度愈高，采食量下降的幅度愈大[1]。而断奶应激也能导致仔猪采食量显著减少，进而导致生产性能下降[2]。

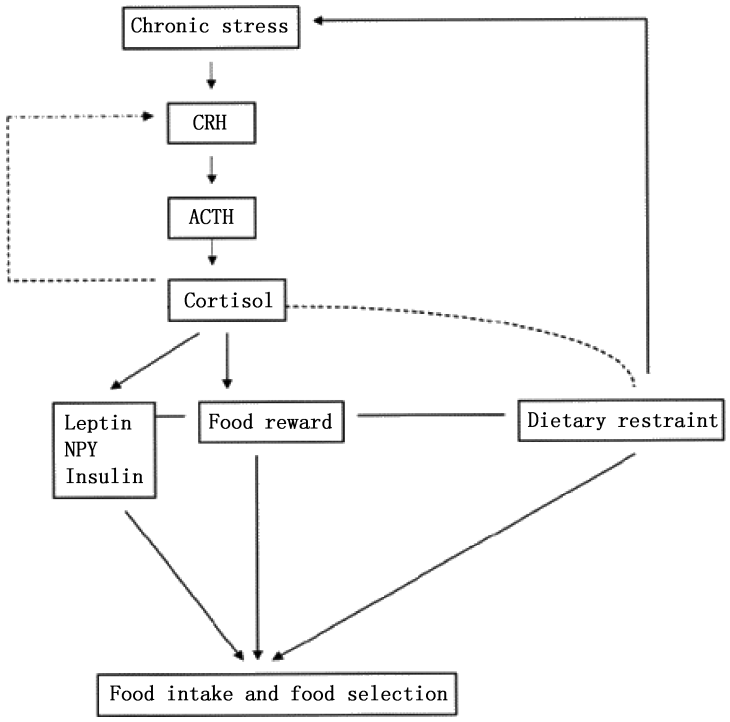
动物机体的应激反应主要由下丘脑－垂体－肾上腺(HPA)轴来调控。下丘脑、垂体和肾上腺皮质通过释放促肾上腺皮质激素释放激素(CRH)、促肾上腺皮质激素(ACTH)和糖皮质激素(GC)这 3 种应激激素来协同调控动物的应激反应。目前认为，应激激素可通过稳态和非稳态两种途径来调节采食行为。稳态途径中应激激素通过调控下丘脑食欲调节肽或者外周能量稳态调节激素来调控采食。下丘脑是稳态途径食欲调节的关键脑区。下丘脑弓状核(arcuate nucleus，ARC)的神经肽 Y(neuropeptide Y，NPY) 和刺鼠基因相关蛋白 (agouti gene-related protein，AgRP) 以及下丘脑外侧区(lateral hypothalamic area，LHA) 中的食欲素(orexin，ORX)和黑色素浓集激素(melanin-concentrating hormone，MCH)是下丘脑中重要的能促进食欲的神经肽[3-5]。另外，下丘脑分泌的阿片促黑素皮质素原(proopiomelanocortin，POMC)、可卡因安非他明调节转录肽(cocaine and amphetamine regulated transcript，CART)以及下丘脑室旁核(paraventricular nucleus，PVN)中的 CRH 和催产素(oxytocin，OT)能够参与抑制采食[4,6]。外周调节途径则包括瘦素、胰岛素及其他饱感信号。瘦素和胰岛素等能参与能量平衡调节，从而对促进食欲或抑制食欲的神经肽产生调节作用[6]。非稳态途径是通过影响中脑多巴胺的分泌而调控采食产生的愉悦感(奖赏系统)，进而影响食欲。中脑腹侧被盖区(ventral tegmental area，VTA) 在奖赏系统中发挥重要作用[7-10]，激活 VTA 中多巴胺神经元会增加其投射到伏隔核细胞外的多巴胺，活化奖赏系统，产生愉悦感。应激激素对采食行为的调控见图 1。

1 CRH 对采食的调节作用

CRH 是一种广泛分布于中枢及外周组织的 41 肽。有研究表明，在中枢，CRH 主要存在于 PVN 的小细胞，此外在下丘脑其他神经核团也有少量存在。外周组织如肾上腺、睾丸间质细胞和消化道中也有 CRH 的分布[12]。

CRH 是一种抑制食欲的神经内分泌因子，通常在进食后表达上调；但也有研究表明，大鼠进食高脂日粮后 CRH 表达并没有明显增加。进食没有引起 CRH 升高，其对食欲素表达的抑制作用则减弱，这可能就是高脂饮食容易导致过度采食的原因[13]。反过来，CRH 也影响动物的采食。在下丘脑腹内侧核给予 0.5 μg 以上的 CRH 会显著降低大鼠的采食量[14]；而在终纹床核给予 0.05～0.10 μg CRH 就能显著降低大鼠的采食量[14]。热应激条件下，大鼠 ARC 中 CRH mRNA 表达量显著增加而采食量显著降低[15]，CRH 在进入 ARC 后会抑制 NPY/AGRP 的表达[16-17]，并促进 CART 的表达[18]，从而抑制采食。还有研究表明，热应激雏鸡 PVN 中 CRH mRNA 表达增加，采食量显著下降，但 PVN 中 CART 的表达量没有显著变化[19]。

来自 CRH 家族的尿皮质素(urocortin，UCN)也有抑制食欲的作用[20-21]。有研究表明，与 CRH 相比，UCN1 能更有效地抑制小鼠的采食[22]。UCN1、UCN2 和 UCN3 可能通过抑制下丘脑促肾上腺激素释放激素二型受体(corticotropin releasing hormone receptor 2，CRHR2)来影响食欲[21]。另外，UCN 中枢给药能够抑制大鼠饥饿素(ghrelin，GHRL)分泌，可能会阻止 GHRL 引起的食欲增强[23]。还有研究发现 UCN 外周给药作用于肠中的 CRHR2 会刺激大鼠循环 GHRL 的增加[24]。



Chronic stress,慢性应激;Cortisol,皮质酮;Leptin,瘦素;Insulin,胰岛素;Food reward,食物奖赏;Dietary restraint,限制饮食;Food intake and food selections,进食和食物选择

图 1　HPA 轴与采食行为之间的关系[11]

Fig. 1　A model for the possible relationship between HPA axis functioning and eating behavior[11]

有关 CRH 对愉悦采食调控作用的报道较少,大多数研究都集中于应激与药物成瘾(药物奖赏)之间的关系。应激后,下丘脑 CRH 会加剧阿片类药物成瘾大鼠对药物的依赖[25],也能促进大鼠对适口性好的食物(混合的巧克力奶油和花生酱)的摄入[26]。CRH 通过 VTA 中促肾上腺激素释放激素 1 型受体(corticotropin releasing hormone receptor 1,CRHR1)的介导能促进可卡因成瘾[27-28];而在 CRH 浓度较高的情况下,CRHR2 可通过促进 GABA 的释放来减少谷氨酸释放到 VTA 多巴胺神经元上,从而抵消由 CRHR1 引起的兴奋作用[27-29]。也有研究证明,CRHR1 和 CRHR2 的信号能调节酒精成瘾[30-31]。反过来,慢性尼古丁暴露又会进一步促进小鼠 VTA 中多巴胺能神经元CRH mRNA 的表达[28]。

有研究表明,摄入可口食物可以缓解应激[32-36]。而在应激条件下,VTA 中 CRH 的水平升高会促进多巴胺神经元活化,而 CRHR1 颉颃剂可以阻断这种作用[37]。伏隔核中的 CRH 能促进多巴胺释放并增加小鼠食欲,但这种作用在应激暴露后消失[38]。

由此可见,CRH 对动物食欲的影响是双重的。在下丘脑能量稳态调节中枢,CRH 主要扮演着抑制食欲的角色;而在中脑多巴胺奖赏系统,CRH 又扮演着促进奖赏的角色,加剧药物成瘾,增加采食愉悦感。但值得关注的是,应激条件下 CRH 并不能促进小鼠愉悦奖赏,推测强弱程度不同的应激或者中枢不同浓度的 CRH 会对中脑奖赏系统存在不同的调节作用。

2　ACTH 对采食的调节作用

ACTH 由 39 个氨基酸组成,在中枢也参与饱腹感的形成,抑制采食。有研究表明,74%的患有神经性厌食症和神经性贪食症的人群血液中可发现抗 ACTH 的自身抗体[39]。此外,POMC 外显子 2 突变导致的 ACTH 功能不全会导致早发性肥胖[40]。

稳态调节途径中,ACTH 对小鼠黑皮质素-4(melanocortin 4,MC-4)受体具有与 α-黑色素细胞刺激素(alpha-melanocyte-stimulating hormone,α-MSH)类似的亲和力,故 ACTH 在能量稳态调节中也可能发挥一定作用[41]。下丘脑 POMC 在前转变素酶 1 的作用下会分解为 α-MSH 和 ACTH,通过对 MC-4 受体的调节抑制采食[41]。也有研究证明,ACTH 中枢给药会抑制大鼠的采食[42]。在 PVN 中单次和重复注射 ACTH 颉颃剂会导致大鼠

在光照期间的采食量持续增加[43]。另外,热应激抑制蛋鸡采食,并能够显著增加血浆 ACTH 水平[44]。可见,ACTH 在中枢和外周都能够抑制动物的采食。

在非稳态途径方面,据报道,静脉注射可卡因可引起血浆 ACTH 的升高,尽管 CRH 可能参与可卡因诱导的 ACTH 的释放,但 CRH 并不是唯一能促进 ACTH 释放的因子[45]。中枢或者外周 ACTH 是否影响中脑奖赏系统、调控愉悦采食行为还未见报道。

3 GC 对采食的调节作用

GC 是由肾上腺皮质分泌的类固醇激素。与 CRH 和 ACTH 不同,GC 在中枢对于食欲调控作用的报道均是正向的。

在稳态途径中,中枢 GC 给药能增加下丘脑中促进食欲基因 *NPY* 的转录从而提高肉仔鸡的采食量[46]。在采食时,GC 会通过大鼠 ARC 中腺苷酸激活蛋白激酶的活化上调该区域中的 NPY 和 AGRP 表达,进一步增强食欲[47-49]。此外,有研究表明,应激后大鼠 GC 分泌增加会导致 GHRL 水平升高,而升高的 GHRL 水平会导致 NPY/AGRP 表达增加,并且提高采食量[50-52]。

非稳态途径方面,药物奖赏和自然奖赏(例如食物)都能增加伏隔核中细胞外多巴胺的浓度,有趣的是,伏隔核多巴胺的释放也会伴随着 GC 的释放而增加,这表明 GC 会影响奖赏行为[53]。已有研究发现,GC 会引起大鼠多巴胺的释放[54-55];诱导应激后,小鼠增加了对适口性好的食物的摄入[56]。雄性大鼠的肾上腺切除术减少了多巴胺能神经传递,而这种效应可以通过 GC 给药来恢复[54],故推测 GC 与奖赏系统之间有着密不可分的关系。据报道,GC 可以促进杏仁核、伏隔核和终纹床核等脑区中 CRH 的表达[57-58],因此,应激和 GC 可能通过激活 CRH 从而强化与奖赏相关行为。

外周 GC 主要通过调控胰岛素和瘦素等能量代谢调节激素的水平而影响食欲。GC 能促进瘦素发出饱腹感信号,从而抑制食欲[59]。而血液中 GC 会降低小鼠采食诱导的下丘脑 ARC 中产生促进食欲的神经肽的表达,并且增加促进厌食的神经肽如 POMC 的表达[60]。虽然 GC 能刺激小鼠脂肪组织中瘦素的释放从而降低食欲,但它们会降低大脑对瘦素的敏感性,从而导致瘦素抵抗[59]。胰岛素是另一种受 GC 影响的食欲调节激素,胰岛素通常作用于下丘脑来降低食物摄入量[61]。外周 GC 给药会刺激大鼠胰腺分泌胰岛素[61],具有抑制食欲的作用。

综上,能量稳态途径中 GC 对中枢和外周的作用是相反的,而这可能是中枢 GC 增加会抑制下丘脑 CRH 的含量、促进 NPY 分泌,并且阻碍中枢神经系统中瘦素和胰岛素减退食欲的机制[46]。HPA 激活和 GC 可能导致暴饮暴食、药物成瘾[57,62]。

4 小 结

应激激素对采食行为的调节是双向的。在下丘脑能量稳态调节中枢,CRH 和 ACTH 均发挥着抑制食欲的作用,而 GC 通过负反馈作用抑制 CRH 和 ACTH 的作用,从而促进食欲;在中脑奖赏效应调节中枢,大量研究证明了 CRH、ACTH 和 GC 在药物奖赏方面的促进作用,但有关食物奖赏的报道还很少。明确应激激素在食物奖赏方面的调控作用,将有助于为畜禽采食调控技术和产品研发提供新的靶点。

参考文献(References):

[1] RENAUDEAU D, GOURDINE J L, ST-PIERRE N R. A meta-analysis of the effects of high ambient temperature on growth performance of growing-finishing pigs[J]. *Journal of Animal Science*, 2011, 89(7): 2220-2230.

[2] 钱朝海,李四元,李 文,等. 仔猪断奶应激的探析及其防治措施[J]. 中国畜牧兽医,2006,33(9):58-60.
QIAN C H, LI S Y, LI W, et al. Researching piglets ablactation stress syndrome produce reasons and prevention[J]. *China Animal Husbandry & Veterinary Medicine*, 2006, 33(9): 58-60. (in Chinese)

[3] GEHLERT D R. Role of hypothalamic neuropeptide Y in feeding and obesity[J]. *Neuropeptides*, 1999, 33(5): 329-338.

[4] VALASSI E, SCACCHI M, CAVAGNINI F. Neuroendocrine control of food intake[J]. *Nutrition, Metabolism and Cardiovascular Diseases*, 2008, 18(2): 158-168.

[5] SMITH P M, FERGUSON A V. Neurophysiology of hunger and satiety[J]. *Developmental Disabilities Research Reviews*, 2008, 14(2): 96-104.

[6] SCHWARTZ M W, WOODS S C, PORTE D J R, et al. Central nervous system control of food intake[J]. *Nature*, 2000, 404(6778): 661-671.

[7] KOOB G F, ZORRILLA E P. Neurobiological mechanisms of addiction: Focus on corticotropin-releasing factor[J]. *Current Opinion in Investigational Drugs*, 2010, 11(1): 63-71.

[8] SPANAGEL R, NOORI H R, HEILIG M. Stress and alcohol interactions: Animal studies and clinical significance[J]. *Trends in Neurosciences*, 2014, 37(4): 219-227.

[9] GOLD P W, CHROUSOS G P. Organization of the stress system and its dysregulation in melancholic and atypical depression: High vs low CRH/NE states[J]. *Molecular Psychiatry*, 2002, 7(3): 254-275.

[10] KELLY E A, FUDGE J L. The neuroanatomic complexity of the CRF and DA systems and their interface: What we still don't know[J]. *Neuroscience and Biobehavioral Reviews*, 2018, 90: 247-259.

[11] NIEUWENHUIZEN A G, RUTTERS F. The hypothalamic-pituitary-adrenal axis in the regulation of energy balance[J]. *Physiology & Behavior*, 2008, 94(2): 169-177.

[12] BAIGENT S M. Peripheral corticotropin-releasing hormone and urocortin in the control of the immune response[J]. *Peptides*, 2001, 22(5): 809-820.

[13] 廖丽萍. 高脂饮食对大鼠下丘脑前增食欲素原及CRH表达的影响[J]. 福建医药杂志, 2010, 32(1): 86-87.
LIAO L P. Effect of high-fat diet on the expression of orexin and CRH in rat hypothalamus[J]. *Fujian Medical Journal*, 2010, 32(1): 86-87. (in Chinese)

[14] CICCOCIOPPO R, FEDELI A, ECONOMIDOU D, et al. The bed nucleus is a neuroanatomical substrate for the anorectic effect of corticotropin-releasing factor and for its reversal by nociceptin/orphanin FQ[J]. *Journal of Neuroscience*, 2003, 23(28): 9445-9451.

[15] SUWANAPAPORN P, CHAIYABUTR N, THAMMACHAROEN S. A low degree of high ambient temperature decreased food intake and activated median preoptic and arcuate nuclei[J]. *Physiology & Behavior*, 2017, 181: 16-22.

[16] HEINRICHS S C, MENZAGHI F, PICH E M, et al. Corticotropin-releasing factor in the paraventricular nucleus modulates feeding induced by neuropeptide Y[J]. *Brain Research*, 1993, 611(1): 18-24.

[17] CURRIE P J. Integration of hypothalamic feeding and metabolic signals: Focus on neuropeptide Y[J]. *Appetite*, 2003, 41(3): 335-337.

[18] MO C, CAI G, HUANG L, et al. Corticotropin-releasing hormone (CRH) stimulates cocaine- and amphetamine-regulated transcript gene (CART1) expression through CRH type 1 receptor (CRHR1) in chicken anterior pituitary[J]. *Molecular and Cellular Endocrinology*, 2015, 417: 166-177.

[19] CRAMER T, KISLIOUK T, YESHURUN S, et al. The balance between stress resilience and vulnerability is regulated by corticotropin-releasing hormone during the critical postnatal period for sensory development[J]. *Developmental Neurobiology*, 2015, 75(8): 842-853.

[20] WENINGER S C, MUGLIA L J, JACOBSON L, et al. CRH-deficient mice have a normal anorectic response to chronic stress[J]. *Regulatory Peptides*, 1999, 84(1-3): 69-74.

[21] RICHARD D, LIN Q, TIMOFEEVA E. The corticotropin-releasing factor family of peptides and CRF receptors: Their roles in the regulation of energy balance[J]. *European Journal of Pharmacology*, 2002, 440(2-3): 189-197.

[22] TANAKA C, ASAKAWA A, USHIKAI M, et al. Comparison of the anorexigenic activity of CRF family peptides[J]. *Biochemical and Biophysical Research Communications*, 2009, 390(3): 887-891.

[23] YAKABI K, NOGUCHI M, OHNO S, et al. Urocortin 1 reduces food intake and ghrelin secretion *via* CRF (2) receptors[J]. *American Journal of Physiology Endocrinology and Metabolism*, 2011, 301(1): E72-E82.

[24] WANG L, STENGEL A, GOEBEL S M, et al. Intravenous injection of urocortin 1 induces a CRF2 mediated increase in circulating ghrelin and glucose levels through distinct mechanisms in rats[J]. *Peptides*, 2013, 39: 164-170.

[25] KOOB G F. Neurobiological substrates for the dark side of compulsivity in addiction[J]. *Neuropharmacology*, 2009, 56(Suppl 1): 18-31.

[26] PUCCI M, MICIONI DI BONAVENTURA M V, GIUSEPPONI M E, et al. Epigenetic regulation of nociceptin/orphanin FQ and corticotropin-releasing factor system genes in frustration stress-induced binge-like palatable food consumption[J]. *Addiction Biology*, 2016, 21(6): 1168-1185.

[27] LEONARD M Z, DEBOLD J F, MICZEK K A. Escalated cocaine "binges" in rats: Enduring effects of social defeat stress or intra-VTA CRF[J]. *Psychopharmacology*, 2017, 234(18): 2823-2836.

[28] GRIEDER T E, HERMAN M A, CONTET C, et al. VTA CRF neurons mediate the aversive effects of nicotine withdrawal and promote intake escalation[J]. *Nature Neuroscience*, 2014, 17(12): 1751-1758.

[29] CONTARINO A, KITCHENER P, VALL E M, et al. CRF1 receptor-deficiency increases cocaine reward[J]. *Neuropharmacology*, 2017, 117: 41.

[30] RINKER J A, MARSHALL S A, MAZZONE C M,

et al. Extended amygdala to ventral tegmental area corticotropin-releasing factor circuit controls binge ethanol intake[J]. *Biological Psychiatry*, 2017, 81(11): 930-940.

[31] OSTROUMOV A, THOMAS A M, KIMMEY B A, et al. Stress increases ethanol self-administration *via* a shift toward excitatory GABA signaling in the ventral tegmental area[J]. *Neuron*, 2016, 92(2): 493-504.

[32] MARTIN J, TIMOFEEVA E. Intermittent access to sucrose increases sucrose-licking activity and attenuates restraint stress-induced activation of the lateral septum[J]. *American Journal of Physiology Regulatory Integrative and Comparative Physiology*, 2010, 298(5): R1383-R1398.

[33] TRYON M S, STANHOPE K L, EPEL E S, et al. Excessive sugar consumption may be a difficult habit to break: A view from the brain and body[J]. *Journal of Clinical Endocrinology and Metabolism*, 2015, 100(6): 2239-2247.

[34] ULRICH-LAI Y M, CHRISTIANSEN A M, OSTRANDER M M, et al. Pleasurable behaviors reduce stress *via* brain reward pathways[J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2010, 107(47): 20529-20534.

[35] FOSTER M T, WARNE J P, GINSBERG A B, et al. Palatable foods, stress, and energy stores sculpt corticotropin-releasing factor, adrenocorticotropin, and corticosterone concentrations after restraint[J]. *Endocrinology*, 2009, 150(5): 2325-2333.

[36] ULRICH-LAI Y M, OSTRANDER M M, THOMAS I M, et al. Daily limited access to sweetened drink attenuates hypothalamic-pituitary-adrenocortical axis stress responses[J]. *Endocrinology*, 2007, 148(4): 1823-1834.

[37] WANAT M J, HOPF F W, STUBER G D, et al. Corticotropin-releasing factor increases mouse ventral tegmental area dopamine neuron firing through a protein kinase C-dependent enhancement of Ih[J]. *Journal of Physiology*, 2008, 586(8): 2157-2170.

[38] LEMOS J C, WANAT M J, SMITH J S, et al. Severe stress switches CRF action in the nucleus accumbens from appetitive to aversive[J]. *Nature*, 2012, 490(7420): 402-406.

[39] FETISSOV S O, HALLMAN J, ORELAND L, et al. Autoantibodies against alpha-MSH, ACTH, and LHRH in anorexia and bulimia nervosa patients[J]. *Proceedings of the National Academy of Sciences of the United States of America*, 2002, 99(26): 17155-17160.

[40] KRUDE H, BIEBERMANN H, LUCK W, et al. Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans[J]. *Nature Genetics*, 1998, 19(2): 155-157.

[41] GANTZ I, KONDA Y, TASHIRO T, et al. Molecular cloning of a novel melanocortin receptor[J]. *Journal of Biological Chemistry*, 1993, 268(11): 8246-8250.

[42] AL-BARAZANJI K A, MILLER J E, RICE S Q, et al. C-terminal fragments of ACTH stimulate feeding in fasted rats[J]. *Hormone and Metabolic Research*, 2001, 33(8): 480-485.

[43] SCHULZ C, PAULUS K, LOBMANN R, et al. Endogenous ACTH, not only alpha-melanocyte-stimulating hormone, reduces food intake mediated by hypothalamic mechanisms[J]. *American Journal of Physiology Endocrinology and Metabolism*, 2010, 298(2): E237-E244.

[44] SAHIN K, KUCUK O. A simple way to reduce heat stress in laying hens as judged by egg laying, body weight gain and biochemical parameters[J]. *Acta Veterinaria Hungarica*, 2001, 49(4): 421-430.

[45] MANETTI L, CAVAGNINI F, MARTINO E, et al. Effects of cocaine on the hypothalamic-pituitary-adrenal axis[J]. *Journal of Endocrinological Investigation*, 2014, 37(8): 701-708.

[46] 刘 磊. 糖皮质激素在应激家禽食欲调控中的作用机制[D]. 泰安: 山东农业大学, 2014.
LIU L. Mechanism of glucocorticoids regulating appetite in stressed poultry[D]. Tai'an: Shandong Agricultural University, 2014. (in Chinese)

[47] SAVONTAUS E, CONWELL I M, WARDLAW S L. Effects of adrenalectomy on AGRP, POMC, NPY and CART gene expression in the basal hypothalamus of fed and fasted rats[J]. *Brain Research*, 2002, 958(1): 130-138.

[48] KONNO J, YOSHIDA S, INA A, et al. Upregulated expression of neuropeptide Y in hypothalamic-pituitary system of rats by chronic dexamethasone administration[J]. *Neuroscience Research*, 2008, 60(3): 259-265.

[49] SHIMIZU H, ARIMA H, WATANABE M, et al. Glucocorticoids increase neuropeptide Y and agouti-related peptide gene expression *via* adenosine monophosphate-activated protein kinase signaling in the arcuate nucleus of rats[J]. *Endocrinology*, 2008, 149(9): 4544-4553.

[50] KRISTENSSSON E, SUNDQVIST M, ASTIN M, et al. Acute psychological stress raises plasma ghrelin in the rat[J]. *Regulatory Peptides*, 2006, 134(2-3): 114-117.

[51] LUTTER M, SAKATA I, OSBORNE-LAWRENCE S, et al. The orexigenic hormone ghrelin defends against depressive symptoms of chronic stress[J]. *Nature Neuroscience*, 2008, 11(7): 752-753.

[52] OCHI M, TOMINAGA K, TANAKA F, et al. Effect of chronic stress on gastric emptying and plasma ghrelin levels in rats[J]. *Life Sciences*, 2008, 82(15-16): 862-868.

[53] BALSEVICH G, PETRIE G N, HILL M N. Endocannabinoids: Effectors of glucocorticoid signaling[J]. *Frontiers in Neuroendocrinology*, 2017, 47: 86-108.

[54] BARROT M, MARINELLI M, ABROUS D N, et al. The dopaminergic hyper-responsiveness of the shell of the nucleus accumbens is hormone-dependent[J]. *European Journal of Neuroscience*, 2000, 12(3): 973-979.

[55] NAISH K R, LALIBERTE M, MACKILLOP J, et al. Systematic review of the effects of acute stress in binge eating disorder[J]. *European Journal of Neuroscience*, 2018, Epub Ahead of Print.

[56] SOMINSKY L, SPENCER S J. Eating behavior and stress: A pathway to obesity[J]. *Frontiers in Psychology*, 2014, 5: 434.

[57] DALLMAN M F, PECORARO N C, LA FLEUR S E. Chronic stress and comfort foods: Self-medication and abdominal obesity[J]. *Brain, Behavior, and Immunity*, 2005, 19(4): 275-280.

[58] MAKINO S, SCHULKIN J, SMITH M A, et al. Regulation of corticotropin-releasing hormone receptor messenger ribonucleic acid in the rat brain and pituitary by glucocorticoids and stress[J]. *Endocrinology*, 1995, 136(10): 4517-4525.

[59] JEQUIER E. Leptin signaling, adiposity, and energy balance[J]. *Annals of the New York Academy of Sciences*, 2002, 967: 379-388.

[60] UCHOA E T, SILVA L E, DE CASTRO M, et al. Glucocorticoids are required for meal-induced changes in the expression of hypothalamic neuropeptides[J]. *Neuropeptides*, 2012, 46(3): 119-124.

[61] STRACK A M, SEBASTIAN R J, SCHWARTZ M W, et al. Glucocorticoids and insulin: Reciprocal signals for energy balance[J]. *American Journal of Physiology*, 1995, 268(1-2): 142-149.

[62] MARINELLI M, PIAZZA P V. Interaction between glucocorticoid hormones, stress and psychostimulant drugs[J]. *European Journal of Neuroscience*, 2002, 16(3): 387-394.

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