

doi: 10.13241/j.cnki.pmb.2022.10.004

高脂饮食联合光照周期改变对不同性别小鼠体重的影响*

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摘要 目的:随着夜间光照与肥胖现象日趋普遍化,机体内的昼夜节律与生理代谢均受到不同程度的影响,其中不同性别间的差异有待进一步研究。本文旨在通过比较高脂饲料喂养,以及改变光照周期从而对不同性别小鼠体重产生的影响来模拟高脂肪饮食时人类受到夜间光照的性别差异。**方法:**随机选取 C57BL/6 小鼠雌鼠、雄鼠各 12 只,分别按照性别、喂养饲料随机均分成 4 组,其中随机选取一组雌鼠和一组雄鼠喂养 60%高脂饲料作为实验组,另外的一组雌鼠和一组雄鼠喂养普通饲料作为对照组,连续喂养 8 周,观察并记录各组小鼠体重变化;第 1~6 周将实验小鼠置于 24h/0h 光照周期下生活,第 6~8 周实验小鼠生活的光照周期改为 12h/12h。**结果:**在高脂饲料喂养以及光照周期失调(24h/0h)的条件下,雌、雄鼠体重均有增长($P<0.05$),但雄鼠体重增加量是雌鼠的三倍。当光照周期恢复正常(12h/12h)后,雌、雄小鼠体重增长量均下降。不同性别的小鼠食用高脂饲料以及生物节律被打乱时体重均增加,但雄鼠体重增加量明显大于雌鼠,提示同在高脂饲料饮食的条件下,雌鼠受生物节律影响比雄鼠更大。**结论:**高脂饮食实验小鼠模型中雌鼠受生物节律的影响比雄鼠更大。

关键词:高脂饮食;光照周期;体重变化;性别差异

中图分类号:R-332;R151;R493 **文献标识码:**A **文章编号:**1673-6273(2022)10-1817-04

Effects of High Fat Diet Combined with Light Cycle Change on Body Weight of Mice with Different Sex*

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ABSTRACT Objective: With the increasing prevalence of night light and obesity, circadian rhythm and physiological metabolism in the body are affected to varying degrees, and the differences between different genders need to be further studied. The aim of this study was to simulate the sex differences in human exposure to nocturnal light on a high-fat diet by comparing the effects of high-fat diet and photoperiod change on body weight in mice of different genders. **Methods:** Twelve female and male C57BL/6 mice were randomly divided into 4 groups according to sex and feeding diet. One group of female mice and one group of male mice were randomly fed with 60% high-fat diet as the experimental group, and the other group of female mice and one group of male mice were fed with ordinary diet as the control group. The body weight of each group was observed and recorded for 8 weeks. The mice were exposed to 24h/0h light cycle during the 1st to 6th weeks, and the light cycle was changed to 12h/12h during the 6th to 8th weeks. **Results:** The body weight of both male and female rats increased under the condition of high fat diet and irregular light cycle (24h/0h) ($P<0.05$), but the body weight of male rats increased three times as much as that of female rats. After light cycle returning to normal (12h/12h), the amount of mouse body weight increment reduced. Mice of different genders gained weight when they were fed high-fat diet and their biological rhythms were disrupted, but the weight gain of male mice was significantly greater than that of female mice under the condition of high fat diet. **Conclusions:** Female mice were more affected by biorhythm than male mice in the high-fat diet mouse model.

Key words: High fat diet; Circadian rhythms; Weight change; Gender difference

Chinese Library Classification (CLC): R-332; R151; R493 **Document code:** A

Article ID:1673-6273(2022)10-1817-04

前言

构建小鼠高脂模型现已成为实验室常用的方法之一,能模

拟人体疾病的发生发展,为临床治疗提供可靠的参考依据^[1-4]。有大量研究表明,高脂饮食会使小鼠体重增加^[5]。同时,大量研究表示,性别是否影响高脂血症的发病机制仍然存在争议。蒙

* 基金项目:国家自然科学基金青年基金项目(31501913);湖南省自然科学基金项目(No.2020JJ4441);湖南省教育厅重点项目(20A304);

2019 年湖南省大学生创新创业训练计划项目(20191115)

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(收稿日期:2021-07-28 接受日期:2021-08-25)

秀坚等研究表明,男女高血脂症患病率之间,无显著性差异($P>0.05$)^[6]。而安晓兰等研究认为,男性的高血脂症发病率显著高于女性^[7];然而,关于性别是否影响小鼠高脂模型建立的研究较少,刘靖等研究认为性别对实验小鼠高脂血症模型的建立及效果无明显影响^[8]。但 Casimiro I 等研究显示与雌性小鼠相比,雄性小鼠在高脂饲料喂养时体重增加得更早。与正常饮食相比,雄性小鼠保持其热量食物摄入量同时减少运动活性,而雌性小鼠的运动活性在高脂喂养时没有显著变化^[9]。

生物体中存在昼夜节律系统,受环境光照的刺激,与外界昼夜循环周期相适应,从而调控相应的生命活动。如今人们夜间暴露在光照条件下已成为一种普遍现象。据文献报道显示,夜间延长照明时间增加了睡眠障碍和体重指数,提高了高脂血症和肥胖等临床疾病的患病风险^[10,11]。而相关研究表明,夜间照明的增加与小鼠的昼夜节律失调、神经免疫变化^[12]、运动活性改变^[13]、情绪变化、体重增加等有关^[14-17]。

本研究通过构建高脂饲料诱导的动物模型,并辅以昼夜照明改变,观察比较生物节律紊乱情况下,高脂饮食对不同性别小鼠体重的变化的影响。

1 材料与方法

1.1 实验动物及方法

C57BL/6 雌、雄小鼠各 12 只购于湖南斯莱克景达实验动物公司(许可证编号:SYXK(湘)2019-0004),并饲养于湖南师范大学医学院动物房(许可证编号:SYXK(湘)2019-0008)。

C57BL/6 小鼠饲养于具有恒温($21^{\circ}\text{C}\sim 25^{\circ}\text{C}$),恒湿(40%~70%)的 SPF 级动物房(使用许可证编号:SCXK(湘)2019-0008)中,皆自由摄食饮水^[18,19]。将 C57BL/6 雌、雄小鼠按

性别随机分为 4 组,分别为雄鼠对照组(Male-Control Diet, Male-CD)、雄鼠实验组(Male-High Food Diet, Male-HFD)、雌鼠对照组(Female-Control Diet, Female-CD)和雌鼠实验组(Female-High Food Diet, Female-HFD)。对照组和实验组分别喂食普通饲料和高脂饲料(60%脂肪,20%蛋白质和 20%碳水化合物)(MolDiets 公司, M10160),连续喂养 8 周。

第 1~6 周小鼠生活在 24h/0h 光照周期的环境中,第 7~8 周小鼠生活在 12h/12h 光照周期的环境中。每 3 天对小鼠体重进行一次称量。第 8 周结束实验,分析实验数据。

1.2 统计学分析

使用 GraphPad 软件建立数据库,所有数据用平均值 $\pm$ 标准差($\bar{x}\pm s$)表示。比较两组之间的差异,使用 t 检验(和非参数检验)分析; $P<0.05$ 被认为差异具有统计学意义。

2 结果

2.1 高脂饲料喂饲后雌、雄小鼠体重变化差异

将 C57BL/6 雌、雄小鼠按性别随机分组并连续喂养 8 周,建立高脂动物模型,建模流程图见图 1。

本实验比较了小鼠体重与初始体重的增长量之间的差异。由图 2A 可见,喂饲正常饲料的雄鼠和雌鼠两组体重无明显变化($P>0.05$),基本呈直线水平;相较于喂饲正常饲料的对照组,高脂饮食喂养中雌鼠和雄鼠的体重均有不同程度的增加,且雄鼠体重增加量是雌鼠的三倍。由图 2B 可见,在两组雄性小鼠中,相较于喂饲普通饲料的对照组,喂饲高脂饲料的实验组小鼠体重呈持续上升的趋势($P<0.05$),且升高显著、稳定。由图 2C 可见,在两组雌性小鼠中,与对照组相比,喂饲高脂饲料的实验组体重基本呈持续升高趋势($P<0.05$)。

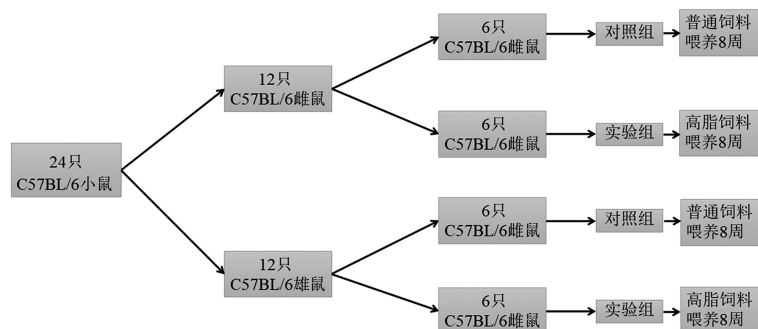


图 1 高脂动物建模流程图

Fig.1 Flowchart of high-fat animals modeling

2.2 光照周期改变对小鼠体重增长量有影响

在建立高脂模型的同时,本研究探讨了光照周期对小鼠体重的影响。在第 1~6 周,小鼠的光照周期为 24h/0h,而在第 7~8 周小鼠的光照周期则改为 12h/12h,其光照实验流程图见图 3。

本实验比较光照周期失调前后对各组小鼠体重增长量的影响。由图 4 可知,在喂养普通饲料的条件下,与 CD(24h/0h)组相比,CD(12h/12h)组的体重增加量减少,雄性小鼠的体重减重量更大($P=0.07$),且雌性、雄性小鼠无明显差异。在高脂饲料喂养以及光照周期失调(24h/0h)的条件下,雌、雄鼠体重均有增长($P<0.05$)。然而,喂食高脂饮食的雌鼠和雄鼠,在光照周

期恢复正常(12h/12h)后,雄性小鼠体重增长量呈现缓和趋势,而雌性小鼠体重继续呈上升趋势(相比于 HFD(24h/0h)组, $P<0.001$)。

从实验结果中可见:食用高脂饲料以及打乱生物节律均会使体重增加,且雌鼠受生物节律影响比雄鼠更大;且从另一面说明,食用高脂饮食对小鼠体重的影响大于生物节律紊乱的影响。

3 讨论

随着现代生活方式的改变,人们对高脂肪食物的摄入量也

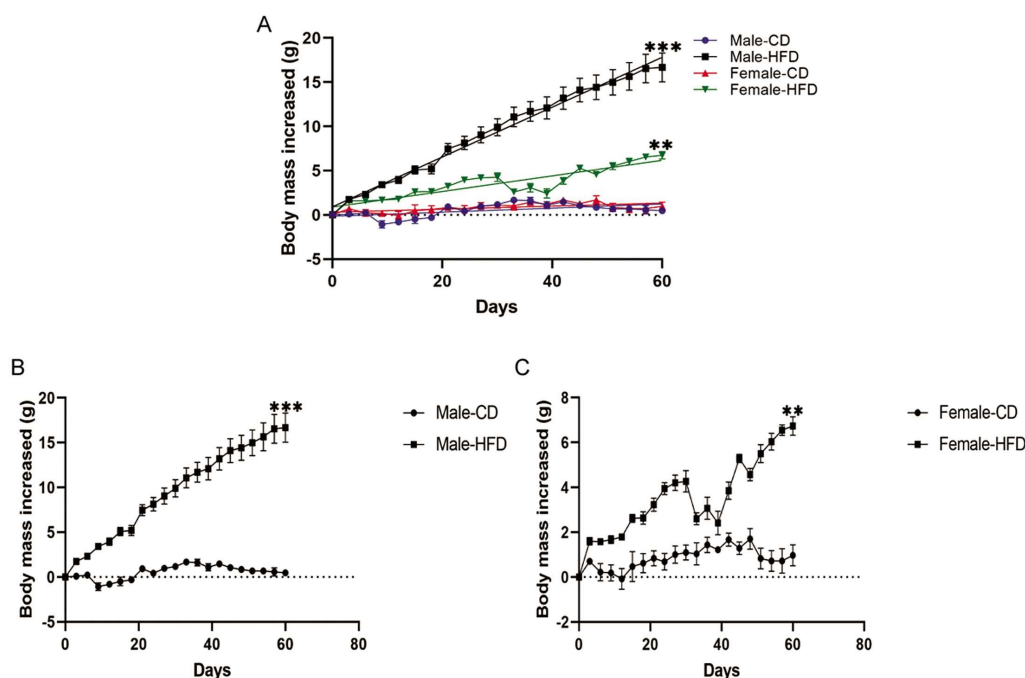


图2 各组小鼠体重增长量的动态变化

Fig.2 Dynamic changes in the body mass increased of mice in each group

(A) The change curve of the body mass increased of mice in all groups. (B) Comparison of the body mass increased between the control group and the experimental group of male mice. (C) Comparison of the body mass increased between the control group and the experimental group of female mice.

: $P < 0.01$ vs. Male-CD; *: $P < 0.001$ vs. Female-CD.

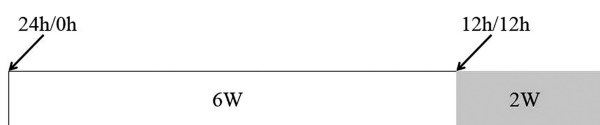


图3 光照实验流程图

Fig.3 Flow chart of illumination experiment

逐渐增加,肥胖人数也日益增加。高脂饮食(HFDs)导致的肥胖症会扰乱机体正常生理代谢,引起相应的代谢类疾病,如脂肪肝、高脂血症、II型糖尿病和动脉粥样硬化等疾病,严重影响人类健康^[20]。为向临床提供更精准的诊断、治疗和预防机制,建立高脂饮食诱导的动物模型是研究高脂饮食引起相关代谢类疾病过程中不可缺少的重要手段。我们选用高脂饲料喂养对肥胖易感的 C57BL/6 小鼠以构建高脂饮食实验动物模型,并着重研究性别因素的差异,旨在模拟性别在人类高脂饮食相关临床疾病中的差异以达到个性化治疗,同时为动物实验中受光照改变而影响数据准确性的现象提供一定参考性。通过比较连续 8 周高脂饮食对雌、雄小鼠体重变化差异的影响,研究结果表明:给予高脂饮食后,不同性别小鼠的体重均有增加,并且与雌性小鼠相比,雄性小鼠体重增加更加稳定和明显。此结果与临床研究报告中,男性的高血脂症发病率显著高于女性的结论相一致。

地球在围绕太阳和地轴旋转时每日产生的昼夜变化,被称为光/暗循环。地球上的生物为适应光/暗循环体内产生了生物钟系统,使内分泌系统活动、睡眠-觉醒周期等生理活动与光照变化同步。以人类为例,位于视网膜的感光神经节细胞在感受到外界传来的光信号时,会将其传递给下丘脑视交叉上核(SCN)^[21]。而 SCN 作为内源性生物钟系统的中枢,根据外源性光信号的强弱控制分子水平的时钟基因,而时钟基因表达变化

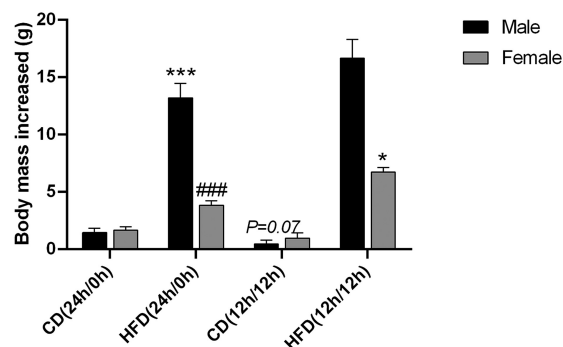


图4 光照周期改变前后各组小鼠体重增长量变化

Fig.4 Changes in body mass increased of mice in each group before and after the change of light cycle; ***: $P < 0.001$ vs. Male-CD(24h/0h);

###: $P < 0.001$ vs. Female-CD(24h/0h);

* $P < 0.001$ vs. Female-HFD(24h/0h).

通过神经-体液途径来控制外周器官组织、细胞的生理功能和维持相对稳态。经典的时钟基因主要包括昼夜节律运动输出周期故障基因(昼夜节律运动输出周期 kaput, clock)、脑和肌肉组织芳香烃受体核转运蛋白的类似蛋白 1 基因(brain and muscle ARNT-like 1, bmal1)^[22]。clock 与 bmal1 时钟基因转录并形成 CLOCK-BMAL1 异二聚体,激活 per、cry 基因并转录形成 PER-CRY 蛋白二聚体,两组基因形成负反馈回路来调控相应的生理代谢^[23,24]。

饮食与昼夜节律有着双向的影响。高热量食物摄入和昼夜节律紊乱都可能导致食物摄入时间的改变,高脂饮食改变了机体对有助于同步与衔接中枢与外部组织昼夜时钟的光线信号的反应,从而钝化进食/禁食周期,对啮齿动物的昼夜节律造

成有害的影响^[25]。当外界环境光照周期改变时,也会相应地引起机体昼夜节律紊乱,进而影响机体新陈代谢,导致能量代谢失调,但在去除夜间光照的影响时,又可逆转代谢失调^[26,27]。本研究中,小鼠恢复明暗交替后,体重增加呈现缓和趋势,但高脂的摄入基本无法改变体重增加。其机制可能与高脂饮食与夜间光照共同影响昼夜节律,从而使得作为生物钟系统中枢的 SCN 与其下游的外周器官组织生物节律缺乏相对校准所致体重增加明显^[13];当外周光照恢复正常后,其生物节律受到影响相对较小,体重增加量较平缓。

随着现代电力系统的不断强大、夜间人造照明的普及化,夜间过度光照对人类健康有一定的影响。据文献报道,夜间光照与体重增加^[28]、心脏病和癌症的患病率增加有关^[29-31]。本实验在构建高脂动物模型的同时,研究光照周期改变对不同性别小鼠体重增长的影响,旨在模拟光照周期改变对人类高脂相关代谢类疾病的影响及性别差异,为指导临床治疗高脂代谢类疾病中光照的影响提供理论机制。研究结果表明,夜间暴露于光照下改变机体生物昼夜节律后,会增加小鼠体重,而且与雄鼠相比,雌鼠更易受此生物节律的影响,其机制可能与雌激素相关^[32-34]。因此,我们推测:雌性动物受光照改变的影响多于雄性,尤其是在高脂饮食引起体重增加及代谢类临床疾病中显著体现。

综上所述,建立高脂饮食动物模型时,喂食 8 周后高脂饲料对小鼠体重的影响性别差异不明显,但使用雄鼠进行构建模型与实验时,更易获得明显、稳定的实验结果。同时,夜间光照时间的延长影响了昼夜节律,导致小鼠体重增加,而雌鼠对此生物节律的改变更为敏感,更易受其影响。

参考文献(References)

- [1] 刁婷婷, 闵清. 高脂血症动物模型研究进展 [J]. 湖北科技学院学报 (医学版), 2018, 32(06): 541-545
- [2] 司原成, 苗维娜. 肥胖动物模型选择的研究进展 [J]. 湖南中医杂志, 2016, 32(09): 200-201
- [3] 潘磊, 张金彪, 崔荣岗, 等. 非酒精性脂肪肝 C57BL/6 小鼠模型的建立[J]. 中国组织工程研究, 2016, 20(40): 6054-6059
- [4] 董明, 刘东, 梁运海, 等. 高脂饮食喂养肥胖模型小鼠的构建: 分析营养因素和代谢综合征的关系 [J]. 中国组织工程研究, 2015, 19(40): 6542-6546
- [5] 崔莉, 陈爱群, 庞婧, 等. 高脂饮食影响小鼠体内能量代谢的性别差异[J]. 山西医科大学学报, 2017, 48(07): 658-664
- [6] 蒙秀坚, 何启亮, 周梓婷. 健康体检中高脂血症发病情况与风险管理模式分析[J]. 临床合理用药杂志, 2020, 13(21): 15-18
- [7] 安晓兰. 脂肪肝和高血脂与性别及年龄的相关分析 [J]. 甘肃科技, 2018, 34(24): 156-157
- [8] 刘靖, 陆大祥, 戚仁斌, 等. 性别对小鼠高脂血症动物模型的影响 [J]. 中国比较医学杂志, 2010, 20(09): 16-18
- [9] Casimiro I, Stull N D, Tersey S A, et al. Phenotypic sexual dimorphism in response to dietary fat manipulation in C57BL/6J mice [J]. J Diabetes Complications, 2021, 35(2): 107795
- [10] Fonken L K, Aubrecht T G, Melendez-Fernandez O H, et al. Dim light at night disrupts molecular circadian rhythms and increases body weight[J]. J Biol Rhythms, 2013, 28(4): 262-271
- [11] Wyse C A, Selman C, Page M M, et al. Circadian desynchrony and metabolic dysfunction; did light pollution make us fat? [J]. Med Hypotheses, 2011, 77(6): 1139-1144
- [12] Chen R, Weitzner A S, McKennon L A, et al. Light at night during development in mice has modest effects on adulthood behavior and neuroimmune activation[J]. Behav Brain Res, 2021, 405: 113171
- [13] Maroni M J, Capri K M, Arruda N L, et al. Substrain specific behavioral responses in male C57BL/6N and C57BL/6J mice to a shortened 21-hour day and high-fat diet [J]. Chronobiol Int, 2020, 37(6): 809-823
- [14] An K, Zhao H, Miao Y, et al. A circadian rhythm-gated subcortical pathway for nighttime-light-induced depressive-like behaviors in mice[J]. Nat Neurosci, 2020, 23(7): 869-880
- [15] Cleary-Gaffney M, Coogan A N. Limited evidence for affective and diurnal rhythm responses to dim light-at-night in male and female C57BL/6 mice[J]. Physiol Behav, 2018, 189: 78-85
- [16] Aubrecht T G, Jenkins R, Nelson R J. Dim light at night increases body mass of female mice[J]. Chronobiol Int, 2015, 32(4): 557-60
- [17] Emmer K M, Russart K L G, Walker W H, et al. Effects of light at night on laboratory animals and research outcomes[J]. Behav Neurosci, 2018, 132(4): 302-314
- [18] 孙奥, 马玉兰, 胡晓琴, 等. C57BL/6 小鼠在肥胖建模过程中常见问题及处理对策[J]. 实验动物科学, 2020, 37(01): 61-65
- [19] 蔡琳琳. SPF 级实验动物房的设计与建设研究 [J]. 科技与企业, 2015, 19: 237+9
- [20] Conway B, Rene A. Obesity as a disease: no lightweight matter[J]. Obes Rev, 2004, 5(3): 145-151
- [21] Buijs R M, Soto Tinoco E C, Hurtado Alvarado G, et al. The circadian system: From clocks to physiology[J]. Handb Clin Neurol, 2021, 179: 233-247
- [22] Pan X, Mota S, Zhang B. Circadian Clock Regulation on Lipid Metabolism and Metabolic Diseases[J]. Adv Exp Med Biol, 2020, 1276: 53-66
- [23] Cox K H, Takahashi J S. Circadian clock genes and the transcriptional architecture of the clock mechanism[J]. J Mol Endocrinol, 2019, 63(4): R93-R102
- [24] 徐晴, 付波, 杨丹凤, 等. 昼夜节律紊乱的小分子调节剂研究进展 [J]. 国际药学研究杂志, 2020, 47(01): 1-7
- [25] Potter G D, Cade J E, Grant P J, et al. Nutrition and the circadian system[J]. Br J Nutr, 2016, 116(3): 434-442
- [26] Borniger J C, Maurya S K, Periasamy M, et al. Acute dim light at night increases body mass, alters metabolism, and shifts core body temperature circadian rhythms[J]. Chronobiol Int, 2014, 31(8): 917-925
- [27] Obayashi K, Sacki K, Iwamoto J, et al. Exposure to light at night, nocturnal urinary melatonin excretion, and obesity/dyslipidemia in the elderly: a cross-sectional analysis of the HEIJO-KYO study [J]. J Clin Endocrinol Metab, 2013, 98(1): 337-44
- [28] Rybnikova N A, Haim A, Portnov B A. Does artificial light-at-night exposure contribute to the worldwide obesity pandemic? [J]. Int J Obes (Lond), 2016, 40(5): 815-23
- [29] Szkiela M, Kusidel E, Makowiec-Dabrowska T, et al. Night Shift Work-A Risk Factor for Breast Cancer [J]. Int J Environ Res Public Health, 2020, 17(2)

- [12] Bekelman DB, Allen LA, McBryde CF, et al. Effect of a Collaborative Care Intervention vs Usual Care on Health Status of Patients With Chronic Heart Failure: The CASA Randomized Clinical Trial[J]. *JAMA Intern Med*, 2018, 178(4): 511-519
- [13] 李世军. 老年心力衰竭流行病学和病理生理学及预后的研究进展[J]. *中华老年心脑血管病杂志*, 2021, 23(3): 318-320
- [14] Vongmany J, Hickman LD, Lewis J, et al. Anxiety in chronic heart failure and the risk of increased hospitalisations and mortality: A systematic review[J]. *Eur J Cardiovasc Nurs*, 2016, 15(7): 478-485
- [15] Lossnitzer N, Feisst M, Wild B, et al. Cross-lagged analyses of the bidirectional relationship between depression and markers of chronic heart failure[J]. *Depress Anxiety*, 2020, 37(9): 898-907
- [16] Eisele M, Harder M, Rakebrandt A, et al. Association of depression and anxiety with adherence in primary care patients with heart failure-cross-sectional results of the observational RECODE-HF cohort study[J]. *Fam Pract*, 2020, 37(5): 695-702
- [17] Mazaheri R, Schmied C, Niederseer D, et al. Cardiopulmonary Exercise Test Parameters in Athletic Population: A Review[J]. *J Clin Med*, 2021, 10(21): 5073
- [18] Mitchell RA, Apperley ST, Dhillon SS, et al. Case Studies in Physiology: Cardiopulmonary exercise testing and inspiratory muscle training in a 59-year-old, 4 years after an extrapleural pneumonectomy[J]. *J Appl Physiol* (1985), 2021, 131(6): 1701-1707
- [19] 俞连芳, 丁彩华, 马云云. 老年慢性心力衰竭患者述情障碍对其正负性情绪的影响[J]. *浙江临床医学*, 2019, 21(6): 817-819
- [20] Dellafore F, Chung ML, Alvaro R, et al. The Association Between Mutuality, Anxiety, and Depression in Heart Failure Patient-Caregiver Dyads: An Actor-Partner Interdependence Model Analysis [J]. *J Cardiovasc Nurs*, 2019, 34(6): 465-473
- [21] Müller-Tasch T, Löwe B, Lossnitzer N, et al. Anxiety and self-care behaviour in patients with chronic systolic heart failure: A multivariate model[J]. *Eur J Cardiovasc Nurs*, 2018, 17(2): 170-177
- [22] Petruzzo A, Biagioli V, Durante A, et al. Influence of preparedness on anxiety, depression, and quality of life in caregivers of heart failure patients: Testing a model of path analysis [J]. *Patient Educ Couns*, 2019, 102(5): 1021-1028
- [23] Sala L, Gorwood P, Vindreau C, et al. Mindfulness-based cognitive therapy added to usual care improves eating behaviors in patients with bulimia nervosa and binge eating disorder by decreasing the cognitive load of words related to body shape, weight, and food [J]. *Eur Psychiatry*, 2021, 64(1): e67
- [24] 潘洁丽, 吕靖. 正念减压疗法对慢性心力衰竭患者疲乏状况及睡眠质量的影响[J]. *医学临床研究*, 2021, 38(3): 449-452
- [25] 魏双, 王家宁, 何琼, 等. 个体化心脏运动康复训练对慢性稳定型心力衰竭病人心肺功能及生活质量的影响[J]. *中西医结合心脑血管病杂志*, 2019, 17(20): 3159-3161
- [26] 沈玉芹, 倪奕, 王乐民, 等. 峰值氧耗量和无氧代谢阈值对慢性心力衰竭患者预后的预测价值 [J]. *中华老年多器官疾病杂志*, 2015, 5(3): 179-183
- [27] 刘永选, 王彩虹. 基于基础疗法的芪苈强心胶囊综合用药对慢性充血性心力衰竭患者 HR、LVEF、LVEDD 水平的影响 [J]. *世界中医药*, 2019, 14(2): 442-445
- [28] 王子健, 肖鹏, 杨冬林. 正念认知疗法对抑郁症患者心理状态和生活质量的干预效果评价[J]. *中国健康教育*, 2021, 37(9): 850-853
- [29] Sheikhzadeh M, Zanjani Z, Baari A. Efficacy of Mindfulness-Based Cognitive Therapy and Cognitive Behavioral Therapy for Anxiety, Depression, and Fatigue in Cancer Patients: A Randomized Clinical Trial[J]. *Iran J Psychiatry*, 2021, 16(3): 271-280
- [30] Wang Y, Fu C, Liu Y, et al. A study on the effects of mindfulness-based cognitive therapy and loving-kindness meditation on depression, rumination, mindfulness level and quality of life in depressed patients [J]. *Am J Transl Res*, 2021, 13(5): 4666-4675
- [31] Li J, Cai Z, Li X, et al. Mindfulness-based therapy versus cognitive behavioral therapy for people with anxiety symptoms: a systematic review and meta-analysis of random controlled trials [J]. *Ann Palliat Med*, 2021, 10(7): 7596-7612
- [32] Docteur A, Gorwood P, Mirabel-Sarron C, et al. Mindfulness-based cognitive therapy efficacy in reducing physiological response to emotional stimuli in patients with bipolar I disorder and the intermediate role of cognitive reactivity [J]. *J Clin Psychol*, 2021, 77(11): 2442-2454

(上接第 1820 页)

- [30] Garcia-Saenz A, Sanchez De Miguel A, Espinosa A, et al. Evaluating the Association between Artificial Light-at-Night Exposure and Breast and Prostate Cancer Risk in Spain (MCC-Spain Study) [J]. *Environ Health Perspect*, 2018, 126(4): 047011
- [31] Erren T C, Lewis P. Hypothesis: ubiquitous circadian disruption can cause cancer[J]. *Eur J Epidemiol*, 2019, 34(1): 1-4
- [32] Chen F, Yu H, Zhang H, et al. Estrogen normalizes maternal HFD-induced cardiac hypertrophy in offspring by regulating AT2R [J]. *J Endocrinol*, 2021, 250(1): 1-12
- [33] Krizo J A, Mintz E M. Sex differences in behavioral circadian rhythms in laboratory rodents [J]. *Front Endocrinol (Lausanne)*, 2014, 5(234)
- [34] Blattnner M S, Mahoney M M. Estrogen receptor 1 modulates circadian rhythms in adult female mice [J]. *Chronobiol Int*, 2014, 31(5): 637-44