

综述

八段锦可能通过调控*Bmal1*基因改善2型糖尿病患者的睡眠质量

董子萱, 马占科*

宁夏师范大学体育学院, 固原 756099

摘要: 糖尿病的发病率不断上升, 而糖尿病患者的睡眠质量通常会受到影响。八段锦可能通过调控*Bmal1*基因表达作用于机体生物节律、骨骼肌糖代谢、骨骼肌纤维以及视交叉上核(suprachiasmatic nucleus, SCN)脑区, 对2型糖尿病(type 2 diabetes mellitus, T2DM)患者的血糖水平和昼夜节律进行调节, 并改善T2DM患者的各项生理机能。本文综述八段锦对糖尿病患者*Bmal1*基因表达调控作用及机制, 探讨八段锦通过调控*Bmal1*基因表达改善T2DM患者睡眠质量的可能性。本综述可为中国传统气功八段锦的临床应用提供新的领域, 为糖尿病的运动疗法提供新的科学依据。

关键词: 八段锦; *Bmal1*; 糖尿病; 睡眠质量

Baduanjin improves sleep quality in patients with type 2 diabetes possibly via regulating *Bmal1* gene

DONG Zi-Xuan, MA Zhan-Kc*

Institute of Physical Education, Ningxia Normal University, Guyuan 756099, China

Abstract: The incidence of diabetes mellitus is increasing, and the sleep quality of patients with diabetes mellitus is often affected. Baduanjin may act on biological rhythm of the body, skeletal muscle glucose metabolism, skeletal muscle fibers and suprachiasmatic nucleus (SCN) by regulating the expression of *Bmal1* gene, thus regulating the blood glucose level and circadian rhythm of patients with type 2 diabetes mellitus (T2DM) and improving their physiological functions. This article reviews the regulatory effect and mechanism of Baduanjin on *Bmal1* gene expression in diabetes patients, and discusses the possibility of Baduanjin to improve the sleep quality of T2DM patients by regulating *Bmal1* gene expression. This review can provide a new field for the clinical application of traditional Chinese Qigong Baduanjin, and provide a new scientific basis for exercise therapy of diabetes.

Key words: Baduanjin; *Bmal1*; diabetes mellitus; sleep quality

随着生活水平的提高, 糖尿病患者数量逐年增加, 其发病风险、进展速度和危害性明显增加^[1]。糖尿病是一组多病因引起的以慢性高血糖为特征的代谢性疾病, 由胰岛素分泌和(或)作用缺陷所引起, 其中2型糖尿病(type 2 diabetes mellitus, T2DM)是一种常见的代谢综合征^[2]。目前, T2DM是发病率较高的慢性疾病之一, 引发该病的因素包括胰岛素因素、遗传因素和基础代谢因素等^[3]。随着病情的恶化, T2DM可能会导致视力模糊、糖尿病足等多

种并发症, 并增加心脑血管疾病的风险。研究表明, 糖尿病患者还易出现昼夜节律紊乱, 睡眠质量受影响^[4, 5]。睡眠质量是评估身体健康的重要标准, 也是反映患者治疗效果和疾病预后的重要指标。研究显示, T2DM患者的睡眠质量与心血管疾病发生的风险密切相关^[6]。睡眠障碍是T2DM患者的常见症状, 会导致生活质量下降、身体素质变差、并发症增多。研究表明, T2DM患者的睡眠障碍会导致胰岛素抵抗和糖脂代谢异常, 增加心血管疾病患

This work was supported by the Scientific Research Project of Higher Education Department of Ningxia Hui Autonomous Region, China (No. NYG2024171).

*Corresponding author. E-mail: 82001014@nxnu.edu.cn

的风险, 同时也会通过多种途径影响糖代谢和脂代谢^[7]。因此, 改善睡眠质量对于 T2DM 患者具有重要意义。

研究表明, 脑和肌肉芳香烃受体核转位蛋白样 1 (brain and muscle aryl hydrocarbon receptor nuclear translocator-like protein 1, *Bmal1*) 基因是调节机体能量代谢的重要基因, 可以通过多种途径影响 T2DM 患者的代谢状态。Gao 等^[8]研究显示, *Bmal1* 基因突变与 T2DM 患者的糖脂代谢紊乱有关, 但与空腹血糖水平无关, 提示 *Bmal1* 基因可能通过影响胰岛素分泌和骨骼肌胰岛素抵抗参与 T2DM 患者的血糖调控。此外, 研究表明, *Bmal1* 基因突变还可能增加多种疾病的风险, 包括心脑血管疾病、血脂异常、肾脏疾病和神经系统病变等^[9]。当前, 有许多研究聚焦如何改善 T2DM 患者的睡眠质量, 但对于八段锦调控 *Bmal1* 基因表达, 改善 T2DM 患者的睡眠质量的分子机制尚未明确阐述。本综述通过总结整理国内外最新文献, 梳理 *Bmal1* 对 T2DM 患者睡眠质量作用的机制, 探讨八段锦通过调控 *Bmal1* 基因表达改善 T2DM 患者睡眠质量的可能性, 为八段锦改善 T2DM 患者睡眠质量的靶点筛选提供有价值的参考。

1 *Bmal1* 基因在改善 T2DM 患者睡眠质量的研究概况

机体内存在着一种被生物钟调控的昼夜节律, 使机体可以适应生存环境的改变。研究表明, 生物钟与太阳的周期变化和物质代谢有关, 需要机体与其保持同步^[10]。血糖在物质和能量代谢过程中扮演着重要角色。血糖水平与生物钟基因的表达密切相关, 生物钟基因的异常会影响胰岛素分泌和昼夜节律。因此, 生物钟昼夜节律紊乱是导致糖尿病的一个重要因素。生物钟是一种高度专门化、分层的生物起搏器网络, 可以引导并维持有机体在多个方面的稳态, 同时也可以受到诸如光、食物和温度之类的外部信号刺激^[11, 12]。研究表明, 生物钟的主要作用是对外部环境的每日变化进行预测, 从而保持内稳态的稳定, 并对波动的环境作出恰当的生理反应, 例如基因表达、睡眠觉醒、激素合成、能量代谢、免疫调节以及细胞因子释放等^[13–15]。这些生物节律的具体分类包括年周期、季节周期、月周期和昼夜周期等。研究表明, 昼夜节律的调控是通过生物钟分子完成的, 这些分子由时钟基因编码, 对机体能

否保持各器官的协调有序运转具有重要意义^[16–18]。

时钟基因包括 *Bmal1* 基因、生物钟循环输出蛋白 (circadian locomotor output cycle kaput, *Clock*)、周期基因 1 (Period 1, *Per1*)、周期基因 2 (Period 2, *Per2*)、周期基因 3 (Period 3, *Per3*)、隐色素基因 1 (Cryptochrome 1, *Cry1*)、隐色素基因 2 (Cryptochrome 2, *Cry2*)、酪蛋白激酶 1ε (casein kinase 1 ε, *CK1ε*)、*NPAS2* (neuronal PAS domain protein 2)、*TIM* (Timeless)、*DEC1* (differentially expressed in chondrocyte 1)、*DEC2* (differentially expressed in chondrocyte 2)、*Rev-erba* 等^[19]。在人体中, 时钟基因的最核心元素是 *Clock* 和 *Bmal1* 基因。这些基因调控着许多生理活动, 包括睡眠 - 觉醒周期、糖代谢、胰岛素分泌、学习记忆等^[20]。*Bmal1* 是结构域转录因子 bHLH-PAS (basic helix-loop-helix-per-arrnt-sim) 的其中一种, 表达于脑、心、肝、肾等多个组织中, 并在生物钟调节中扮演着重要角色。*Bmal1* 与 *Clock* 协同作用, 共同作为活化因子来调控昼夜节律^[21]。*Bmal1* 与 *Clock* 形成二聚体, 并与 E-box 蛋白相互作用, 形成转录 - 翻译反馈环路, 随后在细胞核内激活 *PERs* 和 *CRYs*, 并使其进行转录翻译, 形成一条周期为 24 h 的“转录 - 翻译 - 翻译后反馈抑制”的负反馈环路^[22]。在 *Bmal1* 和 *Clock* 的共同调控下, 时钟基因进行转录和节律性表达, 此过程称为时钟控制基因 (clock controlled genes) 的转录表达^[23](图 1)。

2 八段锦改善 T2DM 患者睡眠质量的研究概况

八段锦是源于我国的一种古老的导引术功法, 因其能增强体质, 且招式简单, 易于上手, 所以在民间广为流传, 历经数千年, 成为我国健康养生文化的瑰宝。八段锦属于一种灵活和刚柔相济的健身养生方法, 强调“练身、练气、练意”, 用身体的动作来配合自己的呼吸, 而在练习健身气功中, 调息是必不可少的一部分, 调息是指在意念的引导下, 通过膈肌上下摆动和腹部起伏对腹部的肠胃、肝胆、肾脏、膀胱等器官进行按摩, 提高消化、排泄、生殖系统的功能, 抑制大脑兴奋和外周交感神经活动, 从而使人达到一种宁静的状态。长期练习八段锦, 可以调节情绪, 促进心理健康^[24]。运动疗法作为一种重要的治疗方式, 在糖尿病患者的治疗中起到了积极的作用。运动是目前国际上公认的改善脂质代谢的有效手段^[25]。八段锦对糖尿病患者的血液循环

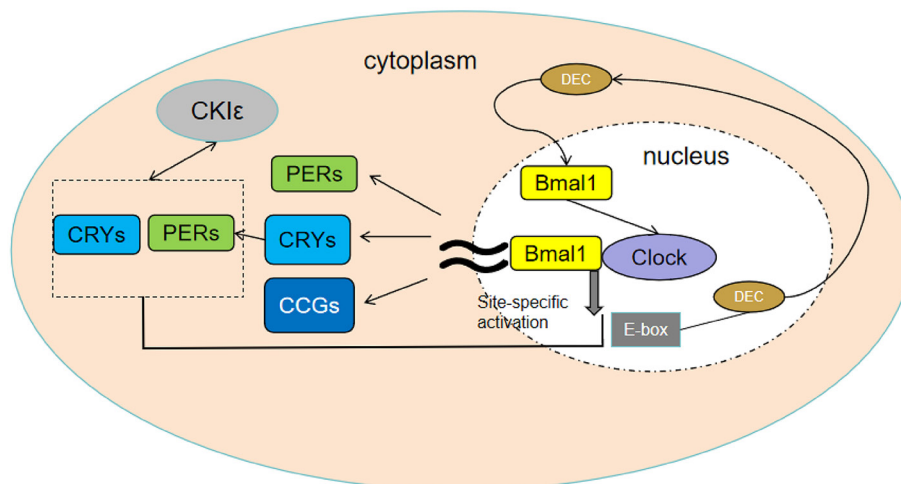


图 1. *Bmal1*基因正负反馈环路示意图

Fig. 1. Schematic diagram of positive and negative feedback loops of *Bmal1* gene. Bmal1 and Clock form dimers and interacts with E-box protein, forming a transcription and translation feedback loop. PERs and CRYs in the cell nucleus are activated, bind to CK1ε to form a complex, and form “transcription-translation-suppression” negative feedback loop, with a cycle for 24 h. On the other hand, Bmal1 regulates the transcription of other target genes in the E-box region to form CCGs (clock controlled genes) with Clock. At the same time, DEC acts on Bmal1 and Clock, regulating energy metabolism at the level of cells, tissues and organisms, and enriching the regulatory network of life activity metabolism. CRYs, Cryptochromes; PERs, Periods; CK1ε, casein kinase 1 ε; DEC, differentially expressed in chondrocyte.

有一定的促进作用，有助于提高人体的代谢能力，进而调控机体的糖脂代谢水平以及昼夜节律^[24]。T2DM 老年患者通过社区管理下八段锦锻炼，可有效改善血糖水平及心理状态^[26]。研究显示，长期练习八段锦能有效提高睡眠时长并改善睡眠质量^[27, 28]，同时在运动过程中对机体的自我控制可起到宁心静神的效果，有利于提升自身整体心理健康、调整情绪^[29-31]。研究表明，八段锦可有效改善各种人群的心理健康状况，减少焦虑，缓解抑郁，提升情绪调节的能力^[24, 32-34]，同时可提高 T2DM 患者睡眠质量^[35]。

在练习形神合一的过程中，八段锦可调节机体生理机能，刺激大脑皮质，对中枢神经系统进行调控，改善下丘脑垂体功能，进而改善胰岛β细胞功能，达到降低血糖的作用^[36, 37]，并减弱在下丘脑内的视交叉上核 (suprachiasmatic nucleus, SCN) 附近的昼夜节律振荡器的控制，对昼夜节律进行调控，减弱患者时钟控制中 *Bmal1* 和 *Per2* 的表达信号，从而达到改善患者睡眠质量的作用^[38]。随着身体运动时间的延长，机体保持动态平衡时，糖异生作用会持续增强，从而避免低血糖的发生，逐步使机体适应运动，改善机体血糖水平^[39, 40]。在练习八段锦这种

平稳、舒缓的运动过程中，血糖和代谢水平逐渐稳定，机体各项功能逐渐恢复到正常水平，从而调节 T2DM 患者昼夜节律，改善睡眠质量^[41]。

3 八段锦可能通过上调*Bmal1*基因表达改善 T2DM 患者睡眠质量

3.1 *Bmal1*基因上调通过调控生物昼夜节律改善睡眠质量

Bmal1 基因是生物钟的核心基因，它可以通过在多器官组织中产生作用，形成一条“转录 - 翻译”的反馈环路，参与调控机体的生物节律，干预机体睡眠质量^[18]。Tahara 等人^[42] 研究显示，运动可调控生物昼夜节律，参与调控机体的昼夜节律紊乱，并改善睡眠质量。近年来研究聚焦于运动对 *Bmal1* 基因的调控。研究显示，昼夜节律紊乱和睡眠障碍是导致慢性代谢性疾病患病率显著增加的危险因素，而这些疾病都与 *Bmal1* 基因异常表达有关^[43, 44]。对于 T2DM 患者而言，由于血糖水平发生异常，*Bmal1* 在调节糖脂代谢的过程中也会异常表达^[45]，造成机体的糖脂代谢紊乱，并进一步影响机体的生物节律，从而影响 T2DM 患者的睡眠质量。研究显示，运动可通过上调 *Bmal1* 表达调整生物节律，从

而改善生物钟昼夜节律异常和相关的代谢疾病^[46]。*Bmal1* 与 *Clock* 的共同作用可有效提高机体的糖脂代谢率^[47], 并调控机体内的胰岛素敏感性, 进而改善糖尿病患者的血糖水平^[48]。研究显示, 上调 T2DM 患者 *Bmal1* 基因表达可调整昼夜节律, 提高机体糖脂代谢, 同时增加机体对胰岛素的敏感性, 从而降低血糖水平, 改善患者睡眠质量^[49]。在机体正常血糖水平下, *Bmal1* 基因也可维持 T2DM 患者的正常生物节律, 改善睡眠质量^[50]。

Bmal1 基因表达和转录在调节 T2DM 患者的血糖水平和昼夜节律方面扮演着关键的角色。研究显示, 运动强度可对 *Bmal1* 基因表达造成影响, 适宜强度的运动可刺激 *Bmal1* 基因表达上调^[51], 提示八段锦这种低强度的有氧运动可能激活 *Bmal1* 基因, 调节人体生物节律, 当 *Bmal1* 基因表达水平上调后, 昼夜节律将更加趋于稳定, 有助于 T2DM 糖尿病患者维持血糖水平, 从而达到改善睡眠质量的的目的。因此, 我们推断八段锦可能上调 *Bmal1* 表达水平, 从而调控生物节律, 改善糖尿病患者的血糖水平和睡眠质量, 这需要进行进一步的研究来验证。

3.2 八段锦上调*Bmal1*基因表达, 调控骨骼肌糖代谢

T2DM 是一种慢性疾病, 易发多种并发症, 如视网膜病变、神经系统紊乱、心血管系统疾病、骨钙代谢紊乱、骨密度降低等, 患者容易产生消极的情感, 如焦虑、抑郁、恐惧、孤独等^[52, 53]。研究表明, 适当的运动可以缓解压力, 提高大脑神经系统的功能, 让患者在心理上产生充实感和满足感, 减轻压力, 增强心理承受能力, 增强自制力、记忆力和创造力等^[54-56]。运动反射性会引起大脑皮层和丘脑、下丘脑部位的兴奋性增加, 而下丘脑是调节内脏、内分泌活动的较高级中枢, 也可调节躯体活动。运动可提高骨骼肌对胰岛素的敏感性, 促进肝糖原的分解, 并促进末梢组织对糖的利用, 从而降低血糖^[57]。同时, 运动可促进局部血液流动, 提高胰岛素和肌细胞膜上受体的结合强度^[58], 改善血糖代谢。

运动可增强脂蛋白酶的活性, 加速脂肪分解速度, 促进脂肪和胆固醇游离脂肪酸的利用, 以弥补能量供应不足^[59]。运动可以改善焦虑情绪, 提高 1 型糖尿病患者对胰岛素的敏感性, 同时促进脂肪和胆固醇游离脂肪酸的利用^[60]。对于 T2DM 患者, 运动对情绪和睡眠质量的积极影响, 使其可能成有效治疗手段。八段锦作为一种中国传统的气功功法,

属于低强度的有氧运动, 易于被广大 T2DM 患者接受。我们推测八段锦能够作为一种促进 T2DM 治疗的运动。研究表明, 运动参与 *Bmal1* 基因的调控和表达^[61]。耐力运动与急性运动可通过调控时钟基因来提高骨骼肌的代谢, 降低冠状动脉疾病和 T2DM 等慢性疾病的患病风险^[62, 63], 小鼠的昼夜节律和神经精神损伤检测^[8]和葡萄糖代谢实验结果^[64]显示, 骨骼肌中 *Bmal1* 过表达对 T2DM 患者的睡眠具有促进作用。由此可见, *Bmal1* 是一个重要的调节因子, 可调控骨骼肌糖代谢。我们猜测, 八段锦可能会上调 *Bmal1* 基因表达, 增加骨骼肌糖原的储存和利用, 改善睡眠质量, 另一方面, 八段锦还可能通过提高身体的代谢率促进血糖的消耗和降低血糖浓度, 从而提高 T2DM 患者睡眠质量。

3.3 八段锦可能通过调节*Bmal1*在骨骼肌中的作用改善睡眠质量

Bmal1 可激活 Wnt 信号通路, 促进肌肉生成和分化^[65]。活化肌肉中的卫星细胞对肌肉纤维的再生与修复有促进作用^[66], *Bmal1* 也是促进肌肉生成的一个重要因子, 可预防和治疗肌肉萎缩^[67]。同时, *Bmal1* 对骨骼肌细胞结构和功能进行日常维护^[68]。研究显示, 运动小鼠肌纤维数量明显增加, 其睡眠质量也较正常小鼠明显提高, 提示运动上调 *Bmal1* 表达, 促进骨骼肌生成, 并具有调控睡眠的功能^[69]。而 *Bmal1* 表达异常可引发骨关节炎^[70]、骨质疏松症等骨代谢疾病^[71], *Bmal1* 的表达缺失不仅会抑制骨和软骨的发育, 导致骨量低下、骨密度降低, 还可促进骨吸收增加患病风险, 而在 *Bmal1* 基因过表达后也可能产生骨密度变化^[72-74], 骨骼肌与骨骼的 *Bmal1* 基因缺失或过表达导致的结果有所差别 (表 1)。

八段锦可提高骨骼肌的结构和功能适应性, 并在此基础上提高有氧运动耐力^[79]。在有氧运动过程中, 骨骼肌所使用的能源物质是糖原, 而肌糖原的储量和代谢直接影响有氧运动的耐力。研究显示, 敲除骨骼肌 *Bmal1* 导致葡萄糖转运、糖酵解和有氧氧化能力下降, 从而降低糖耐量, 使机体产生胰岛素抵抗, 表明 *Bmal1* 是调控骨骼肌糖代谢的重要转录因子^[80-83]。以上研究提示, 八段锦作为一种相对简单的有氧运动, 可促进骨骼肌中的肌糖原代谢, 进而可能改善机体糖耐量以及胰岛素水平, 维持机体正常的生物昼夜节律, 达到改善 T2DM 患者睡眠质量的目的。

表1. *Bmal1*基因缺失/过表达后的病理变化
Table 1. Pathological changes after deletion/overexpression of *Bmal1* gene

Body parts	Experimental model	Experimental subject	Pathological change	References
Whole body	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mutant mice	Skeletal muscle contractility↓	[68]
	Acupuncture	Male Sprague-Dawley rats	Blood glucose level↓	[75]
	Acupuncture	C57BL/6J male mice	Amount of sleep↑	[76]
	<i>Bmal1</i> ^{-/-}	Male (<i>Bmal1</i> ^{-/-}) mice	Blood glucose level↑	[77]
Bone	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mice	Chondrocyte proliferation↓	[70]
	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mice	Apoptosis↑	
	<i>Bmal1</i> overexpression	Male 8-week-old Wistar rats	Proinflammatory factor expression↓	[74]
	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mice	Bone mass↓	[72]
Skeletal muscle	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mice	Glucose uptake and metabolism↓	[47]
	<i>Bmal1</i> ^{-/-}	<i>Bmal1</i> ^{-/-} mice	Amount of sleep↑	[78]

Note: ↑ indicates increase; ↓ for mitigation.

3.4 八段锦可能通过调节*Bmal1*基因在SCN脑区中作用改善睡眠质量

生物钟与睡眠质量密切相关，是机体内部的一种内源性调节系统^[84]。SCN是哺乳动物昼夜节律调节系统的中枢结构，表达多种生物钟调节基因，这些基因能够调节身体内的各种昼夜节律活动^[23]。睡眠是由昼夜节律基因调控的^[85]；在哺乳动物机体内部，生物钟系统的结构较为复杂，是由SCN和附属的外周生物钟系统组成^[86, 87]。研究表明，SCN中*Clock*和*Bmal1*基因的表达紊乱与昼夜节律失调密切相关，其中的*Bmal1*基因与睡眠时长与睡眠质量联系紧密^[88, 89]。正常的昼夜节律上调SCN中生物钟基因*Bmal1*表达，从而对睡眠产生抑制^[90]。在血糖水平正常的机体内，*Bmal1*基因属于SCN中的兴奋性调节基因，当其表达超出正常范围时，会引起神经兴奋性的增强，从而造成睡眠质量下降、睡眠时间减少^[91]。研究表明，T2DM患者体内出现不同程度的*Bmal1*基因损害，由于T2DM患者通常伴有失眠症状，患者的SCN中*Bmal1*表达水平明显低于正常人，*Bmal1*表达紊乱可导致睡眠-觉醒失调，造成昼夜节律紊乱^[92, 93]。

上调*Bmal1*基因表达可调节SCN昼夜节律活动调控，从而达到改善T2DM患者睡眠节律紊乱的目的^[94, 95]。另一方面，SCN通过休息-活动周期驱动进食-禁食节律，并且通过光照以及昼夜节律刺激，使糖代谢水平出现昼夜差异，对T2DM患者体内的血糖水平进行调节，同时糖皮质激素通过血清反应因子信号转导通路也对昼夜节律进行一定程度的调控^[95, 96]。八段锦可稳定T2DM患者的血糖水平，由此通过糖皮质激素受体与血清反应因子信号转导

通路对T2DM患者的昼夜节律进行调控，并上调*Bmal1*基因^[97]，从而改善睡眠-觉醒周期，提高睡眠质量。良好的睡眠觉醒周期能够有效改善T2DM患者血糖水平、增强免疫、改善睡眠质量，并且对情绪调节、身体机能恢复等多方面都具有不可替代的调控作用^[98]。

4 总结与展望

八段锦可不同程度地改善T2DM患者心理健康状态，降低焦虑水平，减轻抑郁情绪，提高情绪调节能力，促进机体的心理健康调节，从心理因素方面对T2DM患者睡眠质量有一定程度的改善作用^[28, 99]，八段锦也可能通过调控T2DM患者机体内*Bmal1*基因表达，调节骨骼肌糖代谢、机体的生物昼夜节律、骨骼肌纤维数量以及SCN昼夜节律调节中枢对*Bmal1*基因表达和血糖水平等多方面进行干预调节。一方面，八段锦可调动T2DM患者全身骨骼肌运动，并且促进骨骼肌糖代谢，提高机体代谢将体内的血糖和血脂消耗，降低血糖水平，改善睡眠质量；另一方面，根据已有研究，我们推测八段锦可能通过上调*Bmal1*基因表达水平来调整生物节律，从而改善T2DM患者的睡眠质量。最后，八段锦也可能具有提高患者的骨骼肌纤维数量、改善机体糖耐量和胰岛素水平的作用，从而进一步改善睡眠质量（图2）。

睡眠是人体自我修复和恢复的重要过程，在睡眠时，*Bmal1*基因表达水平逐渐上调，这对于维持良好的睡眠质量至关重要。虽然有氧运动和生物钟的联合调控可以促进机体能量代谢，但目前单一调控机制对*Bmal1*的具体作用仍不清楚。根据已有研

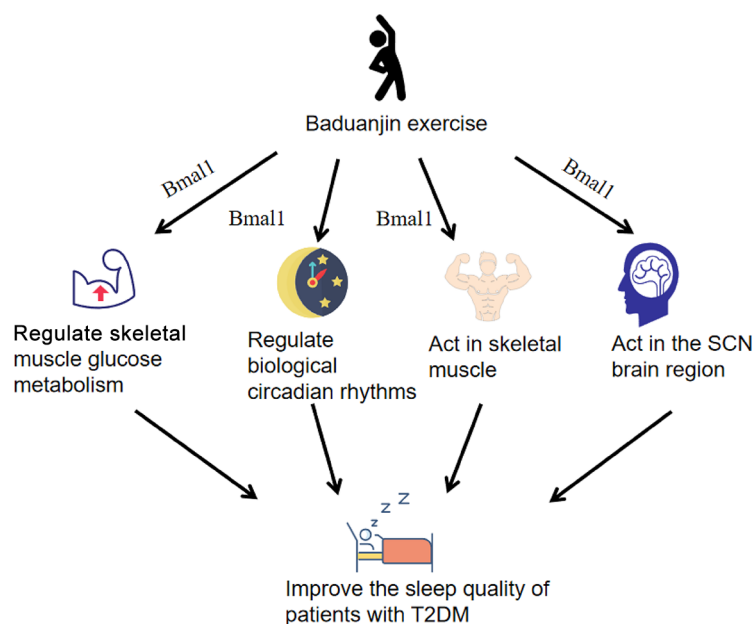


图 2. 八段锦通过调控Bmal1表达提高2型糖尿病(T2DM)患者睡眠质量

Fig. 2. Baduanjin improves sleep quality of type 2 diabetes mellitus (T2DM) patients by regulating the expression of Bmal1. Baduanjin exercise regulates *Bmal1* gene, regulates skeletal muscle glucose metabolism, biological circadian rhythm, skeletal muscle and supra-chiasmatic nucleus (SCN) brain region, and improves the sleep quality of T2DM patients in many aspects.

究, 我们推测八段锦可能对 T2DM 患者 *Bmal1* 基因表达有调控作用, 可改善患者的血糖水平和整体各项身体指标, 改善睡眠质量。需要指出的是, 八段锦治疗 T2DM 患者的整体效果较为常见, 已有较多文献报道, 但是改善 T2DM 患者睡眠质量的直接证据不足, 需要进一步的研究来验证和揭示具体机制。

参考文献

- Ning G (宁光), Xing XP. Endocrine Medicine. Beijing: People's Health Publishing House, 2022 (in Chinese).
- Huang XY (黄新一), Li Y, Liu Y, He Y, Liu X, Zheng M. Study on the mechanism of exercise-mediated insulin receptor-independent glucose uptake in skeletal muscle. *Bull Sports Sci Technol Liter* (体育科技文献通报) 2022; 30(10): 237–241 (in Chinese).
- Li M (李敏), Chen K, Wang YH, Yang ZQ, Huang XY, Liu LH, Wang J. Signing the family doctor service mode for elderly patients with type 2 diabetes vascular lesions associated risk factors exist rate. *Chin J Gerontol* (中国老年学杂志) 2021; 41(6): 1318–1322 (in Chinese).
- Antza C, Kostopoulos G, Mostafa S, Nirantharakumar K, Tahrani A. The links between sleep duration, obesity and type 2 diabetes mellitus. *J Endocrinol* 2021; 252(2): 125–141.
- Zhuang Z, Dong X, Jia J, Liu Z, Huang T, Qi L. Sleep patterns, plasma metabolome, and risk of incident type 2 diabetes mellitus. *J Clin Endocrinol Metab* 2023; 108(10): e1034–e1043.
- Huang HZ (黄慧真). Diabetes care platform that occupy the home in the early onset of type 2 diabetes patients continue nursing application. *Diabetes New World* (糖尿病新世界) 2022; 25(22): 131–134 (in Chinese).
- Paschou SA, Bletsas E, Saltiki K, Kazakou P, Kantreva K, Katsaounou P, Rovina N, Trakada G, Bakakos P, Vlachopoulos CV, Psaltopoulou T. Sleep apnea and cardiovascular risk in patients with prediabetes and type 2 diabetes. *Nutrients* 2022; 14(23): 4989.
- Gao X, Wei Y, Sun H, Hao S, Ma M, Sun H, Zang D, Qi C, Ge J. Role of Bmal1 in type 2 diabetes mellitus-related glycolipid metabolic disorder and neuropsychiatric injury: Involved in the regulation of synaptic plasticity and circadian rhythms. *Mol Neurobiol* 2023; 60(8): 4595–4617.
- Fan R, Peng X, Xie L, Dong K, Ma D, Xu W, Shi X, Zhang S, Chen J, Yu X, Yang Y. Importance of Bmal1 in Alzheimer's disease and associated aging-related diseases: Mechanisms and interventions. *Aging Cell* 2022; 21(10): e13704.
- Schiaffino S, Blaauw B, Dyar K A. The functional significance of the skeletal muscle clock: lessons from Bmal1 knockout models. *Skelet Muscle* 2016; 6: 33.

- 11 Chatterjee A, Lamaze A, De J, Mena W, Chélot E, Martin B, Hardin P, Kadener S, Emery P, Rouyer F. Reconfiguration of a multi-oscillator network by light in the *Drosophila* circadian clock. *Curr Biol* 2018; 28(13): 2007–2017.e4.
- 12 Chen S, Feng M, Zhang S, Dong Z, Wang Y, Zhang W, Liu C. Angptl8 mediates food-driven resetting of hepatic circadian clock in mice. *Nat Commun* 2019; 10(1): 3518.
- 13 Hor CN, Yeung J, Jan M, Emmenegger Y, Hubbard J, Xenarios I, Naef F, Franken P. Sleep-wake-driven and circadian contributions to daily rhythms in gene expression and chromatin accessibility in the murine cortex. *Proc Natl Acad Sci U S A* 2019; 116(51): 25773–25783.
- 14 Daut RA, Hartsock MJ, Tomczik AC, Watkins LR, Spencer RL, Maier SF, Fonken LK. Circadian misalignment has differential effects on affective behavior following exposure to controllable or uncontrollable stress. *Behav Brain Res* 2019; 2(359): 440–445.
- 15 Evans MC, Anderson GM. Integration of circadian and metabolic control of reproductive function. *Endocrinology* 2018; 159(11): 3661–3673.
- 16 Xue Y (薛阳). Persistent postprandial state of CLOCK/BMAL1 pathways regulating role in type 2 diabetes and its mechanism [D/OL]. Yinchuan: Ningxia Medical University (宁夏医科大学), 2022 (in Chinese). https://kns.cnki.net/kcms2/article/abstract?v=K_cp52o2S7_eLRkWtwjEa-Jr-Tl2KACg-9s-JsUW5eNKERbP4Tr8VoK6QMUTBo-0Plw2EO1mg65qlZq_GIXQoZaSvryqtm59XmzjiW8rDU-3wmB90EWIUXWWA==&uniplatform=NZKPT&language=gb
- 17 Ray S, Valekunja UK, Stangherlin A, Howell SA, Snijders AP, Damodaran G, Reddy AB. Circadian rhythms in the absence of the clock gene *Bmal1*. *Science* 2020; 367(6479): 800–806.
- 18 Trott AJ, Menet JS. Regulation of circadian clock transcriptional output by CLOCK:BMAL1. *PLoS Genet* 2018; 14(1): e1007156.
- 19 Jiang H (江杭), Jin F. Research progress and clinical application of clock gene. *Modern Cancer Med* (现代肿瘤医学) 2017; 25(4): 641–644 (in Chinese).
- 20 Herzig KH. Circadian rhythms-daylight saving time, health and body clocks. *Acta Physiol (Oxf)* 2019; 225(1): e13221.
- 21 Cao X, Yang Y, Selby C P, Liu Z, Sancar A. Molecular mechanism of the repressive phase of the mammalian circadian clock. *Proc Natl Acad Sci U S A* 2021; 118(2): e2021174118.
- 22 Sharma A, Sethi G, Tambuwala MM, Aljabali AAA, Chellappan DK, Dua K, Goyal R. Circadian rhythm disruption and Alzheimer's disease: The dynamics of a vicious cycle. *Curr Neuropharmacol* 2021; 19(2): 248–264.
- 23 Pan X, Mota S, Zhang B. Circadian clock regulation on lipid metabolism and metabolic diseases. *Adv Exp Med Biol* 2020; 1276: 53–66.
- 24 Li R (李锐), Lu BC. Research progress on the effect of health qigong on human physical and mental health. *Chin J Gerontol* (中国老年学杂志) 2022; 42(18): 4638–4644 (in Chinese).
- 25 Magkos F, Hjorth MF, Astrup A. Diet and exercise in the prevention and treatment of type 2 diabetes mellitus. *Nat Rev Endocrinol* 2020; 16(10): 545–555.
- 26 Yang H (杨晗), Li P, Fang Z, Wu YC. Effects of Baduanjin exercises under community management on clinical efficacy, psychological state and blood glucose indexes in elderly patients with type 2 diabetes mellitus. *Chin J Gerontol* (中国老年学杂志) 2019; 39(14): 3433–3435 (in Chinese).
- 27 Wang YW (王英伟), Li XD, Bi XJ. Effect of Baduanjin health Qigong on sleep quality and memory function of community elderly. *Chin J Gerontol* (中国老年学杂志) 2019; 39(14): 3435–3437 (in Chinese).
- 28 Fan B, Song W, Zhang J, Er Y, Xie B, Zhang H, Liao Y, Wang C, Hu X, McIntyre R, Lee Y. The efficacy of mind-body (Baduanjin) exercise on self-reported sleep quality and quality of life in elderly subjects with sleep disturbances: a randomized controlled trial. *Sleep Breath* 2020; 24(2): 695–701.
- 29 Guo Y (郭郁), Wei ZR, Hu QC, Zhang JL, Wei YL. To analyze the “regulating heart” effect of Baduanjin on college students with different neurotic personality based on the δ and θ band EEG power spectrum. *Chin J Trad Chin Med* (中华中医药杂志) 2019; 34(11): 5454–5459 (in Chinese).
- 30 Liu J, Yang Y, Zhu Y, Hou X, Li S, Chen S, Yang J. Effectiveness of Baduanjin (a type of qigong) on physical, cognitive, and mental health outcomes: A comprehensive review. *Adv Mind Body Med* 2023; 37(2): 9–23.
- 31 Luo X, Zhao M, Zhang Y, Zhang Y. Effects of baduanjin exercise on blood glucose, depression and anxiety among patients with type II diabetes and emotional disorders: A meta-analysis. *Complement Ther Clin Pract* 2023; 50: 101702.
- 32 Yang YH (杨玉赫), Leng DS, Zhang RX, Che ZY, Bai Y, Yu QM. Research progress on the effect of health cultivation exercises of traditional Chinese medicine on depression of college students. *Chin J Basic Med Trad Chin Med* (中国中医基础医学杂志) 2020; 26(8): 1214–1217 (in Chinese).
- 33 Yang T (杨涛). Effect of six-character formula of health qigong on patients with type 2 diabetes mellitus and depression [D/OL]. Shenyang: Liaoning University of Traditional Chinese Medicine (辽宁中医药大学), 2018 (in Chinese). https://kns.cnki.net/kcms2/article/abstract?v=K_

- cp52o2S7-fLhKpnlvVz9k4RejJZ5cXGSdzPNs0jPm6gx-ChDILdeVEZSaVrQkkz5HfaPbcMUSn6gwg_HflncUQ-sAKnsOpcwt5Ou4-pO7V9CSO6UOi4JQ==&uniplat-form=NZKPT&language=gb
- 34 Kong L, Ren J, Fang S, He T, Zhou X, Fang M. Effects of traditional Chinese mind-body exercise-Baduanjin for type 2 diabetes on psychological well-being: A systematic review and meta-analysis. *Front Public Health* 2022; 10: 923411.
 - 35 Wang F (王芳), Wang WD, Zhang RR, Lin YN, Hong L, Zhao Y, Ni Q, Ishi Y, Kosikawa F, Kisi T, Tututi T, Suzukia K, Haruki T. Different regimens of sleep quality in patients with type 2 diabetes mellitus associated with insomnia. *J Beijing Univ Chin Med* (北京中医药大学学报) 2009; 32(9): 636–640 (in Chinese).
 - 36 Li Q (李勤), Wu R, Wang F, Shi B, An R. Clinical observation of the intervention effect of Baduanjin on patients with prediabetes in community. *Shanghai J Trad Chin Med* (上海中医药杂志) 2022; 56(5): 49–53 (in Chinese).
 - 37 Yu DD, You LZ, Huang WQ, Cao H, Wang FJ, Tang XQ, Fang ZH, Shen GM, Guan YX. Effects of traditional Chinese exercises on blood glucose and hemoglobin A1c levels in patients with prediabetes: A systematic review and meta-analysis. *J Integ Med* 2020; 18(04): 292–302.
 - 38 Ma Q, Li H, Gao Y, Zou Y. Effects of Baduanjin on glucose and lipid metabolism in diabetic patients: A protocol for systematic review and meta-analysis. *Medicine (Baltimore)* 2021; 100(4): e23532.
 - 39 Suh SH, Paik IY, Jacobs K. Regulation of blood glucose homeostasis during prolonged exercise. *Mol Cells* 2007; 23(3): 272–279.
 - 40 Tappy L. Metabolism of sugars: A window to the regulation of glucose and lipid homeostasis by splanchnic organs. *Clin Nutr* 2021; 40(4): 1691–1698.
 - 41 Yin TT (尹甜甜), Deng SL, Zhang JM, Chen SS. A meta-analysis of the effects of Tai chi exercise on physical function in patients with type 2 diabetes mellitus. *Bull Sport Sci Technol* (体育科技文献通报) 2022; 30(11): 68–72 (in Chinese).
 - 42 Tahara Y, Aoyama S, Shibata S. The mammalian circadian clock and its entrainment by stress and exercise. *J Physiol Sci* 2017; 67(1): 1–10.
 - 43 Zimmet P, Alberti KGMM, Stern N, Bilu C, El-Osta A, Einat H, Kronfeld-Schor N. The circadian syndrome: is the metabolic syndrome and much more! *J Intern Med* 2019; 286(2): 181–191.
 - 44 McHill AW, Wright KP Jr. Role of sleep and circadian disruption on energy expenditure and in metabolic predisposition to human obesity and metabolic disease. *Obes Rev* 2017; 18 Suppl 11: 15–24.
 - 45 Padlom A, Ono D, Hamashima R, Furukawa Y, Yoshimura T, Nishiwaki-Ohkawa T. Level of constitutively expressed BMAL1 affects the robustness of circadian oscillations. *Sci Rep* 2022; 12(1): 19519.
 - 46 Pinto AP, Muñoz VR, Tavares MEA, Dos Santos JR, Rebelo MA, Alberici LC, Simabuco FM, Teixeira GR, Pauli JR, de Moura LP, Cintra DE, Ropelle ER, Freitas EC, Rivas DA, da Silva ASR. Combined physical exercise reverses the reduced expression of Bmal1 in the liver of aged mice. *Life Sci* 2023; 312: 121175.
 - 47 Yin H, Li W, Chatterjee S, Xiong X, Saha P, Yechoor V, Ma K. Metabolic-sensing of the skeletal muscle clock coordinates fuel oxidation. *FASEB J* 2020; 34(5): 6613–6627.
 - 48 Chen X, Yu F, Guo X, Su C, Li SS, Wu B. Clock gene Bmal1 controls diurnal rhythms in expression and activity of intestinal carboxylesterase 1. *J Pharm Pharmacol* 2021; 73(1): 52–59.
 - 49 Erickson ML, Zhang H, Mey JT, Kirwan JP. Exercise training impacts skeletal muscle clock in adults with prediabetes. *Med Sci Sports Exerc* 2020; 52(10): 2078–2085.
 - 50 Angelousi A, Kassi E, Nasiri-Ansari N, Weickert MO, Randeva H, Kaltsas G. Clock genes alterations and endocrine disorders. *Eur J Clin Invest* 2018; 48(6): e12927.
 - 51 Fu ZT (傅泽铤), Xia Y, Ding HL. The role of clock gene BMAL1 in exercise-induced skeletal muscle injury recovery. *Chin J Appl Physiol* (中国应用生理学杂志) 2022; 38(3): 220–226 (in Chinese).
 - 52 Haynes RB, McDonald HP, Garg AX. Helping patients follow prescribed treatment: Clinical applications. *JAMA* 2002; 288(22): 2880–2883.
 - 53 Hu L (胡玲), Yu FX, Jia SG, He ZY, Dou FM, Deng Y, Zhao X, Liu X, Liu YY. Influencing factors of hospitalization expenses of type 2 diabetes mellitus and its complications in Chengdu city. *Modern Prevent Med* (现代预防医学) 2022; 49(11): 2012–2018 (in Chinese).
 - 54 Tomas-Carus P, Ortega-Alonso A, Pietilainen KH, Santos V, Goncalves H, Ramos J, Raimundo A. A randomized controlled trial on the effects of combined aerobic-resistance exercise on muscle strength and fatigue, glycemic control and health-related quality of life of type 2 diabetes patients. *J Sports Med Phys Fitness* 2016; 56(5): 572–578.
 - 55 Sousa RAL, Improta-Caria AC, Souza BSF. Exercise-linked irisin: Consequences on mental and cardiovascular health in type 2 diabetes. *Int J Mol Sci* 2021; 22(4): 2199.
 - 56 Callisaya M, Nosaka K. Effects of exercise on type 2 diabetes mellitus-related cognitive impairment and dementia. *J Alzheimers Dis* 2017; 59(2): 503–513.
 - 57 Bai DD (白丹丹), Xiao WH. Lipid metabolic intermediate regulation of skeletal muscle insulin sensitivity. *Acta Physiol*

- Sin (生理学报) 2022; 74(5): 805–815 (in Chinese).
- 58 Hansen D, De Strijcker D, Calders P. Impact of endurance exercise training in the fasted state on muscle biochemistry and metabolism in healthy subjects: Can these effects be of particular clinical benefit to type 2 diabetes mellitus and insulin-resistant patients? *Sports Med* 2017; 47(3): 415–428.
 - 59 Swift DL, Johannsen NM, Lavie CJ, Earnest CP, Church TS. The role of exercise and physical activity in weight loss and maintenance. *Prog Cardiovasc Dis* 2014; 56(4): 441–447.
 - 60 Lu X, Zhao C. Exercise and type 1 diabetes. *Adv Exp Med Biol* 2020; 1228: 107–121.
 - 61 Brager AJ, Heemstra L, Bhambra R, Ehlen JC, Esser KA, Paul KN, Novak CM. Homeostatic effects of exercise and sleep on metabolic processes in mice with an overexpressed skeletal muscle clock. *Biochimie* 2017; 132: 161–165.
 - 62 Gutierrez-Monreal MA, Harmsen JF, Schrauwen P, Esser KA. Ticking for metabolic health: The skeletal-muscle clocks. *Obesity (Silver Spring)* 2020; 28 Suppl 1 (Suppl 1): S46–S54.
 - 63 Erickson ML, Esser KA, Kraus WE, Buford TW, Redman LM. A role for exercise to counter skeletal muscle clock disruption. *Exerc Sport Sci Rev* 2021; 49(1): 35–41.
 - 64 Rakshit K, Matveyenko AV. Induction of core circadian clock transcription factor *Bmal1* enhances β -cell function and protects against obesity-induced glucose intolerance. *Diabetes* 2021; 70(1): 143–154.
 - 65 Chatterjee S, Nam D, Guo B, Kim JM, Winnier GE, Lee J, Berdeaux R, Yechoor VK, Ma K. Brain and muscle Arnt-like 1 is a key regulator of myogenesis. *J Cell Sci* 2013; 126(Pt 10): 2213–2224.
 - 66 Luo B, Zhou X, Tang Q, Yin Y, Feng G, Li S, Chen L. Circadian rhythms affect bone reconstruction by regulating bone energy metabolism. *J Transl Med* 2021; 19(1): 410.
 - 67 Zhu P, Hamlish NX, Thakkar AV, Steffek AWT, Rendleman EJ, Khan NH, Waldeck NJ, DeVilbiss AW, Martin-Sandoval MS, Mathews TP, Chandel NS, Peek CB. BMAL1 drives muscle repair through control of hypoxic NAD^+ regeneration in satellite cells. *Genes Dev* 2022; 36(3–4): 149–166.
 - 68 Andrews JL, Zhang X, McCarthy JJ, McDearmon EL, Hornberger TA, Russell B, Campbell KS, Arbogast S, Reid MB, Walker JR, Hogenesch JB, Takahashi JS, Esser KA. CLOCK and BMAL1 regulate *MyoD* and are necessary for maintenance of skeletal muscle phenotype and function. *Proc Natl Acad Sci U S A* 2010; 107(44): 19090–19095.
 - 69 Smith JG, Molendijk J, Blazev R, Chen WH, Zhang Q, Litwin C, Zinna VM, Welz PS, Benitah SA, Greco CM, Sassone-Corsi P, Muñoz-Cánoves P, Parker BL, Koronowski KB. Impact of *Bmal1* rescue and time-restricted feeding on liver and muscle proteomes during the active phase in mice. *Mol Cell Proteomics* 2023; 22(11): 100655.
 - 70 Ma Z, Jin X, Qian Z, Li F, Xu M, Zhang Y, Kang X, Li H, Gao X, Zhao L, Zhang Z, Zhang Y, Wu S, Sun H. Deletion of clock gene *Bmal1* impaired the chondrocyte function due to disruption of the HIF1 α -VEGF signaling pathway. *Cell Cycle* 2019; 18(13): 1473–1489.
 - 71 Li X, Liu N, Gu B, Hu W, Li Y, Guo B, Zhang D. BMAL1 regulates balance of osteogenic-osteoclastic function of bone marrow mesenchymal stem cells in type 2 diabetes mellitus through the NF- κ B pathway. *Mol Biol Rep* 2018; 45(6): 1691–1704.
 - 72 Takarada T, Xu C, Ochi H, Nakazato R, Yamada D, Nakamura S, Kodama A, Shimba S, Mieda M, Fukasawa K, Ozaki K, Iezaki T, Fujikawa K, Yoneda Y, Numano R, Hida A, Tei H, Takeda S, Hinoi E. Bone resorption is regulated by circadian clock in osteoblasts. *J Bone Miner Res* 2017; 32(4): 872–881.
 - 73 Martin RA, Viggars MR, Esser KA. Metabolism and exercise: the skeletal muscle clock takes centre stage. *Nat Rev Endocrinol* 2023; 19(5): 272–284.
 - 74 Chen G, Zhao H, Ma S, Chen L, Wu G, Zhu Y, Zhu J, Ma C, Zhao H. Circadian rhythm protein *Bmal1* modulates cartilage gene expression in temporomandibular joint osteoarthritis via the MAPK/ERK pathway. *Front Pharmacol* 2020; 11: 527744.
 - 75 Wang X (王栩), Zhang Y, Liu HD, Li J, Zhao WQ, Zhou QY, Zhang ZL. Effect of acupuncture on circadian rhythm of blood glucose in type 2 diabetic rats based on pancreatic PI3K/AKT/BMAL1 pathway. *Tianjin Trad Chin Med (天津中医药)* 2023; 40(1): 69–74 (in Chinese).
 - 76 Wang C (王畅), Sun XM, Xiu Y, Wang YB, Miao JR, Fan X. Effects of electroacupuncture on the expression of liver Clock and *Bmal1* genes in C57BL/6J mice with circadian rhythm disorder. *Chin J Trad Chin Med (中华中医药学刊)* 2023; 41(08): 243–248 (in Chinese).
 - 77 Liu GJ (刘桂君). Effect of *Bmal1* gene on the function of diabetic microvascular endothelial relaxation and its mechanism [D/OL]. Qingdao: Qingdao University (青岛大学), 2022 (in Chinese). https://kns.cnki.net/kcms2/article/abstract?v=K_cp52o2S79xbhTn33ERPwj-vWgwQGIMJtn-rVsWA0q1D_vGwTII_rDhd1wIfeI6DzY5ExMwyjYOCHB-cR o R j Z B X m E K g 8 D A D V D h d 8 V V 8 X 4 Y z -veiB5qqsYUUG==&uniplatform=NZKPT&language=gb
 - 78 Ehlen JC, Brager AJ, Baggs J, Pinckney L, Gray CL, DeBruyne JP, Esser KA, Takahashi JS, Paul KN. *Bmal1* function in skeletal muscle regulates sleep. *Elife* 2017; 6:e26557.
 - 79 Chambers TL, Burnett TR, Raue U, Lee GA, Finch WH, Graham BM, Trappe TA, Trappe S. Skeletal muscle size,

- function, and adiposity with lifelong aerobic exercise. *J Appl Physiol* (1985) 2020; 128(2): 368–378.
- 80 Riley LA, Esser KA. The role of the molecular clock in skeletal muscle and what it is teaching us about muscle-bone crosstalk. *Curr Osteoporos Rep* 2017; 15(3): 222–230.
 - 81 Dyar KA, Hubert MJ, Mir AA, Ciciliot S, Lutter D, Greulich F, Quagliarini F, Kleinert M, Fischer K, Eichmann TO, Wright LE, Peña Paz MI, Casarin A, Pertegato V, Romanello V, Albiero M, Mazzucco S, Rizzuto R, Salvati L, Biolo G, Blaauw B, Schiaffino S, Uhlenhaut NH. Transcriptional programming of lipid and amino acid metabolism by the skeletal muscle circadian clock. *PLoS Biol* 2018; 16(8): e2005886.
 - 82 Yan L (严露), Zhu RX, Zhang Y. Research progress of exercise, skeletal muscle circadian clock and regulation of glucose metabolism. *J Beijing Sport Univ (北京体育大学学报)* 2021; 44(7): 114–122 (in Chinese).
 - 83 MarcheVA B, Ramsey KM, Buhr ED, Kobayashi Y, Su H, Ko CH, Ivanova G, Omura C, Mo S, Vitaterna MH, Lopez JP, Philipson LH, Bradfield CA, Crosby SD, JeBailey L, Wang X, Takahashi JS, Bass J. Disruption of the clock components CLOCK and BMAL1 leads to hypoinsulinaemia and diabetes. *Nature* 2010; 466(7306): 627–31.
 - 84 Yang F (杨飞). The clinical effect of the treatment of balance acupuncture treatment for primary insomnia [D/OL]. Tianjin: Tianjin University of Chinese Medicine (天津中医药大学), 2022 (in Chinese). https://kns.cnki.net/kcms2/article/abstract?v=K_cp52o2S79PkjMhUqar-rE_A4aGmECI-dq-f5O1zjQzMWYM9ml2JSOT8nYo5tH5zsthYHzgVVheCo-ORF9na210V-1Z7qA3YxISmRG4qCUXgyaAq7kD-9qew=&uniplatform=NZKPT&language=gb
 - 85 Jones JR, Chaturvedi S, Granados-Fuentes D, Herzog ED. Circadian neurons in the paraventricular nucleus entrain and sustain daily rhythms in glucocorticoids. *Nat Commun* 2021; 12(1): 5763.
 - 86 Wang DN (王丹妮), Yang Q, Zhong QM, Song MQ, Tong LG, Jia LL, Niu YY, Feng ML. Effects of isognosin on the improvement of pineal gland injury induced by PCPA and the expression of circadian clock genes in rats. *Chin Pharm (中国药房)* 2020; 31(17): 2081–2086 (in Chinese).
 - 87 Nishide S, Honma S, Honma K I. Two coupled circadian oscillations regulate Bmal1-ELuc and Per2-SLR2 expression in the mouse suprachiasmatic nucleus. *Sci Rep* 2018; 8(1): 14765.
 - 88 Bolsius YG, Zurbruggen MD, Kim JK, Kas MJ, Meerlo P, Aton SJ, Havekes R. The role of clock genes in sleep, stress and memory. *Biochem Pharmacol* 2021; 191: 114493.
 - 89 Duncan MJ, Prochot JR, Cook DH, Tyler Smith J, Franklin KM. Influence of aging on Bmal1 and Per2 expression in extra-SCN oscillators in hamster brain. *Brain Res* 2013; 1491: 44–53.
 - 90 Xiao D (肖迪), Liu J, Zheng TY. This pill on the sleep deprivation mouse suprachiasmatic nucleus clock genes Clock and Bmal 1 expression. *J Hubei Univ Chin Med (湖北中医药大学学报)* 2019; 21(4): 25–29 (in Chinese).
 - 91 Fu XY (傅馨莹), Kuang SD, Liu LM, Yan SY, Zhang W, He QH. Study on the effect of circadian clock system on sleep circadian rhythm from the theory of essence and spirit. *Chin Med J (中医杂志)* 2023; 64(18): 1843–1846 (in Chinese).
 - 92 Engeland WC, Massman L, Miller L, Leng S, Pignatti E, Pantano L, Carlone DL, Kofuji P, Breault DT. Sex differences in adrenal Bmal1 deletion-induced augmentation of glucocorticoid responses to stress and ACTH in mice. *Endocrinology* 2019; 160(10): 2215–2229.
 - 93 Wang Q (汪卿), You QY, Ding L, Xia J, Wang P. Effects of An Mei Dan on circadian rhythm and energy metabolism in zebrafish sleep deprivation model. *Modern Trad Chin Med Mater Med World Sci Technol (世界科学技术-中医药现代化)* 2022; 24(12): 4873–4880 (in Chinese).
 - 94 Liu HX (刘恒旭), Chen PJ, Lu WY, Zhao H, Yin J, Luo J. Physical exercise: temporal cues mediating the molecular clock of circadian rhythm in skeletal muscle. *J Shanghai Univ Sport (上海体育大学学报)* 2022; 46(6): 94–106 (in Chinese).
 - 95 Olejníková L, Polidarová L, Sumová A. Stress affects expression of the clock gene Bmal1 in the suprachiasmatic nucleus of neonatal rats via glucocorticoid-dependent mechanism. *Acta Physiol (Oxf)* 2018; 223(1): e13020.
 - 96 Engeland WC, Massman L, Mishra S, Yoder JM, Leng S, Pignatti E, Piper ME, Carlone DL, Breault DT, Kofuji P. The adrenal clock prevents aberrant light-induced alterations in circadian glucocorticoid rhythms. *Endocrinology* 2018; 159(12): 3950–3964.
 - 97 Kung YY, Shen YC, Li JY, Kao YK, Kuo TBJ, Yang CCH. Effects of mind-body exercise on body constitution and circadian rhythm in people with suboptimal health status. *J Chin Med Assoc* 2024; 87(1): 94–102.
 - 98 Zhang NW (张乃文), Li MY, Li XL, Lu LH, Zhang J, Diao HQ, Chen L. The influence of circadian clock genes on sleep circadian rhythm based on yin-yang, ying-wei theory. *J Beijing Univ Trad Chin Med (北京中医药大学学报)* 2022; 45(4): 376–381 (in Chinese).
 - 99 Kuo CC, Wang CC, Chang WL, Liao TC, Chen PE, Tung TH. Clinical effects of Baduanjin Qigong exercise on cancer patients: A systematic review and meta-analysis on randomized controlled trials. *Evid Based Complement Alternat Med* 2021; 2021: 6651238.