

健康行为缓解焦虑情绪的作用机制

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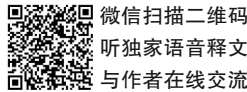
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【摘要】 本文目的是以健康行为干预焦虑情绪作为切入点, 结合国内外最新研究成果, 对健康运动行为、健康饮食行为和健康休闲娱乐行为调控焦虑情绪的作用机制进行综述, 以期从运动选择、饮食控制、休闲娱乐活动参与这三个层面改善焦虑情绪, 为健康行为改善焦虑情绪的规模化应用提供参考。

【关键词】 健康行为; 焦虑; 缓解; 作用机制

开放科学(资源服务)标识码(OSID):



微信扫码二维码

听独家语音释文

与作者在线交流

中图分类号: R749.4

文献标识码: A

doi: 10.11886/scjsws20221018002

Mechanism of health behavior in relieving anxiety mood

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【Abstract】 Taking the intervention of healthy behaviors in anxiety mood as the entry point, this paper aims to review the mechanism of healthy exercise behaviors, healthy eating behaviors, healthy leisure and entertainment behaviors in regulating anxiety mood based on recent national and international research findings, and to summary the alleviation of anxiety mood from the following three aspects: choice of exercise, diet control and participation in leisure and entertainment activities, thus providing a practical basis for the scale application of health behavior treatment for anxiety mood.

【Keywords】 Health behaviors; Anxiety; Alleviation; Mechanism

焦虑情绪是当代社会普遍存在的一种精神卫生问题, 广泛存在于儿童、青少年、中老年人等各个年龄阶段的人群中, 严重时会引起个体精神和身体损害, 影响生活质量。在全球新型冠状病毒肺炎(COVID-19)疫情背景下, 人们面临着经济衰退、就业歧视等压力, 且因 COVID-19 疫情产生焦虑情绪的社会群体人数大幅增加^[1-2]。在时代背景和社会环境的协同作用影响下, 人们对焦虑情绪等心理健康问题的关注程度不断提高。健康行为是以增强个体身体素质和维持身心健康为目的所进行的各种活动, 包括适度运动和均衡饮食等^[3]。既往研究表明, 面对焦虑情绪引起的健康风险, 健康行为干预有助于改善焦虑等负性情绪^[4-5]。

本文以健康行为作为切入点, 探讨健康行为在改善焦虑情绪中的意义, 致力于对健康行为调控焦虑情绪的作用机制进行更深入细致的探讨, 并阐明运动、饮食和休闲娱乐三项健康行为对焦虑情绪的调控效果和作用机制, 为健康行为缓解焦虑情绪的规模化应用提供参考。

1 资料与方法

1.1 资料来源与检索策略

1.1.1 资料来源

于 2022 年 10 月分别对中国知网、万方数据库、PubMed 和 Web of Science 数据库进行检索, 检索时限为 2015 年 1 月-2023 年 3 月。

1.1.2 检索策略

中文检索词: 焦虑、健康、作用机制、运动、饮食、娱乐; 英文检索词: Anxiety、Healthy、Mechanism、Sport、Food、Diet、Drink、Entertainment。

中文检索式: “焦虑” and “健康” and “作用机制” and (“运动” or “饮食” or “娱乐”); 英文检索式: “Anxiety” and “Healthy” and “Mechanism” and (“Sport” or “Food” or “Diet” or “Drink” or “Entertainment”)。

1.2 文献纳入与排除标准

文献纳入标准: ①关于焦虑情绪及健康行为干

预的研究内容以及作用机制;②包含健康行为干预相关作用机制和干预手段等内容的文献。排除标准:①重复文献;②会议摘要。

1.3 文献筛选与质量评估

首先采用EndNote对文献进行去重,通过阅读文献标题及摘要,对其余文献进行初步筛选;根据文献纳入及排除标准选取符合要求的文献。选取的文献整体质量较高,但各文献在研究对象和分析方法等方面同质性较差,不适合进行Meta分析,所以作定性描述。

2 结 果

2.1 纳入文献基本情况

初步检索共获取文献1 811篇,通过删除重复文献,对文献标题、摘要及全文进行阅读,最终纳入文献63篇,其中英文文献56篇,中文文献7篇。文献筛选流程见图1。

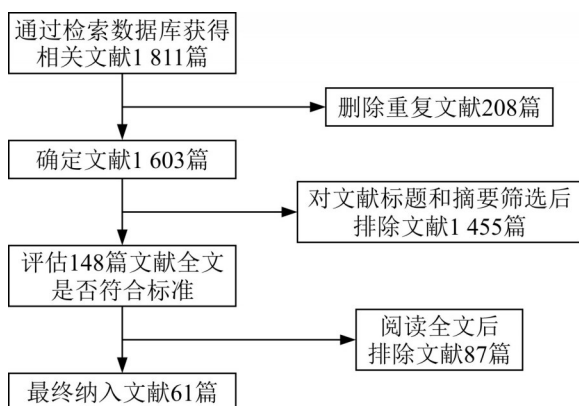


图1 文献筛选流程图

Figure 1 Flow chart of literature screening

2.2 健康运动行为调控机体焦虑情绪相关的分子网络

2.2.1 健康运动行为调控机体的脑区基因表达和信号通路传导

海马体是负责学习、记忆、社会认知和处理情绪障碍的关键脑区,影响焦虑情绪的产生与恢复^[6-7];杏仁核则是控制厌恶情境中生理和行为反应的边缘皮质结构^[8]。一项对大鼠的实验研究表明,低强度跑步干预可通过增加海马区的免疫基因表达,促进海马神经发生,对海马体、前额叶皮质和杏仁核等与认知功能相关的区域产生积极影响并降低应激激素皮质酮水平,进而起到抗焦虑的作用^[9]。连续性运动和间歇性运动也有助于提高大鼠

海马体内过氧化物酶体增殖受体 γ 辅激活因子 α (peroxisome proliferators-activated receptor γ co-activator 1 alpha, PGC-1 α)、Ⅲ型纤连蛋白结构域包含蛋白5 (fibronectin type Ⅲ domain containing 5, FNDC5)与脑源性神经营养因子 (brain-derived neurotrophic factor, BDNF)蛋白的表达,进而改善焦虑样行为^[10]。Constans等^[11]通过比较高强度间歇性有氧运动与中强度连续性有氧运动对SD大鼠的影响,结果显示,间歇性运动会使血液乳酸浓度升高,并激活有丝分裂原活化蛋白激酶 (mitogen-activated protein kinase, MAPK)、细胞外信号调节激酶 (extracellular signal-regulated kinase, ERK)、有丝分裂原和应激活化蛋白激酶 (mitogen- and stress-activated protein kinase, MSK)的信号通路,减轻焦虑样反应。Zebrowska等^[12]的一项对照实验显示,运动训练有助于提高1型糖尿病患者BDNF水平,Tai等^[13]研究表明,运动训练可提高1型糖尿病患者类胰岛素生长因子-1 (insulin-like growth factors-1, IGF-1)水平,提高受损的神经营养水平,并扭转患者的焦虑样行为。此外,Morgan等^[14]对C57BL/6小鼠的实验研究结果显示,适量跑台运动可增加单磷酸腺苷依赖的蛋白激酶 (AMP-activated protein kinase, AMPK)活性,而Azimi等^[15]对Wistar大鼠的实验研究表明,适量跑台运动可上调PGC-1 α 、FNDC5和BDNF表达,促进海马神经发生,改善认知功能和焦虑情绪。互动性体育锻炼也具有增加前扣带皮质 (anterior cingulate cortex, ACC)区域灰质体积的作用,并促进神经细胞信息传递^[16]。

2.2.2 健康运动行为调控机体焦虑情绪相关的激素变化

2.2.2.1 5-羟色胺能活动介导

Fan等^[17]对血管性痴呆SD大鼠进行研究,结果表明,定期体育锻炼可调控5-羟色胺2A受体 (5-hydroxytryptamine 2A receptor, 5-HT_{2A}R)的通路,减轻应激源诱发的焦虑情绪^[18-19],而5-HT_{2A}R在杏仁核区域神经元的突触募集作用也可能介导运动改善焦虑情绪的机制^[20]。Zhou等^[21]对小鼠进行的研究表明,定期有氧运动可促进前扣带回5-HT释放并作用于5-羟色胺7受体 (5-hydroxytryptamine 7 receptor, 5-HT₇R),增强海马神经发生并调节突触可塑性^[22],改善焦虑情绪。

2.2.2.2 内源性大麻素调控通路

内源性大麻素(endocannabinoids, eCBs)由神经细胞膜上的多不饱和脂肪酸(polyunsaturated fatty acids, PUFA)转化而成,包括脂肪酸乙醇酰胺(acid ethanolamides anandamide, AEA)和2-花生四烯酸甘油(2-arachidonoylglycerol, 2-AG),可与突触前神经元上的大麻素 I 型受体结合,进而释放神经递质并抑制突触活性^[23]。一项大型横断面研究显示,成年人每周参加1~2次体育运动,可提高eCBs浓度并缓解焦虑情绪^[24],而eCBs浓度升高已被证实是有氧运动缓解焦虑情绪的机制^[6]。

2.2.2.3 下丘脑-垂体-肾上腺通路活动

下丘脑-垂体-肾上腺(hypothalamic-pituitary-adrenal, HPA)通路在应对压力导致的焦虑等负性情绪时,杏仁核与大脑其他区域会激活下丘脑神经元,导致下丘脑释放促肾上腺皮质激素释放因子(corticotrophin-releasing factor, CRF),促进促肾上腺皮质激素(adrenocorticotrophic hormone, ACTH)释放,此时,血液中ACTH浓度升高并与对应受体结合^[25],进而对海马体和杏仁核的功能产生影响,减轻焦虑情绪^[26]。Safari等^[27]以30只Wistar大鼠为研究对象的实验结果表明,游泳可促进皮质酮分泌。

催产素是一种由垂体后叶分泌、下丘脑合成的神经肽,在HPA轴运作环节中,抑制压力相关的激素分泌,具有调节情绪和社会行为的作用^[28]。实验结果表明,长期运动有助于提高大脑催产素水平,缓解焦虑情绪并改善相应症状^[29]。自发运动行为则可能通过提高血液催产素水平进而抑制焦虑情绪^[30-31]。

2.3 健康饮食行为调控焦虑情绪的作用机制

2.3.1 健康饮食行为调控机体焦虑情绪相关的激素与蛋白质变化

饮食所摄取的维生素D₃可通过抑制海马神经元中I型钙通道表达与一氧化氮合酶合成,改善尼古丁戒断引起的焦虑样行为^[32]。饮食补充鱼油则可通过降低海马细胞外5-HT水平,并促进细胞外调节蛋白激酶(extracellular regulated protein kinase, ERK)活化,抑制焦虑情绪^[33]。Achour等^[34]研究表明,适量饮用迷迭香茶可提高人体血浆中的BDNF和肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)水平,起到抗焦虑的作用。生酮饮食(ketogenic diet,

KD)模式下机体的主要能量来源会由葡萄糖转变为酮体,Gumus等^[35]在研究中联合KD与定期运动,发现小鼠体内 β -羟丁酸(β -hydroxybutyrate, β -HB)水平提高,葡萄糖和胰岛素水平降低,低密度脂蛋白(low-density lipoprotein, LDL)和高密度脂蛋白(high-density lipoprotein, HDL)之间比率下降,焦虑样行为减少。

2.3.2 健康饮食行为调节体内微生物群落环境

人体肠道微生物群因受外界环境变化和益生菌摄入行为等影响而处于动态变化中,健康饮食行为通过影响微生物菌落环境调节机体焦虑情绪的作用机制包含维持能量稳定、促进营养物质代谢、免疫调节、影响HPA轴和内分泌通路等,而焦虑患者多有体内微生物群落失衡的现象^[36-37]。调节体内微生物群落可能是改善焦虑情绪的方式。但并非所有的益生菌都具相同功效,仍需就微生物种类特异性进行研究,进一步探讨适量摄入益生菌改善焦虑情绪的效果。

酸奶是市面上常见的饮品,其发酵所用菌种包含植物乳杆菌、干酪乳杆菌和双歧杆菌等。研究表明,大学男生在跑步训练期间摄入含格氏乳杆菌CP2305的饮料,能够改善肠内微环境,预防应激诱导的外周血白细胞及线粒体功能相关基因表达变化,并提高血清生长激素水平,缓解焦虑情绪^[38]。大鼠摄入副干酪乳杆菌PS23可增加海马糖皮质激素受体(glucocorticoid receptor, GR)、盐皮质激素受体(mineralocorticoid receptor, MR)和BDNF蛋白的表达,增强神经可塑性,促进抗炎与抗氧化基因表达,提高血清素和多巴胺能在海马体、前额皮质以及纹状体中的活性,改善肠道微生物群,同样具有抗焦虑样作用^[39-40]。另有研究指出,成年人摄入植物乳杆菌DR7可在改善认知和记忆功能的同时通过减少血浆皮质醇和促炎细胞因子含量,上调血清素通路和多巴胺通路,进而减轻焦虑情绪^[41]。大鼠实验显示,双歧杆菌三联活菌胶囊具有改善焦虑情绪和认知障碍的作用,其机制与增加海马神经元数量、抑制海马小胶质细胞活化、减少炎症和细胞凋亡有关^[42]。可见,现有研究已初步揭示影响益生菌调节机体内环境功效的因素,部分益生菌能改变海马基因表达,具有缓解焦虑情绪的潜力^[43-44]。

除补充益生菌外,其他健康饮食模式还可通过调节体内微生物菌落环境缓解焦虑情绪。Wang等^[45]将40只C57BL/6小鼠作为研究对象,结果显

示,摄入富含色氨酸的饮食可改变肠道微生物群的结构和成分,增强肠粘膜屏障完整性并促进 BDNF 表达,使色氨酸代谢向 5-HT 途径转移,进而改善焦虑样行为。经常食用花生可增强记忆功能、提高应激反应能力。花生中富含多酚,食用花生后,粪便中短链脂肪酸(Short-chain fatty acid, SCFA)含量增加,多酚可能通过与肠道微生物的相互作用间接影响情绪和认知功能,SCFA 则可能通过调节能量代谢、免疫系统和血脑屏障通透性影响中枢神经系统,并抑制组蛋白去乙酰化、提高前额叶皮层 BDNF 水平,进而缓解焦虑情绪^[46-48]。总体而言,肠道微生物群与脑区功能之间的相互作用可能是调控焦虑情绪的潜在机制^[49]。

2.4 健康休闲娱乐行为调控焦虑情绪的作用机制

2.4.1 健康休闲娱乐行为改变机体激素水平与蛋白质水平

听音乐或音乐治疗具有改善焦虑情绪和增强幸福感的作用^[50]。Wulff 等^[51]对 172 名孕妇的随机对照试验结果显示,在听音乐或参加歌唱干预后,孕妇与焦虑抑制作用相关的皮质醇水平降低,催产素水平提高。音乐信号还可诱导 BDNF 表达并对海马 CA1 区锥体神经元产生影响,防止海马树突棘密度下降,产生生理缓冲,抑制焦虑样行为^[52]。

2.4.2 健康休闲娱乐行为通过感觉信号传导缓解焦虑情绪

感觉信号传导是健康休闲娱乐行为缓解焦虑情绪的主要机制之一,根据现有研究,可将感觉信号传导通路总结为“分子-感觉信号-感觉皮层-脑区处理-缓解焦虑”。研究表明^[53],游戏和绘画有助于缓解焦虑情绪,且简单、经济、高效。刘丽秋^[54]对初中新生进行表达性艺术团体辅导的结果显示,此干预方式有助于缓解该群体的焦虑情绪。大脑解码由视觉信号刺激视觉皮层接收的图像,进而影响焦虑等情绪状态,可能是游戏与绘画缓解焦虑情绪的机制^[55]。听音乐时,音乐信号可从听觉皮层传导至与焦虑情绪处理相关的下丘脑、杏仁核和内侧面额叶皮层区域,研究表明,杏仁核能被听觉信号激活,抑制厌恶性记忆^[56-57]。不同类型的音乐对焦虑情绪改善的机制不同,但都与大脑功能连接性增强相关。例如,中性音乐可致枕叶功率谱密度降低以及枕叶和额叶功能连接增强,令人感到快乐音乐也可增强枕叶和右颞叶功能连接^[58]。

芳香疗法作为新型干预手段可直接对个体的心理状态产生影响。研究表明,吸入香气的类型与抗焦虑作用相关^[59]。芳香疗法可能通过影响杏仁核和前额叶皮质的兴奋性对焦虑情绪产生抑制作用^[60],而中缝核 5-HT 神经元在嗅球和前额叶皮层之间的信号转导中扮演着重要角色,抑制 5-HT 信号通路可预防或减轻小鼠在应激反应中的焦虑情绪,据此推断芳香疗法减轻焦虑的信号环路与分子基础^[61]。在芳香疗法中,香气分子首先被鼻腔内部的黏液溶解,然后与嗅觉受体结合并在受体神经元内产生动作电位和电信号,再传送至嗅觉皮层,经初步处理,最终由杏仁核、海马体和下丘脑等情绪调控相关的脑区进行处理^[62],起到缓解焦虑情绪的作用。

3 小结与展望

临床试验和流行病学研究表明,健康行为可起到调节焦虑情绪的作用,各类健康行为干预主要通过影响与焦虑情绪发生相关的关键脑区,增加其功能连接,从而达到缓解焦虑情绪的目的。而调控焦虑情绪的大脑区域与肠道联系密切,二者之间存在着双向调节关系,这种肠脑交流活动可能与胃肠道的感觉信息传递相关,并由此转化为神经传导、激素分泌和免疫调节信号^[63]。

健康行为干预可以在不摄入药物的情况下以更低的成本达到减轻焦虑情绪的效果,并具有被广泛使用的可能性。未来相关研究可考虑从健康行为干预与调控焦虑情绪的关系出发,进一步探索脑区活动与肠道变化的内在作用机制,将宏观层面的外在情绪改变与微观层面的分子调节机制相结合。健康运动、健康饮食、健康娱乐三位一体的健康行为综合干预措施对焦虑情绪的调控作用效果较好,应考虑在未来的研究中通过实施长期追踪随访以确定该干预措施的远期效果。

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(本文编辑: 陈霞)

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- (收稿日期: 2022-10-30)
(本文编辑: 陈霞)