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•论著•

基于肠道菌群-肠-脑轴双向调节探讨五行音乐疗法治疗高血压伴发焦虑的机制

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摘要: 随着人们生活节奏和压力的增大, 高血压患者易伴发焦虑等情志和心理障碍, 焦虑情绪进一步加剧血压波动, 影响降压药的临床疗效。高血压伴发焦虑的调控与肠道菌群-肠-脑轴间的双向调节密切相关。一方面, 高血压伴发焦虑可激活肠道免疫系统, 改变肠道菌群分布和结构; 另一方面, 肠道菌群经由中枢神经、迷走神经等多种途径对机体血压和情绪产生影响。五行音乐疗法具有辨证施乐、调节机体、动荡血脉的作用, 从而达到治疗高血压和调理情志的效果, 而肠道菌群-肠-脑轴有可能参与了此过程。文章基于肠道菌群-肠-脑轴双向调节的特点, 探讨五行音乐疗法治疗高血压伴发焦虑的可能机制, 为临床治疗高血压伴发焦虑提供借鉴与探索。

关键词: 五行音乐疗法; 高血压; 焦虑; 肠道菌群-肠-脑轴; 非药物疗法; 机制

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Discussion on the mechanism of five elements music therapy with the two-way adjustment of intestinal flora-gut-brain axis in treating hypertension combined with anxiety

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Abstract: With the increase of people's life rhythm and pressure, hypertensive patients are prone to emotional and psychological disorders such as anxiety. Anxiety further aggravates blood pressure fluctuations and affects the clinical efficacy of anti-hypertensive drugs. The regulation of hypertension with anxiety is closely related to the two-way regulation of intestinal flora-gut-brain axis. On the one hand, hypertension accompanied by anxiety can activate the intestinal immune system and change the distribution and structure of the intestinal flora; on the other hand, the intestinal flora affects the blood pressure and mood of the body through various channels such as the central nervous system and the vagus nerve. The five elements music therapy has the effects of syndrome differentiation xerox, regulating the body, and turbulent blood, so as to achieve the effect of treating high blood pressure and regulating emotions, and the intestinal flora-gut-brain axis may participate in this process. Based on the characteristics of the two-way regulation of intestinal flora-intestine-brain axis, this article explores the possible mechanism of the five elements music therapy in the treatment of hypertension with anxiety, and provides reference and exploration for clinical treatment of hypertension with anxiety.

Key words: Five elements music therapy; Hypertension; Anxiety; Intestinal flora-gut-brain axis; Drug-free treatment; Mechanism

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高血压 (high blood pressure, HBP) 是心血管疾病最普遍且可改变的危险因素, 并直接影响心血管及其相关疾病的发病率和病死率, 尽管一直以来医生和患者都在致力于改变生活方式和改进药物治疗, 然而全球范围内的血压控制率仍然很低, 在我国情况也是如此^[1-2]。现有研究显示, 患者的焦虑等不良情绪对HBP有显著诱发作用, 而HBP患者或出于对疾病的担心亦常伴发焦虑^[3]。基于此种情况, 临床药物常使用降压联合抗焦虑治疗, 但血压控制的稳定性并不十分理想, 同时由于药物本身的副作用, 联合用药不良反应事件发生的概率亦随之增加^[4]。已有研究证实, 肠道菌群 (gut microbiota, GM) 通过代谢产物、神经递质、免疫信号通路等多种途径对大脑结构功能产生影响, 进而使得机体血压和情绪产生变化^[5-7]。GM与肠道神经系统 (enteric nervous system, ENS)、中枢神经系统 (central nervous system, CNS) 形成了双向互动交流的新通路: 肠道菌群-肠-脑轴^[8]。五行音乐疗法作为一种非药物干预手段已越来越多地被运用于临床, 其基于中医五行理论, 通过五音影响与之相关的脏腑, 达到防病治病的目的, 能有效改善HBP伴发焦虑状态, 但其具体

机制尚不清楚^[9]。现就GM与HBP伴发焦虑的关系及五行音乐疗法治疗HBP伴发焦虑的可能作用机制进行探讨。

焦虑与HBP的相关性

现代生物-心理-社会医学模式的提出, 主张在生物医学的基础上, 对心理和社会因素的研究调控进行关注。HBP患者通常伴随焦虑等不良情绪改变, 其发生与发展往往随着心理负担的渐进加重伴有精神压力、愉快感缺乏、持久的情绪低落、入睡困难等诸多负面情绪障碍。长期焦虑的不良情绪一方面导致机体自主神经功能和下丘脑-垂体-肾上腺轴 (hypothalamus pituitary adrenal axis, HPA) 功能调节失衡, 过度激活交感神经系统 (sympathetic nervous system, SNS), 使机体心率、心肌收缩力、血管外周阻力过度增加^[10-11]; 另一方面会使机体免疫系统功能发生紊乱, 体内呈慢性炎症状态, 血管平滑肌释放炎症因子被激活, 形成泡沫细胞, 促进了动脉粥样硬化的形成, 使得血管壁的弹性较正常水平下降, 外周血管的阻力随之增高, 导致机体血压波动幅度增大^[12]。焦虑情绪对机体的影响降低了临床药物降压的疗效和患者的依从性, 形成不良循环^[13-14]。

GM调控焦虑及HBP的机制

GM已逐渐成为心血管、情志疾病的研究热点,主要由厚壁菌门、拟杆菌门、放线菌门和变形菌门组成^[15]。影响GM的重要因素包括宿主遗传因素、早期口服抗生素、饮食等^[16-17]。GM组成和结构的改变对机体功能和疾病的发生如高血压、精神疾病等产生影响^[18],这种影响与肠-脑轴双向调节机制密切相关^[19-20]。

肠-脑轴指在胃肠道和CNS间供机体生化信号进行传递交流的通路,经由机体神经、免疫和激素等连接起来的网络,即肠道和大脑之间进行密切地信息交换,广义的肠-脑轴涵盖CNS、神经免疫系统、神经内分泌系统、HPA系统、自主神经系统(autonomic nervous system, ANS)、ENS和GM^[21-23]。ENS又被称为“第二大脑”,它能通过自主调控SNS(如椎前神经)和副交感神经(如迷走神经)与机体CNS发生相互作用,充当了胃肠道与CNS的中间通路^[24]。ENS的感觉神经元受到信号刺激后,吸收调控位于肠道内的30多种神经递质,并将肠道信号向上传递到大脑。肠道内神经递质与大脑内神经递质有很大程度相同,譬如肠道内存在超过50%多巴胺和超过90%五羟色胺,这些神经递质在大脑、肠道间的双重作用不仅对肠-脑轴的协调平衡起着重要的作用,同时亦与情绪调节有着密切的联系^[25-26]。

基于既往研究,GM影响HBP及焦虑情绪的可能机制:①GM代谢产物短链脂肪酸(short chain fatty acids, SCFAs)可以直接扩张血管,降低血压^[27],另外两个代谢产物氧化三甲胺(trimethylamine-N-oxide, TMAO)及脂多糖(lipopolysaccharide, LPS)则主要是促进动脉粥样硬化,增加血小板聚集,并有一定程度升高血压的作用^[28-29];②GM可通过辅助性T细胞17(T-helper type 17, Th17)、调节性T细胞(regulatory T, Treg)等介导的免疫炎症反应影响血压^[30];③GM失衡刺激促炎细胞因子形成,炎症诱导氧化应激,而高氧化应激状态可导致低密度脂蛋白(low density lipoprotein, LDL)氧化,形成氧化低密度脂蛋白(oxidized low density lipoprotein, oxLDL),可能引起血管舒张因子水平降低及血管收缩因子水平升高,进而使得血管外周阻力增加,血压水平随之升高^[31];④焦虑情绪抑制CNS,进一步激活HPA轴和SNS,诱发炎症,改变GM结构和组成,而益生菌也可以通过反向调节,改善焦虑情绪^[32-33](图1)。

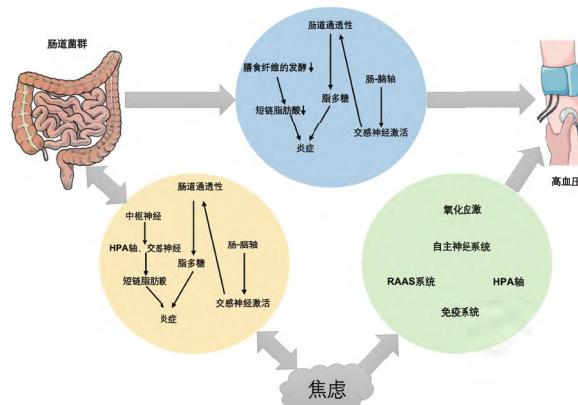


图1 GM、焦虑情绪及高血压相互影响的途径

五行音乐对HBP伴发焦虑的作用研究

1. 五行音乐的中医理论基础 五行音乐疗法是基于中国传统文化和中医《黄帝内经》的五行理论,将音乐归类为木、火、土、金、水五音,与中医五脏(肝、心、脾、肺、肾)、五志(怒、喜、思、悲、恐)相结合,形成的一种身心同调的非药物疗法^[34]。《灵枢·邪客》云:“天有五音,人有五脏;天有六律,人有六腑”,角、徵、宫、商、羽5种不同调式音乐的声波振荡,对生物体内气的运动方式产生影响,这个“气”即包含情绪,亦包含五脏之气^[35]。运用中医五行相生、相克又相互制约的原理及中医临床辨证分型和患者个体化差异,通过适当选择对应木音、火音、土音、金音、水音对机体起到身心同调的作用。音乐经由听觉、神经系统与机体脏器间形成互动、调控,不同调式的音乐对机体会产生不同的调节和影响,其中“角动肝……羽动肾”的理论广为流传。临床实际运用中,自然界天地阴阳二气和人体之气机的运行都会因人因时因地改变,个体差异如性别、年龄、本身情绪状态及症状表现的变化,均可不同程度地对机体气机运化产生影响使其失去平衡。传统的五行音乐治疗遵循中医理论和五行生克制化,根据不同时间、不同个体、不同证型辩证施乐^[36-37]。

2. 五行音乐可以改善患者焦虑情绪,调控HBP 随着人们生活水平的提高和对非药物疗法需求的增加,临床音乐疗法作为一种非药物治疗手段运用于HBP及改善焦虑的研究报道逐渐增多,并取得了一定的进展,音乐疗法被认为是一种有效的非药物调节血压水平的手段^[38-39],其具体可能作用机制如下^[40-41]:①神经系统作用:音乐治疗可使副交感神经兴奋,降低交感神经兴奋度,从而对机体产生镇静、降压等效果。同时能够降低血管紧张素Ⅱ

(angiotensin II, AngII)的水平,使得内分泌系统恢复正常而发挥降压作用。音乐刺激调节大脑皮质功能,缓解焦虑、烦躁的情绪,使得患者的肌肉得到放松,降低其血管壁紧张度,从而使得血压下降。②同频共振作用:音乐是一种声波经由耳源传入体内,当它的振动频率、节律及强度与机体内在振动频率协调一致时,便会发生同步和谐的声波共振,激发机体潜能^[42]。通过振幅的改变又可以影响到脑干网状结构以及大脑边缘系统。③生理心理作用:音乐治疗能够对机体神经系统的活力和细胞兴奋性起到提高作用,进而对机体生理活动产生正向调控作用,降低个体的紧张感,使不良的情绪得到舒缓,达到更好的降压效果。

讨论

HBP的难治性与焦虑密切相关,相互影响,警示临床医生对此类人群应及早识别并重视早期的综合治疗。既往研究已证实,GM与焦虑情绪之间通过肠-脑轴实现相互作用,相互影响,二者对调控血压水平均具有重要作用。益生菌可通过改变GM的组成改善焦虑症状,同时也为HBP的治疗带来了新的进展^[43];与此同时,抗焦虑药物也被用于辅助治疗HBP,且其对GM结构亦产生影响^[44]。尽管治疗方向不同,但调控GM和抗焦虑治疗对HBP的防治都取得了一定进展,这为非药物介入HBP的防治提供了新的可能靶点。

随着更多研究的深入,结合“双心医学”“心脾相关”理论及中土五行模式与GM相关性的探讨,肠道微生态参与人体代谢的途径逐渐成为心血管疾病治疗的药理学靶点^[45]。在HBP伴发焦虑的防治中,五行音乐作为非药物疗法,已被写入治疗HBP伴发焦虑的专家共识^[46]。不仅如此,相关研究也已经证实了五行音乐疗法能够达到身心同治的目的,即有效减轻胃肠道症状的同时调节GM,进而改善患者神经功能紊乱^[47]。基于肠-脑轴的双向调节机制,笔者推测在五行音乐治疗HBP伴发焦虑的同时,也伴随着GM结构及数量的变化。下一步,我们将进一步研究辨证施乐对HBP伴发焦虑不同证型的影响,检测相对应的GM结构和数量的变化,以期为五行音乐治疗HBP伴发焦虑内在机制的研究提供新的视角,也为非药物疗法防治心血管疾病并发病志改变提供更多的选择。

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