·综述·

老年抑郁与衰弱双轨迹的研究进展

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【摘 要】 老年人抑郁和衰弱双重障碍发生率高,且常同时发生,易导致一系列不良健康结局,严重影响其身心健康。基于组轨迹模型为识别两者间的异质性发展轨迹,分析抑郁和衰弱的纵向因果关联,提供了新的研究视角,对于应对老年共病态势具有重要意义。因此,本文从基于组轨迹模型的概念内涵,老年抑郁与衰弱双轨迹现状、相关性机制、关联、影响因素和干预措施进行综述,旨在为临床决策精准化提供方法学上的补充。

【关键词】 老年人;基于组轨迹模型;抑郁;衰弱;疾病轨迹;综述
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Research progress on dual trajectories of depression and frailty in the elderly

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【Abstract】 The prevalence of dual difficulties of depression and frailty is quite high in the elderly, often occurring concurrently, and leading to a series of adverse health outcomes that seriously affect their physical and mental health. Group-based trajectory modeling provides a new research perspective for identifying the heterogeneous developmental trajectories between depression and frailty and analyzing their longitudinal causal relationship, which is of great significance for addressing the comorbidity situation in the elderly. Therefore, in this article, we reviewed the concept connotation based on the group-based trajectory model, current status, correlation mechanism, association, influencing factors and intervention measures of the dual trajectories of elderly depression and frailty, aiming to provide methodological supplements for the precision of clinical decision-making.

【Key words】 aged; group-based trajectory model; depression; frailty; disease trajectory; review
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随着老龄化进程的加速,我国抑郁和衰弱问题愈加严峻[1]。研究表明,抑郁和衰弱共病性显著增加了老年人的死亡风险[2]。因此,识别疾病不同发展轨迹,阐明两者间的发病关联和潜在机制,对追踪老年高危人群、预防疾病及实施个性化护理干预具有重要意义。目前,国内关于抑郁和衰弱的关联多集中于横断面和随访研究,但对两者间的动态发展关系研究不足,而基于组轨迹模型能够有效识别总体中不同的发展轨迹,通过分析抑郁和衰弱疾病双轨迹研究现状,捕捉抑郁和衰弱之间的双向动态依存关系,研究轨迹与预测因素或结果间的联系[3],为不同轨迹组患者提供个性化决策和护理干预具有重要意义。因此,本研究就基于组轨迹模型进行阐述,并就其在国外老年抑郁与衰弱疾病双轨迹的研究进展进行综述。

1 基于组轨迹模型概述

基于组轨迹模型(group-based trajectory modeling, GBTM)又被叫做潜类别增长模型(latent class growth analysis, LCGA),最早由 Nagin 等[4]提出,并将其应用于犯罪学领域,现被广泛应用于心理学[5]及医学[6]。GBTM 在医学中的应用,主要是通过识别目标患者群体结局指标随时间变化的轨迹,将不同轨迹水平的患者分配到轨迹亚组,使亚组间差异显著,而组内患者具有相近的轨迹,为医护人员提供了一种描绘不同疾病发展轨迹与预测因素和结果相关联的便捷化统计工具,以可视化反映患者的疾病变化[7]。

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基于组轨迹模型的老年抑郁与衰弱双轨迹是指构建以时间为横轴,以抑郁程度、衰弱状态为纵轴的轨迹模型[8],研究老年人抑郁程度与衰弱状态随时间的纵向变化情况,通过深入探索抑郁和衰弱的双向关联,阐明老年共病机制,以期为全程、全方位的共病管理提供理论依据。

2 抑郁轨迹与衰弱轨迹的研究现状

2.1 抑郁轨迹的研究现状

抑郁症主要由神经递质功能及体液因子等机制介导,辅以环境和心理因素[9],及时发现老年人抑郁不同发展轨迹,探索不同轨迹的预测因素,将有助于医护人员识别不同轨迹的需求差异,有效逆转抑郁症状的加重。Killeen 等[10]发现,与无感觉障碍的老年人相比,有听力、视觉和双重感觉障碍的老年人,从低抑郁进展为高抑郁的风险明显增加。Lim 等[11]发现性别、年龄、住房拥有率和三种以上的慢性病是区分抑郁不同轨迹组的预测因素。

2.2 衰弱轨迹的研究现状

衰弱作为一种老年综合征,本质上是动态发展的,并且早期衰弱是一个可逆过程[12],因此,识别不同的衰弱轨迹被认为是逆转衰弱、降低衰弱发生、防止衰弱恶化的有效措施。Bae 等[13]发现衰弱和主观认知能力下降有相似轨迹,同时发现快速进行性衰弱组和主观认知能力下降组的抑郁症状和步态速度缓慢的发生率较高,为医护人员提供针对性干预借鉴,即通过增强心理健康和改善步态速度,有效减轻或逆转老年人衰弱和认知能力增加风险。Guo 等[14]发现衰弱存在低而稳定、中等且增加、高且增加 3 条轨迹,发现高龄、女性、教育水平低、农村居住、身体活动水平低以及居住在中国东北等因素与衰弱的快速进展有关,而适度饮酒与低而稳定的衰弱轨迹相关。

3 抑郁和衰弱双轨迹的关联

GBTM 通过识别抑郁和衰弱相似发展轨迹的个体,将其划分为不同的轨迹组,以揭示抑郁和衰弱老年人群内部的异质性。Yuan 等[8]使用 GBTM 多轨迹建模来拟合衰弱、认知障碍和抑郁症状的并发轨迹,得到了 4 种不同的衰弱、认知障碍和抑郁症状轨迹,结果显示,超过七分之一的老年人同时遵循“抑郁”“衰弱恶化”及“认知障碍恶化”的轨迹。Lohman 等[15]发现,抑郁轨迹和衰弱轨迹都与两种不良结果(入院和严重跌倒)的可能性增加有关。Suprawesta 等[16]采用 GBTM 识别潜在的认知衰弱轨迹群,发现即使处在认知衰弱进展轨迹,通过降低抑郁状态也能得到改善。

抑郁和衰弱双轨迹的这种关联性可以通过共同的病理生理机制来解释。(1)神经生物学基础。研究表明[17,18],衰弱的严重程度与总白质高信号的增加和灰质体积的降低相关,特别是在皮质下区域,这显著介导了衰弱与抑郁发生的关联,被认为会影响大脑信息的正常传递,从而导致抑郁的发生。(2)慢性炎症。在抑郁和衰弱两类人群中均存在促炎细胞因子水平增高,主要包括白细胞介素-6(interleukin-6,IL-6)、肿瘤坏死因子-α(tumor necrosis factor-alpha, TNF-α)、C 反应蛋白(C-reactive protein, CRP)等,促炎细胞因子通过增加肌肉蛋白质的降解[19],间接导致衰弱特定表征的缺陷,包括肌肉力量下降、行动迟缓和疲劳等,同时,炎症过程也会对中枢神经系统产生负面影响,特别是基底神经节中的多巴胺功能,从而导致抑郁情绪的发生。(3)线粒体功能障碍。线粒体功能障碍已在抑郁症中被发现[20],抑郁症患者的肌肉活检显示线粒体吸收 O_2 转化为三磷酸腺苷(adenosine triphosphate, ATP)生成的能量转化减少,以及线粒体呼吸受损,与衰弱症状密切相关。(4)下丘脑-垂体-肾上腺轴(hypothalamic-pituitary-adrenal axis, HPA)功能失调。HPA 是介导身体和中枢神经系统(central nervous system, CNS)压力影响的主要生物系统之一,衰弱与 HPA 异常调节造成皮质醇水平增加、胰岛素样生长因子和睾酮水平降低有关,从而导致肌肉功能减退,而抑郁的发生也与 HPA 功能衰退有关[21]。

4 抑郁和衰弱双轨迹的影响因素

4.1 人格特质

研究表明,人格特质是老年人抑郁和衰弱同时出现的危险因素,这可能与人格影响老年人的身体活动、健康行为和情绪变化有关[22]。Stephan 等[23]发现,高神经质、低责任心、低外向性、低开放性和低宜人性与老年人衰弱程度增加有关。Ho 等[24]表明,低外向性、低责任心及高神经质可以显著预测抑郁症状的发生。

4.2 睡眠质量

睡眠是一种受昼夜节律、稳态和神经激素过程调节的生物行为现象[25]。研究显示,睡眠质量、抑郁和衰弱之间存在关联,良好的睡眠质量可使身体和大脑得到恢复和修复,促进身体机能和心理健康的维持,进而减少抑郁和衰弱的发生[26]。Liu 等[27]发现,与身体健康的老年人相比,睡眠质量差和午睡时间长的

老年人出现认知衰弱的风险更高。然而,较短的午睡时间与较低的认知衰弱风险相关。Nielson 等[28]同样表明,睡眠问题和抑郁症状在老年人中常高度并存,短睡眠(<7 h)、长睡眠(>8~9 h)以及失眠症状都是导致老年人抑郁发生的危险因素。

4.3 多病共存

多病被定义为同一人同时发生两种或多种慢性疾病,包括糖尿病、癌症、高血压等,而多病共存会使老年人生理储备量降低从而导致多系统紊乱,进而加速抑郁和衰弱的发展[29]。Gobbens 等[30]发现多病共存与身体衰弱存在强相关性,与心理和社会衰弱相关性较低。同时表明,多种慢性疾病与衰弱变量的关联强度因疾病而异。

4.4 定期锻炼

定期锻炼可影响抑郁和衰弱症状的生物过程,如脑血流量和神经营养因子的升高、灰质体积增加、多巴胺传递增快及促炎细胞因子水平的减少,进而促进神经系统及肌肉功能的恢复[31,32]。Jang 等[33]指出,可将定期锻炼作为纵向识别衰弱轨迹亚组和区分轨迹模式的预测因子。同时,通过长期有规律的体育锻炼,改善老年人的抑郁症状[34]。

5 抑郁和衰弱双轨迹的干预措施

老年抑郁和衰弱是一种复杂且多维的临床综合征,因此,与单一学科、单一干预措施相比,多学科、多领域干预更能有效减少和逆转抑郁和衰弱的发生。多学科干预是指由护士、老年病医师、营养师、物理治疗师及心理学家等组成的多学科团队,对老年抑郁和衰弱共病患者提供疾病全程的身心功能筛查和评估,以便实现综合性医疗服务[35]。多领域干预包括运动干预、营养干预及睡眠干预等[36,37],其中抗阻运动和有氧运动是最常见的运动干预方式,营养干预则包括坚持地中海饮食、生酮饮食及北欧饮食等健康的饮食模式,以及补充蛋白质、ω-3 多不饱和脂肪酸及维生素 B 等,同时,目前常用的睡眠干预方法主要包括光照疗法、睡眠卫生干预、认知行为疗法等。

综上,GBTM 为分析老年抑郁和衰弱的纵向关联提供了新的研究视角,通过描述各轨迹的内在结构特征及其存在的影响因素,有助于揭示轨迹组间的内在异质性,为全面掌握抑郁与衰弱双轨迹的动态发展规律奠定理论依据。老年抑郁与衰弱双轨迹既相互关联又具有各自的特征。然而,目前关于老年人群抑郁症状与衰弱状态的双轨迹研究大多聚焦在两者的关联程度,忽视了两者关联的异质性,未来仍需不断深入研究,以期通过了解两轨迹组间内部复杂结构及疾病严重程度,促进对高危患者的早期识别与干预,预防不良疾病结局的发生。同时,在今后的临床工作中,针对抑郁和衰弱双轨迹的筛查和诊断,应统一指标测量工具和分析框架,提高研究的可信度。此外,加强抑郁与衰弱双轨迹相关预测因素的分析,为两者间的潜在因果关系提供证据支持,同时为医护人员制定针对性的预防和干预措施提供决策支持,进而促进动态干预措施的研究,以更有效的方式应对逐年加剧的老年抑郁和衰弱共病态势。

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