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老年人衰弱与认知障碍之间的联系

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摘　要

随着年龄的增长，在老年人中，衰弱和认知障碍越来越普遍，也逐渐提出了认知衰弱这一新概念，可见，衰弱和认知障碍之间存在一定的联系，本文旨在对老年人衰弱和认知障碍的发生机制、危险因素及两者之间的关系做出综述，希望能为探索衰弱和认知障碍提供新思路，也为有效预防衰弱和认知障碍提供帮助。

关键词

衰弱，认知障碍，联系，发生机制

Association between Frailty and Cognitive Impairment in Older Adults

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Abstract

Frailty and cognitive impairment are becoming more common in the elderly with increasing age. Also gradually put forward the cognitive frailty, a new concept, so there is a certain relationship between frailty and cognitive impairment, the purpose of this paper is to make a review for the relationship between the elderly frailty and the occurrence mechanism of cognitive impairment, risk factors, hoping to provide new thinking for exploring frailty and cognitive impairment, and provide help to effectively prevent frailty, and cognitive impairment.

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Keywords

Frailty, Cognitive Impairment, Link, Mechanism

1. 引言

衰弱(frailty)是一种复杂的与年龄相关的临床疾病，其特征是多个器官系统的生理能力下降，从而导致对应激源的敏感性增加[1]。常见的认知功能障碍包括轻度认知功能障碍(MCI)和痴呆，MCI 是介于认知功能正常和痴呆的中间状态，对 MCI 的干预可延缓痴呆的发生发展[2]。认知障碍可能是身体衰弱的临床特征，或共同的背景因素可能使人们易发生这两种状况[3]。在老年人中，衰弱和认知障碍是相关的，并且经常共存[4]，一项研究发现，53%的体弱多病者有认知障碍[5]。2001 年有人首次提出了“认知衰弱”的概念[6]，直到 2013 年，国际营养与老化学会和国际老年学和老年病学协会第一次提出了认知衰弱的诊断标准：同时存在身体衰弱和轻度认知障碍，即 CDR (临床痴呆评定量表) = 0.5，并除外并发痴呆或其他痴呆[7]。衰弱和认知障碍可致多种不良健康结局的发生，法国一项为期一年的多中心随访的队列研究显示：1306 名年龄在 75 岁或以上的患者，一年后，84 名受试者(34%)经历认知快速下降，377 名(36%)被送入机构，445 名(34%)死亡[8]。故了解身体衰弱和认知障碍之间的联系将有助于制定干预措施[9]。

2. 衰弱和认知障碍的发病机制

轻度慢性炎症、应激相关反应能力降低、线粒体功能障碍、胰岛素抵抗、内分泌途径改变和中枢神经系统衰竭是衰弱的主要背景[10]。“炎症老化”一词是由 Franceschi 和他的研究小组创造的，用来表示年老时炎症反应的上调，由此产生的低度慢性全身促炎症状态[11] [12]，这种状态是大多数年龄相关疾病的基础。炎症和抗炎共同决定了许多具有衰老表型特征的进行性病理生理变化[13]。促炎细胞因子，如白介素-6 (IL-6)和肿瘤坏死因子-α (TNF-α)已广泛涉及社区老年人的身体衰弱[14] [15]，而 TNF-α 的上调在痴呆(AD)患者中已被观察到[16]。在衰弱的发病机制中，内分泌失调的作用也一直是一个广泛研究的课题，在衰弱的老年人中发现血清合成代谢激素胰岛素样生长因子 1 (IGF-1)和脱氢表雄酮硫酸酯(DHEAS)水平较低[17] [18]，与正常对照组相比，AD 患者的 IGF-1 循环水平较低[19] [20]。除了个体的有害影响外，观察到的 IGF-1 和 IL-6 联合降低致残和死亡风险，提示炎症和内分泌失调的潜在叠加效应[21]。此外，在体内和体外都观察到了合成代谢激素和促炎细胞因子之间的复杂关系，包括 IL-6 下调 IGF-1，以及 DHEAS 潜在的免疫调节作用[9]。在 10 年的随访中，较高的水平的白细胞分类计数(WCC)，较低水平的脱氢表雄酮硫酸酯和较高的皮质醇 DHEAS 比率都与衰弱的增加显著相关。WCC 和皮质醇 DHEAS 在随访时可以用于明显区分身体衰弱的个体[10]。身体衰弱的受试者血清胰岛素样生长因子-i (IGF-I)和硫酸脱氢表雄酮(DHEA-S)水平较低，IL-6 水平高于非衰弱的个体。在衰弱的人群中，IGF-I 和 IL-6 呈负相关，而非衰弱的人群中，IGF-I 和 IL-6 呈负相关，这表明内分泌和免疫/细胞因子失调之间可能存在相互作用[22]。在 10 年的随访间，端粒磨损越快，随访时握力越低。在同一时期，当调整炎症水平时，这种关联完全减弱。类似地，较高的炎症水平与随访时较低的握力相关。然而，当端粒磨损调整后，这些相关性保持不变[23]。

人类的老化伴随着典型的大脑结构和神经生理变化以及不同程度的认知衰退[24]。与年龄相关的记忆障碍与大脑和血浆抗氧化剂的减少有关[25]。研究表明，与认知正常的老年人相比，MCI 患者不同脑区的蛋白质羰基水平增加[26] [27]。线粒体功能障碍与正常的大脑衰老和神经退行性疾病有关[28]。

3. 衰弱与认知障碍发生的危险因素

一项有效调查了 1627 位居住于上海社区的 75 岁及以上老年人的研究，采用衰弱表型(PF)及简易智能精神状态量表(MMSE)进行评估，研究结果显示：55.7%存在身体衰弱，40.3%患有轻度认知障碍，另外，高龄、营养不良或营养不良风险、抑郁是身体衰弱和认知障碍的共同影响因素[29]。来自中国西部健康与老龄化趋势(WCHAT)研究的 4103 名 60 岁及以上社区老年人，78.8%既没有衰弱也没有认知障碍、3.9%存在单纯衰弱(PF)、14.5%存在单纯认知障碍(CI)、2.9%两者都存在。单纯 PF、单纯 CI 及两者都存在的患病率与年龄、文化程度和单身有关，不同类型的 PF 和 CI 的在患病率上存在明显的种族异质性。与两者都没有的患者相比，衰弱和/或认知障碍与抑郁、日常生活能力下降和营养不良的相关性更高，值得注意的是，肥胖仅与 PF 显著相关，而与 CI 或两者均不相关[30]。一项在上海及北京多家医院的社区卫生服务中心和养老院，选取就诊的 546 例年龄 ≥ 60 岁的老年人为研究对象，建立了一种老年认知障碍风险简易预测模型，该模型认为对于认知障碍高危人群，应考虑年龄、文化程度、直系亲属痴呆史、主观认知下降、衰弱状态、代谢综合征和低白蛋白血症等因素的综合作用，可以快速、简便评估个体认知障碍风险[31]。文化程度、过去 1 年跌倒史、平衡功能是养老机构衰弱老年人容易发生轻度认知功能障碍的影响因素[32]。

4. 衰弱与认知障碍的关系

多项研究表明，衰弱与认知障碍有关，并认为，认知状态与衰弱呈正相关，认知能力越差衰弱程度越高[33]，与非衰弱老年人相比，衰弱老年人的认知能力普遍较低[34]，衰弱老年人发生 MCI 是无衰弱老年人的 1.6~2.5 倍[35] [36]。衰弱前期受试者认知障碍的患病率高于正常认知老年人，衰弱的人比衰弱前期的人认知功能障碍的患病率更高[3]。体弱多病的人经历认知能力下降的可能性是正常人的两倍[16]。

4.1. 衰弱表型和认知表型方面

巴西圣保罗 384 名居住在社区的 65 岁及以上老年人，衰弱老年人在大多数认知变量方面的表现显著低于衰弱前期及非衰弱老年人。握力和年龄与 MMSE 表现相关，年龄与记忆回忆延迟相关，步态速度与语言流畅性和 CDT (画钟实验)表现相关，教育程度与 CDT 表现相关[37]。衰弱老年人认知领域中的执行能力及记忆力维度得分较非衰弱老年人低[38]。养老机构衰弱老年人容易发生轻度认知功能障碍[32]。对 2737 名认知正常老年人进行为期 4 年的前瞻性研究，身体衰弱，表现为体重过轻、握力较弱、起坐测试较慢、男性步长较短、女性握力较弱，在四年的时间里与认知能力下降有关[39]。同样，在另外一项年龄偏大的老年患者样本中，经过 4 年的随访发现，更好的注意力、处理速度和记忆功能与较慢的握力下降有关[40]。对大量老年女性样本的纵向观察也证实了早期认知障碍的存在，突显出认知能力的下降先于步速和握力的下降[41]。60 岁以上住院患者，衰弱发生率较高，与年龄、文化程度关系密切，可导致总体认知功能障碍，以时间定向力、地点定向力、注意力和计算力、延迟回忆、视空间障碍为主[42]。布什尔老年人健康(BEH)计划的横断面分析中，研究对象为 60 岁人群(N = 2336)，在调整了相关危险因素后，认为认知障碍与衰弱表型中的低体力活动、低握力、低行走速度有关；衰弱与认知障碍表型中的定向力和执行功能有关，而与记忆力无关[3]。当将握力作为连续性变量进行分析时，其每增加 1 kg，认知得分增加 0.07 分，认知障碍的发生风险降低 6%。提示老年人的握力水平与认知功能表现呈正相关，握力较低与认知障碍风险增加相关[43]。最近，一项基于人群的纵向研究证实了上述认知-运动的趋势，并强调了

不同年龄之间的潜在差异：与年轻人相比，老年人(85 岁至 90 岁)认知能力较差与步态速度和握力的急剧下降有关[44]。基于运动认与知的关系，提出了一个新概念，即运动认知风险综合征(MCR)，是一种痴呆前综合征，其特征是无痴呆或行动障碍的老年人同时存在主观认知障碍和步态缓慢。一项基于爱因斯坦老化研究的前瞻性队列研究，患有 MCR 的老年人患痴呆的风险是常人的 3 倍，血管性痴呆的风险是常人的 12 倍[45]。步速缓慢和 MCR 与衰弱风险增加相关。然而，在主观认知下降和衰弱之间没有发现显著的联系[46]。

4.2. 衰弱和认知障碍结局方面

老年墨西哥裔美国人随着 MMSE 分数的下降，衰弱个体的百分比呈线性增加，衰弱和认知障碍是死亡的独立危险因素。与认知障碍相比，衰弱是老年墨西哥裔美国人死亡的一个更强的预测因素[47]。一项对来自耶路撒冷纵向队列研究的 840 名 85 岁及以上社区居民的具有代表性样本进行研究，衰弱、衰弱前期、无衰弱的 5 年死亡率分别为 44.5%、20.4%、13.6%，有和没有认知障碍的衰弱受试者的死亡率分别为 54.2%、54.9%。衰弱的 5 年死亡率危险比为 3.861，认知障碍为 1.25，最后认为衰弱状态与认知功能障碍显著相关，仅衰弱可预测随后的死亡率[48]。衰弱指数似乎对死亡预测的改善最大，其次是衰弱表型、MMSE、握力和行走速度[49]。然而，也有研究显示，身体衰弱的人，如果他们还患有认知、社会或心理衰弱，并不会更容易出现虚弱的负面后果，如日常生活能力的下降、生活质量下降和再住院率[50]。

5. 未来与展望

本文介绍了关于衰弱和认知障碍之间联系的最新研究进展，主要从发病机制、危险因素及两者之间的联系三大方面进行阐述。虽然关于衰弱和认知障碍目前已取得了一定进展，但仍需大规模的流行病学调查，进一步明确衰弱和认知障碍的好发人群，同时也需要简便易于获取的实验室指标早期发现这一人群，另外，还需进一步探索衰弱和认知障碍的预防及干预措施，对这一人群早期采取预防及干预措施，延缓老年综合征的发生。

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