

老年人睡眠问题与主观认知下降的关联研究进展

赵延青

山东大学齐鲁医学院公共卫生学院流行病学系, 山东 济南

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摘要

随着全球人口老龄化的加剧, 老年人的健康问题日益突出, 其中认知健康与睡眠障碍的关联备受关注。主观认知下降(SCD)作为阿尔茨海默病(AD)的临床前阶段, 可显著增加进展为轻度认知障碍(MCI)和AD的风险。本文系统综述了老年人睡眠问题与SCD的关联研究进展。流行病学数据显示, 认知正常的中老年人群中SCD的患病率约为40%~60%, 且存在显著的地区差异。研究表明, 睡眠问题(如睡眠不足、睡眠质量差)与SCD密切相关: 纵向研究显示SCD患者的总睡眠时间和卧床时间显著低于非SCD组, 失眠症状的恶化与自我报告记忆力下降的风险增加相关。但现有研究多基于横断面设计, 缺乏长期随访。未来需结合多组学数据、开展队列研究及个体化干预策略, 以明确睡眠与SCD的因果关联及睡眠干预对SCD的临床转化价值。

关键词

主观认知下降(SCD), 睡眠问题, 阿尔茨海默病(AD), 老龄化, 干预措施

Research Progress of the Association between Sleep Problems and Subjective Cognitive Decline in the Elderly

Yanqing Zhao

Department of Epidemiology, School of Public Health, Cheeloo College of Medicine, Shandong University, Jinan Shandong

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Abstract

With the global acceleration of population aging, health challenges among older adults have become

increasingly prominent, particularly the interplay between cognitive health and sleep disturbances. Subjective cognitive decline (SCD), recognized as a pre-clinical stage of Alzheimer's disease (AD), substantially elevates the risk of progression to mild cognitive impairment (MCI) and AD. This review systematically synthesizes the research progress of the association between sleep-related issues and SCD in older populations. Epidemiological studies indicate that the prevalence of SCD ranges from 40% to 60% among cognitively intact middle-aged and older adults, with marked geographical disparities. Studies demonstrate a robust correlation between sleep impairments (e.g. insufficient sleep duration, poor sleep quality) and SCD: longitudinal analyses reveal significantly reduced total sleep time and time in bed among SCD cohorts compared to non-SCD groups while deteriorating insomnia symptoms are associated with heightened risks of self-reported memory decline. However, current research predominantly relies on cross-sectional designs and lacks long-term follow-up data. Future investigations should integrate multi-omics approaches, prioritize cohort studies, and develop individualized intervention strategies to elucidate causal relationships between sleep patterns and SCD progression and the clinical translational value of sleep interventions for SCD.

Keywords

Subjective Cognitive Decline (SCD), Sleep Problems, Alzheimer's Disease (AD), Aging, Intervention Strategies

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1. 前言

随着全球人口老龄化进程不断加剧,老年人健康问题面临严峻挑战,同时也造成了巨大的经济负担[1][2]。在老年人群中,认知健康问题和睡眠问题[3][4]都是重要的健康问题。在许多研究尤其在老年人中发现,睡眠质量与客观的认知表现有关[4]-[6]。主观认知下降(SCD),是指个体在主观上认为自己与之前正常状态相比,有记忆或认知功能的下降,但客观神经心理测验处于正常范围[7]。SCD被认为是早于轻度认知障碍(MCI)的阿尔茨海默病(Alzheimer's Disease, AD)的临床前阶段,增加了日后认知下降及进展为AD的风险[7][8]。大多数SCD老年人存在睡眠问题,研究表明睡眠障碍可加速认知衰退及痴呆进展[9]。总结睡眠问题与主观认知关系的研究,有利于系统掌握睡眠对SCD的影响现状,阐述对理解认知老化机制、早期干预认知障碍的理论与实践意义。

2. SCD对老年人的健康影响

关于SCD的流行病学研究日益增多。国内针对不同年龄段和地区的研究,SCD患病率有所不同。基于既往人群研究,在我国认知正常的中老年人群中SCD的发病率约在40%~60%[10]-[12]。国际上,有德国和美国的研究[13][14]显示,70岁以上认知正常的老年人中,50%~80%的人自报存在SCD,与我国部分数据相近。但也有研究呈现出较低的SCD患病率,美国一项研究在1915人中SCD的患病率约19.5%[15];荷兰为19.40%[16]。这表明各国对SCD患病率的估计差异较大。

SCD在成人中的患病率受人口统计学特征[17]、遗传等因素的影响。不同种族和民族遗传背景不同,某些基因变异与认知衰退易感性相关,如载脂蛋白APOE基因的 $\epsilon 4$ 等位基因在不同种族分布不同,它是公认的阿尔茨海默病等认知障碍疾病的风险基因[18],携带该等位基因个体的大脑易出现病理变化,导致

认知下降,增加SCD风险。

同时,SCD标准难以统一,也可能是导致差异的重要因素,例如:部分研究采用单一问题快速筛查(如“是否感觉记忆力下降”),虽便于大规模操作,但可能遗漏多维度的认知担忧(如Kielb等[15]的研究);而另一些研究则通过综合问卷(如Blessed记忆测试结合ECog量表)评估,涵盖记忆、日常功能和主观担忧,提高了SCD判定的全面性(van Harten等[13])。部分工具仅关注记忆下降的存在性(如Jonker等[16]基于日常记忆表现分类),而其他研究(如Jessen[14])进一步纳入“对记忆问题的担忧程度”,将SCD细化为“有但不担心”和“有且担心”亚型,这种分类可能影响患病率的统计结论。SCD评估方法的异质性(如工具复杂度、判定维度和文化适应性)是导致患病率差异的主要原因。未来研究需推动评估工具标准化,提升结果的可比性。

SCD是早于MCI的AD的临床前阶段,AD占痴呆病例数的60%~70%[19],最近有研究表明,SCD患者相较于对照组,进展为MCI的风险增加了4.5倍,最终诊断为AD的风险增加了6.5倍[20]-[22];一项荟萃分析显示,在长达4年的研究中,14.1%的SCD患者发展为痴呆,26.6%的SCD患者继续发展为MCI[23]。聚焦AD临床前阶段的动态变化,对减轻痴呆带来的沉重疾病负担意义重大。提出SCD这一概念的关键价值在于进一步推动AD防治的关口前移,促使研究人员在AD尚未发展到明显阶段时就采取行动,极大地促进了AD二级预防相关试验研究,为早期干预和延缓疾病进程提供了新的方向与可能。而探索SCD的影响因素,这对于预防或减缓认知功能下降具有十分重要的临床意义和社会意义。

3. 老年人的睡眠问题

睡眠这一生理过程对维持机体稳态具有多重生物学意义。睡眠在促进能量物质储存、调节免疫系统[24]、记忆形成[25]等方面发挥关键作用。然而,大约有50%的55岁以上的人夜间难以入睡或保持良好的夜间休息。尽管睡眠模式会随着人们年龄的增长而变化,但睡眠障碍和醒来时疲倦并不是正常衰老的一部分[26]。老年人容易难以入睡,睡眠时间较少,并且在夜间或清晨频繁醒来,所有这些都可能导致他们获得较低质量的睡眠,这可能导致一系列健康问题,如跌倒和日间疲劳的风险增加。

睡眠问题与主观认知下降之间存在密切关联,这在多项研究中得到证实。Tsapanou等[3]对认知健康的老年人进行研究,采用医学结局研究睡眠量表(MOS-SS)中的睡眠指数II来衡量睡眠问题,涵盖入睡时长、睡眠安静程度、是否获得充足休息等9个问题,得分范围1~6分,分数越高表示睡眠问题越多。通过多因素回归模型分析发现,睡眠问题与更多的主观认知下降相关,且这种关联在调整了年龄、性别、教育程度、共病、抑郁和焦虑等因素后仍然显著。Bubbico等[27]通过纵向队列研究,对70名社区老年人进行跟踪,其中35人完成2年随访。利用腕部活动记录仪客观测量睡眠参数,发现主观认知下降(SCD)组与非SCD组在总睡眠时间和总卧床时间上存在显著差异,SCD组的总睡眠时间和卧床时间在2年观察期内明显低于非SCD组。

4. 睡眠不足与主观认知关系的研究

睡眠不足是较为突出的睡眠问题,与许多慢性病息息相关。睡眠不足不仅是肥胖症、糖尿病和抑郁症的一个已知的危险因素[28],还有可能提高阿尔兹海默症(AD)的发病风险[12],在中国,关于睡眠不足对认知能力下降影响的研究大多集中在客观认知问题上。Wang等在中国西部成年人中发现了睡眠不足与SCD之间的相关性,虽然这可能不能完全推广到中国人群中[29],但是为将来更大规模的研究提供了方向和参考,因此,需要进一步的研究来证实这些发现,并将其应用于更多的中国老年人。Zhao等[30]基于加拿大老龄化纵向研究的纵向分析显示,失眠与加拿大中老年SCD之间存在联系,基线时无失眠症状而后发展为失眠患者或者睡眠状况恶化者,自我报告记忆力下降的几率增加,自我报告记忆力下降是

SCD 判断中的重要一项, 这表明失眠或可作为干预年龄相关认知下降的早期靶点。Wardle-Pinkston 等进行了一项荟萃分析, 结果表明失眠与主观认知表现的损害有关, 强调了治疗失眠对潜在改善认知结果的效用[31]。

5. 睡眠质量与主观认知关系的研究

睡眠质量差也是典型的睡眠问题。特别是对于老年人而言, 睡眠质量差还可能是认知障碍, 如阿尔茨海默病等的早期预警信号, 与大脑神经细胞的退化和认知功能的衰退存在潜在联系。最近, 针对来自中国上海的 707 名年龄在 60 岁至 99 岁之间的成年人进行的一项横断面研究发现, 老年人较差的睡眠质量与较高的 SCD 发病率相关, 而较高的焦虑/抑郁和担忧患病率介导了这一关系, 这提示了导致 SCD 的可能机制途径[32]。韩国人群中一项横断面研究表明, 较差的睡眠质量与男女和各年龄组 SCD 患病率增加和症状加重有关[33]。相反地, 韩国一项针对 164 名老年人的横断面研究发现, 睡眠质量良好与更好的主观认知功能相关[34]。Wen 等采用 logistic 和线性回归模型对 1165 名无客观认知障碍的受试者进行 41 项影响 SCD 的因素分析, 发现 SCD 的总体患病率很高(42%), 8 个因素最终被确定为 SCD 的危险因素, 包括日间功能障碍[12]。关于睡眠质量与主观认知功能的关联性研究需要其他样本开展更多研究, 尤其是队列研究, 以期更好地建立因果关系。

6. SCD 人群的睡眠检测措施

在对 SCD 群体睡眠现状研究的领域中, 一项聚焦于 SCD 人群睡眠特征的研究成果[35]显示, 在该研究中, 将 SCD 人群与认知功能正常且无 SCD 的人群进行对比时发现, 若单纯依据自主汇报的信息, 二者在睡眠异常方面并未呈现出明显差异。然而, 当采用客观检测手段时, 情况截然不同。通过客观检测可以明确, SCD 受试者在睡眠过程中存在诸多问题, 其睡眠效率相较于认知正常人群更低, 睡眠期间清醒的次数更为频繁, 而且夜间醒来的时长变化幅度也更大。另有一项为期 2 年的观察性研究, 同样针对 SCD 人群展开深入探究, 研究结果表明, 睡眠改变现象在 SCD 群体中较为普遍[35]。具体而言, SCD 受试者的总睡眠时间以及总卧床时间, 均出现了显著下降的情况。综合上述研究可以得出, 对 SCD 人群开展睡眠检测具有重要意义。通过睡眠检测, 能够获取更为准确的睡眠数据, 进而深入了解 SCD 人群的睡眠特征, 为后续制定针对性的干预措施提供有力依据, 对改善 SCD 人群的睡眠质量、减缓认知功能下降进程具有积极作用。

7. 总结与展望

随着全球老龄化, 老年人认知健康和睡眠问题备受关注。SCD 作为早于 MCI 的 AD 临床前期阶段, 研究其影响因素对预防认知减退至关重要。众多研究证实, 睡眠问题与 SCD 之间存在紧密联系。研究提示失眠或许可作为干预年龄相关认知下降的早期切入点; 治疗失眠对改善认知结果具有潜在作用; 良好的睡眠质量与更好的主观认知功能相关。尽管当前睡眠问题与 SCD 关系的研究已取得一定进展, 但二者之间的因果关系还需更多队列研究加以验证。

未来应广泛选取不同地区、种族和文化背景的老年人群作为研究对象, 增强研究结果的普遍适用性。深入挖掘作用机制, 结合基因组(如 APOE ϵ 4 等 AD 风险基因)、蛋白组(如 A β 、tau 蛋白水平)、代谢组(如炎症标志物)数据, 进一步探究睡眠问题影响 SCD 的神经生物学机制, 为制定干预措施筑牢理论根基。开展干预性研究, 针对不同 SCD 风险人群(如携带 AD 生物标志物者), 设计分阶段干预方案。例如, 针对失眠患者: 用认知行为疗法(CBT-I)评估其对主观记忆抱怨的改善效果; 针对昼夜节律紊乱者, 以光照疗法或褪黑素观察其对 SCD 进展的延缓作用, 为临床实践提供切实有效的指导; 重视长期随访工作, 对队列研究进行分层设计, 如按睡眠问题类型(失眠、昼夜节律紊乱)分组, 追踪 SCD 的进展差异; 考虑采用

孟德尔随机化分析睡眠相关基因与 SCD 的关联, 以规避混杂因素进行因果推断, 为延缓认知衰退提供更具说服力的证据。睡眠与主观认知的研究为个体健康管理、公共卫生决策及社会福祉提升提供理论支撑, 实现“以睡眠为切入点, 延缓认知老化”的目标。

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