

青少年肥胖和抑郁症的研究进展

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【摘要】 近年来研究发现青少年肥胖和抑郁症普遍存在双向联系,即发生一种情况时,另一种情况发生的风险显著增加。研究发现两者在遗传、炎症因子、激素和社会环境等方面存在很多共性。分析青少年时期两者的相关性及其原因,不仅可能成为治疗肥胖和抑郁症的重要靶点,而且可能从根本预防两者的发生。然而,这一理论亟需更多的证据支持。现对青少年肥胖和抑郁症的关联性及相关成因进行阐述。

【关键词】 青少年; 肥胖; 抑郁症; 影响因素; 综述

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【Abstract】 In recent years, studies have found that adolescent obesity and depression generally have a two-way connection, that is, when one situation occurs, the risk of the other situation significantly increases. It is found that the two have a lot in common in genetics, inflammatory factors, hormones and social environment. Analyzing the correlation between the two and its causes in adolescence may not only become an important target for obesity and depression treatment, but also can even prevent the occurrence of both. Yet, more evidence is needed to support this theory. In this paper, the correlation and related causes of adolescent obesity and depression are illustrated.

【Key words】 Adolescent; Obesity; Depressive disorder; Influencing factor; Review

体质指数(body mass index, BMI)是衡量人体肥胖程度的重要指标,世界卫生组织将肥胖定义为 $BMI \geq 30 \text{ kg/m}^2$ ^[1]。近30年,全世界青少年肥胖率增长了4倍,其中33%的人为肥胖,近6%的人为重度肥胖($BMI \geq 35 \text{ kg/m}^2$)^[2-3]。中国大约有300万青少年罹患肥胖,主要由于饮食结构的改变和活动减少导致^[4-5]。研究发现,肥胖青少年发生抑郁症的风险增加,表现出较低自我效能、自尊心和较高的身体不满意度^[1]。对比BMI正常的抑郁青少年,肥胖的抑郁患者人数是其3.5倍,且BMI越高,发生抑郁的风险越高^[2-3]。另外,肥胖青少年的BMI越高,成年后发生抑郁症的风险越高^[6],社会心理因素、生活环境以及内环境的改变起着重要的中介作用^[7-8]。

与没有抑郁症的青少年相比,抑郁的青少年出现肥胖的风险是其6倍^[9]。抑郁症患者由于不良的生活方式、炎症因子及神经递质的失衡,导致发生肥胖的风险增加^[10-11]。研究显示,有一部分抑郁症患者由于神经递质瘦素的分泌减少,表现为食欲增强,因此发生肥胖的风险增加,而女性患者在青春

期早期出现更为明显^[12-13]。

这些都证明肥胖和抑郁症呈现双向联系,且肥胖和抑郁症的共病率高达33%。有研究发现抑郁症更容易引起肥胖,即青少年抑郁症患者发生肥胖的风险比肥胖患者发生抑郁症的风险高3%^[14]。

综上所述,分析青少年时期两者的相关性及其原因,不仅可能成为治疗肥胖和抑郁症的重要靶点,而且可能从根本预防两者的发生。现从生物、心理、社会方面来论述肥胖和抑郁症之间可能的关系以及可能的机制。

一、生物学因素

在生长和发育的关键时期,身体和情绪上的压力会对身体生长发育、代谢和行为产生永久性影响,从而导致健康不良后果^[15]。研究表明内分泌系统失调、炎症状态、瘦素受体减少和肠道菌群紊乱,可能是导致抑郁症和肥胖症之间联系的潜在因素。

1. 内分泌系统、炎症因子和瘦素:研究表明青少年肥胖导致内分泌系统下丘脑-垂体-肾上腺(HPA)轴慢性激活^[16],皮质醇过度分泌会导

致性类固醇激素分泌不足,而性类固醇激素波动会增加抑郁症的风险,女性更加明显^[17]。同时也会促使炎症因子水平升高^[11],而增加的脂肪组织也会释放某些炎症标志物,如IL-6、TNF- α 和CRP^[18],这与抑郁症患者血浆中升高的炎症因子种类一致,且炎症因子血液浓度和BMI呈正相关^[11],这可能是增加抑郁风险的诱因。

研究表明抑郁症患儿HPA轴也存在过度激活现象^[19],过高的皮质醇水平会升高单核细胞和巨噬细胞的数量,导致炎症水平增加^[11],炎症标志物可以增加发生肥胖的风险^[20]。而抑郁症也可通过HPA轴直接促进脂肪积累,并通过脂肪组织释放促炎因子激活炎症反应^[11]。这表明抑郁症会通过增加BMI而影响炎症反应,也说明肥胖、抑郁症、炎症因子三者互相关联。另有实验表明带有抑郁情绪的大鼠下丘脑中的瘦素受体蛋白表达下调,大鼠出现食欲增强并导致体重增加^[2]。临床上有些抑郁症患儿也会表现为食欲亢奋^[13],这可能与下丘脑中的瘦素受体蛋白表达下调有关。另外,糖皮质激素虽然诱导瘦素分泌,但会产生“瘦素抵抗”的现象,并引起肥胖^[15]。

同时抑郁症和肥胖的青少年都会增加压力易感性,而压力系统与HPA轴活动密切相关^[19,21]。在外周,HPA轴起始为下丘脑室旁核素激素,末端是糖皮质激素,压力系统长时间激活会促进皮质醇的分泌增加^[22],而皮质醇过度分泌会下调免疫系统的抑制信号,从而对炎症信号过度反应,使免疫系统分泌过多的促炎因子,引发单核细胞和巨噬细胞等免疫细胞做出积极反应,增加炎症因子水平^[11],这反过来也会增加抑郁症和肥胖的风险。另外,皮质醇水平异常也可以直接导致大脑结构和功能的改变,这有助于发展与食物摄入和奖励有关的行为,引发肥胖^[23]。也可以通过降低瘦素受体的敏感性,使下丘脑的瘦素反应性神经元无法被激活,患者饱腹感缺失,刺激进食并增加体重^[23]。

2. 肠道菌群:人类胃肠道拥有超过100万亿个微生物(细菌、酵母菌、单细胞真核生物、寄生虫和病毒),重达2 kg^[24],而青少年以双歧杆菌属和梭状芽孢杆菌属为优势菌群^[25]。抑郁症可以导致肠道菌群紊乱,如拟杆菌、变形杆菌和放线菌属的水平增加,而厚壁菌和费卡菌属的水平降低^[26],导致革兰阴性菌比例增高^[27],并且由于肠道通过性增高^[28],细菌内毒素和废物被释放到体循环中,并触发免疫反应,导致IL-6、IL-12、TNF- α 等炎症因子增高^[27],而炎症反应又会促发脂肪组织堆积,引起肥胖。

研究发现肥胖的青少年肠道菌群也紊乱,如拟杆菌、变形杆菌、肠杆菌科含量提高,而硬毛菌科含

量降低^[29],这导致许多由肠道菌群分泌的神经递质减少,如5-羟色胺(5-HT)、多巴胺、脑源性神经营养因子(brain-derived neurotrophic factor, BDNF)、去甲肾上腺素(norepinephrine, NA)等^[30],而这些递质的缺失和抑郁症密切相关。另外,肥胖会造成HPA轴的激活^[19],而皮质醇上调会影响肠道微生物的定植和肠道屏障的改变^[31],这也会改变肠道菌群的稳定而使神经递质减少和诱发免疫反应。

而且,肠道菌群也对压力十分敏感,青少年肠道菌群不成熟,在环境压力的影响下出现菌群紊乱^[27],减少神经递质的产生,并引起HPA轴亢进,导致肠黏膜桥接蛋白水解,促进肠道对革兰阴性菌的通透性,细菌毒素和废物被释放到体循环中,并触发免疫反应^[28],炎症因子再通过脑-肠轴进入大脑,引起炎症损伤^[27]。此外,促肾上腺皮质激素释放因子(corticotropin-releasing factor, CRF)的释放会激活肥大细胞以释放TNF- α 和蛋白酶,致使正常的负反馈回路受损,导致HPA对糖皮质激素刺激产生抗性,进一步上调皮质醇,出现恶性循环^[28]。

二、社会心理学因素

肥胖/抑郁症不仅会使神经内分泌紊乱,还会使孩子自卑、自闭,影响孩子的社交及个人行为^[32]。研究发现,校园欺凌、偏见、污名化及情绪化饮食可能与抑郁症和肥胖有着潜在的关联。

1. 校园:肥胖的青少年易遭受偏见以及不公平的待遇,并被贴上懒惰、缺乏动力或缺乏意志力的标签^[33]。研究发现,与体重正常的学生相比,肥胖的同伴更少被提供帮助,反而容易受同伴欺负,而欺凌行为可持续5年以上^[34]。这会使他们有无价值感和身体耻辱感^[35],从而增加发生抑郁症的风险,且身体耻辱和沮丧感越强的学生,抑郁症的风险越高^[7]。由于害怕被戏弄和欺凌,逃避社交,甚至为了摆脱基于体重的戏弄和欺凌脱离学校环境,因此更加孤独、自卑和消沉^[32]。校园欺凌也可直接导致青少年抑郁症,并随着欺凌频率的增多而使风险增高^[36]。受凌者大部分选择独自忍受^[37],这会加剧身心的恐惧和痛苦,并感到生活无望,逐渐产生消极观念和自杀的想法^[36]。另外,教师也易对肥胖的学生产生偏见,会降低对他们的期望值,包括对身体、社交和学术能力的期望^[34],这使得学生从老师那获得的关怀减少,降低学生的自尊心,增加抑郁症的风险。

2. 家庭:父母在家庭中具有领导作用,如果父母一方有抑郁症,会增加青少年抑郁症的风险^[38]。青少年具有很强的模仿能力^[39],他们会学习父母的处理事情的方法和态度以及思维方式^[40],当父母一方的认知模式消极时,孩子则容易产生自卑、自责等消极念头^[41]。据调查,患抑郁症的父母饮食往往不

健康且不规律,他们直接给孩子提供不健康的饮食从而增加孩子肥胖的风险^[42]。家庭环境不和谐也会增加青少年患抑郁症的风险。研究显示家庭出现经济问题时,家庭冲突和对青少年施暴的情况增加,青少年出现心理问题的比例随之增高^[43]。此外父母也会对肥胖青少年口头污名化。调查发现有37%的孩子因体重被父母嘲弄,其中53%是母亲,而44%的为父亲^[44]。这容易降低他们的自尊心和对自己身体形象的认识,也会增加抑郁和自杀的风险^[34]。

3. 个人:研究表明肥胖青少年表现为认知和执行功能下降,他们更倾向于冲动,如情绪化暴饮暴食^[45]。并且基于体重的受害行为可能会加剧不健康的饮食行为,从而导致体重增加。调查发现,因肥胖被取笑的女孩更有可能采取不良的饮食行为导致体重增加^[34]。另有调查报道,患抑郁症的青少年更倾向于选择富含碳水化合物的食物来提供愉悦或舒适感^[15],以此应对负面情绪,但这会增加肥胖的风险,而女性情绪化进食预示着更高的BMI^[13]。此外,抑郁症患儿通常表现为久坐少动,例如过分看电视和上网,这些习惯与肥胖有关,尤其是在青春期女孩中^[15]。情绪化饮食行为是应对抑郁和过度情绪的一种方式,因为孩子们认为这种饮食行为可以为痛苦的负面情绪提供分心和舒适感^[15],但在缓解压力的同时,也会诱发BMI升高并最终加剧炎症反应^[11]。另外,随着孩子年龄的增长,食物的选择越来越依赖于孩子的自我控制和冲动。一项关于青少年食品偏爱的研究表明,青少年更爱选择快餐食品和碳酸饮料^[7]。这项结果表明,一旦孩子对食物选择有了更多的控制,他们就更有可能会选择不健康的食物,从而增加肥胖的风险。

三、小结

青少年肥胖和抑郁症两者互相促进,它们不仅体现在神经内分泌、炎症因子方面,如肥胖/抑郁症产生的压力应激可以使HPA亢进,分泌更多的皮质醇,促进炎症因子水平升高,然后透过血脑屏障或间接影响大脑小胶质细胞产生炎症反应,导致抑郁/肥胖。或影响肠道菌群及肠道屏障的稳定,细菌内毒素进入外周循环引发炎症反应,炎症因子通过脑-肠轴的迷走神经进入大脑,导致抑郁/肥胖。也体现在社会心理上,如肥胖青少年易遭受污名化,变得自卑、抑郁,而抑郁症患者因为情绪化饮食而肥胖。

临床医生需谨慎治疗青少年抑郁症患者,因为已知一些常用抗抑郁药会引起体重增加,如阿米替林、米氮平,这会使青少年患者依从性下降,增加治疗难度。可以采用认知行为疗法(CBT)治疗抑郁症和肥胖患者,改变他们的负性认知。

利益冲突 文章所有作者共同认可文章无相关利益冲突

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