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·综述·

孤独症谱系障碍儿童睡眠问题及其行为干预研究进展*

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孤独症谱系障碍(autism spectrum disorder, ASD)是一种通常起病在3岁前的广泛性神经发育障碍,以社会交流、交往缺陷以及限制、重复性的行为、兴趣和活动及感知觉异常为特征的复杂神经发育障碍性疾病^[1]。睡眠对人的整个生命周期的健康运作至关重要^[2],而睡眠问题是ASD儿童最常见的共病之一,据估计,正常发育儿童的睡眠问题患病率在15%—35%,但ASD儿童睡眠问题患病率高达50%—80%^[3]。如果没有有效的治疗,这些问题将持续贯穿整个儿童时期,直至青少年时期^[4],除了普遍存在和持续存在之外,这些问题对ASD儿童本身的成长发育及家庭生活都会产生深远影响。睡眠对大脑的发育和成熟起着重要的作用,影响ASD儿童的记忆、注意力、情绪和行为^[5]。就家庭而言,ASD儿童睡眠问题与家庭成员的压力水平^[6]等相关。因此治疗ASD儿童的睡眠问题至关重要。虽然药物治疗对改善睡眠

问题具有显著的效果,但它们可能最适用于解决阻碍睡眠的生物因素(如补充褪黑激素),而且只依赖药物治疗睡眠问题有一些明显的局限性,例如,一些家庭可能会因为难以清醒、恶心和与其他药物相互作用等副作用而避免服用睡眠药物。作为儿科治疗的一般原则,非药物干预是首选的治疗方案^[7],因此,对ASD儿童睡眠问题的了解及对行为干预方法的掌握具有重要临床意义,本文将从ASD儿童睡眠问题、发病机制、行为干预具体方法、影响因素等进行阐述。

1 ASD儿童睡眠问题临床表现

1.1 ASD儿童睡眠问题常见症状

ASD儿童睡眠问题的患病率不仅远高于正常儿童,并且相比正常儿童这些睡眠问题更可能随着年龄的增长而持续存在^[8]。ASD儿童睡眠问题的临床表现多样,主要包括睡眠

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失调、异态睡眠、睡眠相关呼吸障碍和睡眠相关运动障碍四种^[9-10]。睡眠失调:表现为睡眠启动和维持障碍,即入睡困难或入睡时间延迟、频繁的夜间醒来且醒来的时间增长、早醒、同睡要求,还包括一些睡眠干扰行为,即离开床、玩玩具、大声叫父母和重复发出刻板的声音。异态睡眠:包括非快速眼动期睡眠相关障碍和快速眼动期睡眠相关障碍两种形式^[10],表现为夜惊、噩梦、梦游和磨牙等。睡眠相关呼吸障碍:表现为阻塞性睡眠呼吸暂停或者鼾声过大等。睡眠相关运动障碍:包括癫痫、不宁腿综合征。另外还有一些与睡眠问题相关的身体问题:肠胃问题、尿床、哮喘等^[11]。

1.2 ASD儿童睡眠问题的影响

睡眠失调(如睡前抵抗、频繁醒来、共睡、早起、睡眠时间过短)是ASD儿童最常见的睡眠问题^[12]。睡眠问题会对ASD儿童产生直接的负面影响,ASD儿童的睡眠与其身体健康、行为、认知缺陷和适应功能有关^[13],有睡眠问题的ASD儿童会有更多的焦虑、抑郁、多动、易怒、敌意和注意力不集中等内、外化行为^[14-16]。睡眠问题会直接加重ASD儿童的症状,例如,睡眠不足会加重儿童社交能力障碍并且增加其重复、强迫和仪式性行为^[12]。睡眠问题还会对其家庭成员的心理、身体健康都会造成不良影响^[17]。ASD儿童父母相比普通儿童父母会承受更大的心理压力、更多的抑郁情绪、更严重的身体疲劳以及更差的睡眠质量。儿童睡眠问题还会对家庭功能产生负面影响,包括父母关系^[18]、总体生活质量^[19]和兄弟姐妹的行为问题^[20]。

2 ASD儿童睡眠问题发病机制

鉴于ASD的复杂性质,ASD儿童睡眠问题的病因可能是多因素的,可能与神经生物变化、基因突变、睡眠结构紊乱以及ASD核心症状等有关。

2.1 神经病理机制

2.1.1 睡眠结构紊乱:睡眠结构代表了睡眠在不同睡眠阶段之间的循环模式,包括非快速眼动睡眠(non-rapid eye movement sleep, NREM)和快速眼动睡眠(rapid eye movement sleep, REM)。NREM睡眠逐渐增加,会导致较浅的睡眠,更容易夜醒,更难入睡。循环交替模式(cyclic alternating pattern, CAP)法发现ASD儿童NREM期密度增加、REM期密度减少^[21],并且ASD儿童在REM期可见纺锤状脑电波^[22]以及仅在早产儿和3—8月龄婴儿所特有的脑电活动,且缺少正常儿童REM期的慢波活动和REM爆发活动,可见ASD儿童存在睡眠结构紊乱问题。

2.1.2 生物异常及相关基因突变:神经递质如血清素、褪黑素、伽马氨基丁酸(γ -aminobutyric acid)以及GABA都会影响ASD儿童的昼夜节律。血清素又名5-羟色胺(5-hydroxytryptamine, 5-HT)是一种参与个体睡眠—觉醒的单胺神经递

质^[23],ASD儿童血清素信号系统失调,血液血清素水平升高以及血清素通路的基因产生突变(如转运基因SLC6A4)^[24]。褪黑素是分泌于松果体的内源性神经激素,ASD儿童的褪黑激素的主要代谢物(6-羟基硫酸褪黑素)的分泌显著减少,ASD儿童的褪黑素合成通路、受体调控区域存在基因突变(如ASMT、CYP1A2、MTNR1A、MTNR1B等)^[25]。GABA^[26]是中枢神经系统中主要的抑制性神经递质,ASD个体的15q染色体中有一个含有GABA基因产生突变,可能导致GABA抑制功能的中断,进而导致ASD的睡眠问题。

2.2 ASD核心症状

ASD儿童的核心症状,如重复和仪式化行为可能会导致ASD患者遵循常规和仪式,不遵循则会导致严重痛苦从而影响睡眠;活动之间的转换困难可能会导致问题行为从而延迟就寝时间;重复的认知活动,包括侵入性思维,可能导致生理上的高唤醒和情绪上的高反应,导致睡眠延迟;感觉过度反应也可能影响ASD儿童的睡眠障碍^[27];此外,与父母沟通的能力不足也可能会加剧睡眠问题。

2.3 共患病

共病注意缺陷障碍(attention deficit hyperactivity disorder, ADHD)的儿童由于过度活跃引起的高水平觉醒可能会加重睡眠障碍,哌醋甲酯等治疗多动症的药物也会扰乱睡眠,并可能加剧睡眠问题^[28]。ASD儿童常共患躯体疾病比如:胃肠道功能紊乱、癫痫等以及、抑郁、焦虑、强迫、感觉敏感、情绪调控不良等,这些共患病均可影响患者睡眠^[29-30]。

3 睡眠问题的评估与测量

目前关于评估、测量ASD儿童睡眠问题的方法分为客观测量和主观报告两种。多导睡眠图(polysomnography, PSG)利用脑电波和眼球运动等生理变量来测量睡眠,体动记录仪记录活动模式并估计睡眠参数。主观测量问卷,如儿童睡眠习惯问卷^[31](children's sleep habits questionnaire, CSHQ)、修正后的西蒙茨睡眠问卷(Simonds and Parraga sleep questionnaire, MSPSQ)^[32]、比尔斯睡眠问卷(BEARS questionnaire)^[33]均被广泛使用。睡眠日记,是由患者或年轻患者的父母填写的关于睡眠和清醒活动的每日记录^[34],因为睡眠日记可以连续几天每天填写,它们可能比在某个时间点填写调查问卷提供的信息更准确。睡眠日记与其他睡眠评估工具如睡眠活动记录仪或睡眠问卷相结合时具有更高的评估价值。此外有研究者建议除了主观与客观评估外还需要筛查儿童的共病情况,包括胃肠反流、便秘、腹痛、癫痫、打鼾、夜间咳嗽、牙痛、湿疹,以及患者是否服用含铁复合维生素。这些症状中的任何一种都可能导致睡眠不佳,应根据实际情况提出适当对策^[35]。

4 行为干预

4.1 行为干预具体措施

行为干预的目的是培养积极的睡眠习惯,以及放松和自我安抚的技能。

4.1.1 睡眠常规建立:认识和建立良好的睡前常规是其他睡眠干预成功的基础,因此,改善睡眠习惯应该始终是治疗的第一步^[36]。如确定就寝程序和睡眠时间、确保睡眠环境黑暗和安静、避免睡前刺激活动等。对于ASD儿童,可能需要调整睡眠卫生习惯,以适应儿童和家庭的独特需求,例如,有些儿童会过度关注日常活动的细节,在睡前常规元素中引入小的变化(例如,让孩子穿不同的睡衣),以防止常规成为不可打破的仪式。

4.1.2 消退与强化:消退分为标准消退与逐步消退。标准消退,指ASD儿童一旦上床,父母便忽视所有的睡觉干扰,不进行任何互动直至第二天起床,但这可能会导致ASD儿童暴怒大哭等消极行为的增加,并可能对有自我伤害行为的儿童造成威胁。逐步消退,指父母在规定的时间内忽视所有不希望看到的睡眠行为如哭泣、吵闹并且当儿童在夜间或醒后有需求时,逐渐延长其等待时间^[37],同时父母逐渐增加自己和孩子的距离,直到孩子能独自入睡。这种方法可以减少ASD儿童的夜间醒来、同睡和就寝前的阻力等睡眠问题^[38]。

强化,是利用睡前就寝卡的一种正强化手段,在儿童就寝时发给他们的一张卡片或其他类似物品,可以用来换取儿童在就寝后的一次免费下床旅行或其他形式的父母安慰。儿童使用就寝卡后,家长应该迅速带其回到床上。这种干预可用于教导儿童在入睡困难或夜间频繁醒来时进行自我安慰和卧床休息^[39]。

4.1.3 有节律唤醒:有节律唤醒通常用于减少唤醒障碍发作:儿童从慢波睡眠中突然觉醒,伴随着强烈的恐惧,如尖叫或哭泣。在儿童通常发生睡眠惊恐发作之前30min前将其唤醒,如此反复,可以有效降低ASD儿童的夜惊频率,减少恐惧反应^[37]。

4.1.4 就寝时间调整、反应代价与睡眠限制:调整就寝时间首先要求确定一个上床时间,儿童可能会在上床后15min内入睡。一旦儿童在这个时候毫无抗拒地睡着就提早就寝时间直到达到理想的就寝时间。此外,每日清晨于同一时间将儿童唤醒,且不允许在设定时间之外睡觉。反应代价指如果该儿童不能在15min之内入睡则规定其起床活动30min以上,然后重新尝试睡眠,反复如此直到睡着。睡眠限制也涉及到睡眠时间的减少,类似于反应代价但基于的是睡眠时间而不是就寝时间。它要求将儿童在床上的清醒时间限制在儿童总睡眠时间基线的10%,如果儿童在床上一直保持清醒,则引导其下床从事安静活动直到疲惫。这种方法可以明显减短被试睡眠启动时间、睡眠潜伏期,减少频繁夜醒、陪

睡、睡眠抵抗行为和睡眠相关破坏性行为^[40]。

4.1.5 认知策略指导:纠正儿童有关睡眠的负性相关信念(例如,他/她无法改善睡眠的信念),还包括一些应对策略,如放松技巧的教授;呼吸、放松肌肉群等^[37]。

4.2 行为干预影响因素

4.2.1 ASD症状严重程度:ASD儿童的某些核心特征与特定的睡眠问题有关,这表明睡眠问题是ASD诊断中固有的一部分。Mayes等^[41]认为与其他可能的预测因素相比,父母报告的ASD症状严重程度是ASD儿童睡眠问题最有效的预测因素。具体来说,ASD儿童的沟通障碍与较短的睡眠时间有关,社会交流问题与更多的睡前抵抗行为有关,对感官刺激的敏感性与睡眠焦虑有关。

4.2.2 ASD儿童年龄:与正常发育儿童相比,ASD儿童的睡眠问题不太可能随着年龄的增长而缓解。ASD青少年与ASD儿童都在睡眠潜伏期、总睡眠时间和睡眠效率等方面有明显的障碍^[42]。但是ASD儿童所经历的睡眠问题类型随着年龄的不同有所不同。ASD青少年在入睡、获得充足睡眠和白天嗜睡等方面有更显著的问题,而ASD的年幼儿童更多与睡前抵抗、睡眠潜伏期长、睡眠焦虑、夜间醒来和异态睡眠有关^[43]。

4.2.3 其他因素:研究发现ASD儿童早晨和/或中午之后的身体活动与更早的睡眠发作有关,这表明较低的身体活动水平可能是ASD儿童睡眠潜伏期紊乱的风险因素^[44]。在室内接触电子游戏、电视和电脑也与睡眠障碍呈正相关,比如学龄期和青少年男性ASD患者睡眠时间会减少^[45]。此外,性别^[46]、智商^[47]、躯体疾病:胃肠道紊乱与躯体疼痛^[48]、精神病共病症^[49]等均与ASD儿童的睡眠问题有相关关系。但是目前的研究结果还不够统一,研究数量也相对较少。

5 小结

上述研究发现表明,ASD儿童睡眠问题的发生率较高,既影响ASD儿童的生活质量并且加重核心症状,还可能影响患儿父母亲属及家庭功能。使用基于ABA行为疗法(applied behaviour analysis)的干预手段结合家长教育培训具有最佳的治疗效果。采用这种方式治疗ASD儿童的睡眠问题可能会在其他功能方面产生附带的好处,如改善内在症状、不当行为、ASD症状严重程度和儿童生活质量。然而,由于目前研究结果的质量和数量的限制,如缺乏大样本、多中心的随机对照研究;随访时间不足,现有研究对治疗疗效的持续性观察时间都较短;缺少对影响因素背后的变化机制的研究,还不能够有力的就间接治疗效果得出有关行为干预的决定性结论。需要更多的高质量的研究丰富行为干预的研究结果,特别是注重对治疗附带效应的实验控制的研究。这需要未来的研究者不断在临床实践与科研过程中总结,为临床

医师和ASD儿童亲属提供更多精准、有效的治疗手段。

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