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·综述·

儿童错𬌗畸形合并阻塞性睡眠呼吸暂停综合征的诊疗研究进展

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【摘要】 儿童错𬌗畸形在口腔科较常见，而部分错𬌗畸形合并有阻塞性睡眠呼吸暂停综合征（obstructive sleep apnea hypopnea syndrome，OSAHS）的儿童常由于缺乏多学科诊疗而未得到恰当的治疗，导致睡眠期间通气异常，影响儿童中枢系统、心血管发育，甚至产生神经行为问题。儿童OSAHS与上呼吸道结构变窄、面部骨骼和神经肌肉因素相关，与错𬌗畸形有一定相关性；儿童OSAHS临床表现和病因多样，因此诊断和治疗呈现多学科交叉、个性化和专业化的特点。通过问卷和体格检查能够进行初步筛查，儿童口腔科和耳鼻喉科检查则是发现该疾病的前哨。多导睡眠监测（polysomnography，PSG）是目前诊断的直接方法。儿童OSAHS治疗方法多样，对因腺样体扁桃体肥大引起的OSAHS，以腺样体扁桃体切除术为主；下颌前导装置治疗、上颌扩弓治疗等正畸治疗对合并错𬌗畸形的OSAHS儿童有较好效果。目前儿童错𬌗畸形与OSAHS相关性的研究较少，多学科联合疗法可能会提高治愈率但缺乏足够文献证明。未来应进一步阐明OSAHS的发病机制，推进多学科联合治疗的研究，以期通过多学科协作，对于潜在及已发病患者做到早干预、早治疗。

【关键词】 儿童；　错𬌗畸形；　阻塞性睡眠呼吸暂停低通气综合征；　睡眠障碍；
多导睡眠监测；　腺样体扁桃体切除术；　多学科诊疗；　正畸治疗
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Research progress on the diagnosis and treatment of pediatric malocclusion combined with obstructive sleep apnea-hypopnea syndrome

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【Abstract】 Pediatric malocclusion is common in dentistry. Some children with malocclusion combined with obstructive sleep apnea-hypopnea syndrome (OSAHS) often fail to receive appropriate treatment due to a lack of multidisciplinary diagnosis and treatment. It can cause abnormal ventilation during sleep, affecting the central nervous system and cardiovascular development and even causing neurological and behavioral problems. Pediatric OSAHS is caused by the narrowing of the upper respiratory tract, characterized by specific facial bone characteristics and neuromuscular factors and correlated with malocclusion. Due to its diverse clinical manifestations and etiology, the diagnosis and treatment of pediatric OSAHS require an interdisciplinary, personalized, and specialized approach. Questionnaires and physical examinations can be used for preliminary screening. Moreover, children's stomatology and otorhinolaryngology examinations are the basis for disease diagnosis. Polysomnography (PSG) is currently the direct diagnostic method. There are var-

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ious treatment methods for OSAHS in children, and for OSAHS caused by adenoid tonsil hypertrophy, adenoidectomy and tonsillectomy are the main treatments. Othodontic treatment including mandibular advancement and rapid maxillary expansion et al is also effective for OSAHS in children with malocclusion. Currently, there is limited research on the correlation between childhood malocclusion and OSAHS, and multidisciplinary combination therapy may improve the cure rate, but there is a lack of sufficient evidence. In the future, the pathogenesis of OSAHS should be further elucidated, and research on multidisciplinary combination therapy should be promoted to achieve early intervention and treatment for potential and existing patients.

【Key words】 children; malocclusion; obstructive sleep apnea hypopnea syndrome; sleep disorder; polysomnography; adenotonsillectomy; multidisciplinary diagnosis and treatment; orthodontic treatment

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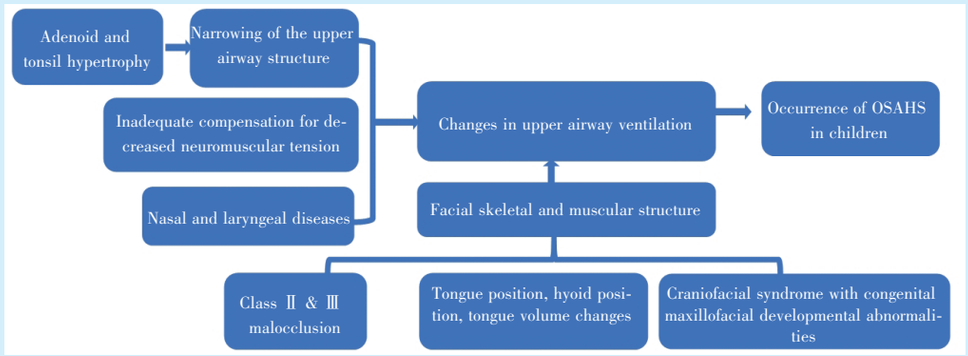
儿童及青少年错𬌗畸形发生率较高，世界范围内发生率约为56%，无性别差异[1]。口腔正畸科及儿童口腔科就诊的未成年错𬌗畸形患者中部分合并有阻塞性睡眠呼吸暂停低通气综合征（obstructive sleep apnea hypopnea syndrome，OSAHS）。OSAHS是一种常见的儿童疾病，其特征是在睡眠期间反复发生部分或完全上呼吸道阻塞，导致通气和睡眠模式异常。OSAHS会影响儿童中枢神经系统、心血管发育及代谢[2-5]，错𬌗畸形合并OSAHS儿童的诊疗值得重视。OSAHS发病因素机制复杂，涉及耳鼻喉科、儿童口腔科、正畸科、呼吸科、睡眠科等多学科，其中正畸科和儿童口腔科在错𬌗畸形合并OSAHS儿童的多学科诊疗中扮演重要角色。目前有关儿童错𬌗畸形合并OSAHS多学科诊疗的文献较少，诊断标准不一，各种治疗方法效果尚不明确。本研究旨对儿童错𬌗畸形合并OSAHS多学科联合诊疗的相关研究进展进行综述，为临床提供参考。

1　儿童OSAHS相关发病因素及与错𬌗畸形相关性

上呼吸道结构变窄及上呼吸道神经肌张力下降代偿不足是OSAHS发病的重要因素[6]。腺样体和腭、舌部的扁桃体肥大是儿童上呼吸道变窄的重要易感因素之一：在非肥胖儿童中，腺样体、扁桃体大小与呼吸暂停低通气指数（apnea hypopnea index，AHI）之间存在相关性；较严重的OSAHS患儿气道较窄，特别是在软腭后区、腺样体和扁桃体重叠区域。上气道的解剖和功能特性与OSAHS严重程度相关，学者发现OSAHS患儿上气道第3段（即鼻后孔和悬雍垂之间的重叠区域）体积较小，上气道平均横截面积较小[7]。另外，OSAHS患者的咽气道变窄，可在软腭后方、舌根后方或下咽区等一个或多个层面发生收缩，这样的气道在负压下更容易发生机械塌陷，伴随的张力降低和异常肌肉行为进一步会引起睡眠时气道阻塞[7]。其他影响上气道通气情况的还包括一些鼻部疾病（如鼻炎、鼻中隔偏曲、鼻息肉等）和喉部疾病，这些也是影响儿童OSAHS的发病因素。

另外，面部骨骼和肌肉结构也与OSAHS存在相关性。对OSAHS有重要诊断意义的骨骼特征包括下颌平面角更大、下颌平面更陡、上颌狭窄、面下1/3高度增加和颅颈角增加[8]。在咬合类型方面，OSAHS儿童主要表现为Ⅱ类错𬌗畸形。在学龄前儿童中，与无OSAHS的对照组相比，OSAHS组的SNB角显著减小，ANB角显著增大，但SNA角未发现显著差异[6,9]。Ⅲ类错𬌗患者也可能与OSAHS有关。对于错𬌗畸形患者，颅面发育不良也常伴有舌、舌骨异常，如Ⅱ类和Ⅲ类错𬌗通常伴有舌低位，这可能是由于当上气道堵塞时，舌低位便于口呼吸代偿[10-12]。二者的区别在于，Ⅱ类错𬌗由于上气道堵塞舌骨下陷，通常拥有更低的舌骨位。另外，Ⅱ类患者舌体积大于口腔气道体积，这与OSAHS成人气道体积较小、舌体积与气道体积之比明显大于正常成人特征相似[11]。而Ⅲ类错𬌗有着相比更靠前的舌骨位。气道容积是由咽腔的内在解剖结构和神经肌肉控制共同决定的，其更靠前的舌骨位置或许是因为气流阻塞引起神经肌肉反应，以恢复气道通畅所导致[13]，体现了面部骨骼和肌肉结构对于通气的调节性。此外，相比正常儿童，先天颌面部发育异常的颅面综合征患儿（如非

综合征性腭裂、Pierre Robin综合征以及21三体综合征等)更容易患OSAHS[14]。儿童OSAHS相关发病因素及与错𬌗畸形相关性如图1所示。



OSAHS: obstructive sleep apnea hypopnea syndrome

Figure 1　Schematic diagram of the correlation between OSAHS related factors and malocclusion in children

图1　儿童OSAHS相关发病因素及与错𬌗畸形相关性示意图

2　儿童OSAHS诊断

儿童OSAHS临床表现相对多样,其诊断相对成人也更为复杂,具有多步骤、多学科交叉的特点(表1),具体内容详述如下。

2.1　问卷和体格检查

在儿童OSAHS中,儿科睡眠问卷(pediatric sleep questionnaire,PSQ)是使用最广泛的,由家长填写。在对多项问卷的评估分析中,儿童睡眠问卷的睡眠相关呼吸障碍量表(sleep-related breathing disorder scale of the pediatric sleep questionnaire,SRBD-PSQ)表现良好,是使用AHI≥1诊断阈值对儿童OSAHS最敏感的筛查问卷[15]。在评估病史和问卷后,仍需进行一般体格检查,包括评估身高和体重增长、神经行为因素、心脏病和肺疾病等,其中肥胖是儿童OSAHS的危险因素之一[16]。神经行为后遗症常出现在儿童OSAHS中,其损伤主要包括行为和神经认知[3, 17]。问卷和体格检查能够对儿童OSAHS进行初步筛查,但相关危险因素的出现并不能做出完善的判断,需要进一步进行诊断。

2.2　多学科联合诊断

儿童OSAHS诊断需要多学科协同检查。近年来家长对患儿错𬌗畸形关注度较高,牙齿不齐、面型不佳、甚至“地包天”或“小下颌”等错𬌗畸形是OSAHS患儿的典型表现,此类患儿通常在正畸科及儿童口腔科就诊,故需正畸专科临床检查及上气道的影像学分析,包括唇、舌、牙弓等口内外检查以及头颅定位侧位X线片、头影测量、锥形束CT和磁共振成像等。儿童口腔科、正畸科是可能发现潜在OSAHS或OSAHS患儿的前哨[18]。耳鼻喉科检查包括上呼吸道评估、鼻内窥镜检查腺样体是否肥大以及使用Brodsky评分对儿童扁桃体大小进行分级。然而,近期研究表明儿童OSAHS严重程度与扁桃体或腺样体大小相关性较弱[19],不适用于对患儿症状进行分级诊断。

2.3　多导睡眠监测

多导睡眠监测(polysomnography,PSG)是诊断OSAHS的“金标准”,所监测的参数包括脑电图衍生、心电图追踪、氧饱和度、潮末二氧化碳、身体位置和运动、睡眠分期和结构以及呼吸暂停类型(阻塞性、混合性和中心性)等。美国耳鼻喉头颈外科学会(American Academy of Otolaryngology-Head and Neck Surgery, AAO-HNS)和中华医学会耳鼻喉头颈外科分会小儿学组均使用阻塞性呼吸暂停低通气指数(obstructive apnea hypoventilation index,OAHI)>1次/h作为儿童OSAHS的诊断界值,更适合用于儿童OSAHS的诊断[20-21];此外AHI、阻塞性呼吸暂停指数(obstructive apnea index,OAI)和最低血氧饱和度对儿童OSAHS的诊断也具有重要参考意义。然而,多导睡眠图结果的严重程度并不总是与发病程度相关[22]。多项研究使用AHI将OSAHS分为轻度(AHI 1~4.9)、中度(AHI 5~9.9)或重度(AHI>10),该分级对指导OSAHS患儿预后风险评估具有重要意义。研究表明,由于儿童焦虑情绪较少,PSG监测相对容易,准确性高于成

人[23]。然而，PSG数据采集需要在专门的睡眠实验室进行，往往需要父母整夜照顾儿童，并且PSG数据采集需要连接至少15个测量通道，这些通道通过传感器进行物理接触。因费用昂贵且耗时，降低了PSG家庭中的实用性，不适合大规模筛查。由于PSG实用性较低，有研究表明，超过80%的OSAHS患者未被诊断[24]。

表1　儿童OSAHS诊断方法评价

Table 1　Evaluation of diagnostic methods for OSAHS in children

Diagnostic method	Concerns	Method evaluation
PSQ	Sleep status (including whether or not snoring, snoring frequency, Apnea, etc.)	Preliminary screening of OSAHS; SRBD-PSQ is the most sensitive screening questionnaire for pediatric OSAHS using AHI ≥ 1 diagnostic threshold
Physical examination	Assess signs such as gain in height and weight, neurobehavioral factors, heart and lung diseases	Preliminary screening of OSAHS, but not as a diagnostic tool for children with OSAHS
Orthodontic examination	Orthodontic clinical examination and imaging analysis of upper airway, focusing on the presence of maxillofacial deformities (such as "crossbite" or "mandibular retrognathia" malocclusion)	Sentinel for personalized diagnosis of OSAHS in children
Otolaryngology examination	Assessment of the upper respiratory tract, nasal endoscopy for adenoid hypertrophy, and grading of tonsil size in children using the Brodsky score	Personalized outpost of disease development (OSAHS severity is weakly correlated with tonsil or adenoid size, which is not suitable for grading diagnosis)
PSG	Parameters monitored included EEG derivation, ECG tracking, oxygen saturation, end-tide carbon dioxide, body position and movement, sleep stage and structure, and apnea type	The "gold standard" for the diagnosis of OSAHS in children. The diagnostic threshold for OSAHS in children is AHI>1 time/h, and the severity is classified as mild (AHI 1-4.9), moderate (AHI 5-9.9), and severe (AHI > 10)
Emerging sleep monitoring technologies such as wristwatch sleep monitors	Based on biomedical signal processing technology and artificial intelligence technology, which can objectively record sleep patterns and obtain sleep parameters	Not yet widespread and devices are diverse, which can reduce the number of signals and the complexity of the diagnostic process, providing diagnostic priority reference for children awaiting diagnosis of PSG

OSAHS: obstructive sleep apnea hypopnea syndrome. PSQ: pediatric sleep questionnaire. SRBD-PSQ: sleep-related breathing disorder scale of the pediatric sleep questionnaire. AHI: apnea-hypopnea index. PSG: polysomnography. EEG: electroencephalogram. ECG: electrocardiograph

2.4　其他诊断技术

近年来，生物医学信号处理技术的普及以及人工智能的发展为OSAHS的初步诊断及筛查提供了新方法。基于XGBoost算法的机器学习诊断模型以心率和血氧数据为主要特征，对于不同严重程度的OSAHS患儿的识别准确率可达85%以上[24]。腕表式睡眠监测仪通过程序算法估计获取睡眠参数（总睡眠时间、睡眠效率、睡眠中断次数等），能够客观记录睡眠模式，测定的总睡眠时间与PSG具有较强相关性，能对OSAHS做初步诊断和评估治疗结果[25]。此外，采用带血氧饱和度监测功能的运动手环进行的睡眠呼吸筛查试验（sleep apnea screening test，SAST）能够对患儿进行快速筛查，心肺耦合分析（cardiopulmonary coupling，CPC）也可筛查症状相对严重的患儿[26]，给治疗方案的确定提供参考。以上新兴方法减少了信号的数量和诊断过程的复杂性，为患者提供了更多有效的睡眠呼吸监测手段。但由于儿童诊断标准不断更新、便携性检测设备的多样性，设备检测结果提示程度严重的患儿仍需完善PSG检查，确诊后治疗[24]。

3　多学科治疗方法

OSAHS病因多样，包括肥胖、颅颌面解剖结构异常、扩张肌对气道梗阻反应不足、呼吸驱动的皮质觉醒阈值低或气道狭窄导致的过早觉醒等[27]。患者的表型各种各样，施以同样治疗方法的疗效也因人而异。因此，个性化及专业化的多学科治疗尤为重要。

3.1　腺样体扁桃体切除术

对因腺样体扁桃体肥大引起的OSAHS，腺样体扁桃体切除术是最常见的手术治疗方法，大约80%的病例可以被治愈。一项对照研究证实，对于学龄前轻度OSAHS患儿，腺样体扁桃体切除术可改善白天行为、睡眠呼吸暂停症状、多导睡眠监测中的觉醒次数和整体健康水平[28]。然而，腺样体扁桃体切除术后OSAHS仍存在的发生率尚未完全确定（可能达到30%～60%）[29]。其中，颅面结构

异常与肥胖是患儿术后未治愈或复发的风险因素。下颌骨和舌的大小、位置和形态的改变可导致腭后区增厚，导致气道梗阻；肥胖患儿咽部软组织水平脂肪的存在减少了管腔的口径，胸壁和腹壁脂肪的增加也显著降低了这些患者的呼吸功能，这阻碍了气道堵塞的痊愈[30]。一项Meta分析证明，与正常体重患儿相比，术前肥胖患儿腺样体扁桃体切除术后OSAHS仍持续存在的风险是其4.11倍（OR = 4.11，95%CI 1.68~10.08，P < 0.01）[20]。一项基于人群的队列研究发现，腺样体扁桃体切除术还有可能带来体重的增长，试验组儿童的身高体重评分较对照组均有增加。因此，预防超重OSAHS患儿在术后体重的增长是有必要的[31]。

3.2　下颌前导装置治疗

在正畸治疗中应用的下颌前导装置不仅能改善下颌后缩伴有OSAHS的青少年患者的面型，减小固定正畸的难度，还可改善OSAHS症状。一项跟踪调查显示，经过9个月的下颌前导装置治疗后，患者睡眠呼吸质量明显提高，AHI下降，84%的患者在治疗结束几年内没有出现任何呼吸困难或呼吸声音大的情况[32]。此外，两项系统评价发现，各种类型的下颌前导装置治疗可以增加上呼吸道的尺寸并改善AHI指数，但是由于样本量小，缺乏对照组和长期结果，所以暂时不能认为下颌前导装置治疗是一种长期有效的治疗方法[33-34]。近来，Liu等[35]发现患者对下颌前导装置治疗具有较高依从性，并且医生的交流、随访能提高依从性。综上，现有研究显示，下颌前导装置疗法可能是治疗儿童OSAHS和下颌后缩的有效手段，但其长期稳定性尚待确定。

3.3　上颌扩弓治疗

上颌扩弓在儿童正畸中用于治疗上颌牙弓狭窄，它可以改善牙弓宽度、舌位和鼻宽，从而缓解上呼吸道阻塞。上颌快速扩弓（rapid maxillary expansion，RME）能够降低AHI、低通气阻塞指数和唤醒指数，而且这种效果在治疗后甚至在治疗结束后10年仍存在[36]。最近，Yoon等[37]发现RME治疗的另一个长期治疗效果是可以缓解腺样体和扁桃体肥大，这可能可以解释为什么RME可使轻度至中度腺样体和扁桃体肥大的OSAHS患儿症状减轻。此外，一项系统评价证实，腺样体扁桃体切除术和正畸治疗联合使用比单独使用能更有效地改善患儿OSAHS[38]。对于手术后仍然存在的OSAHS症状，通常需要进行颅面骨手术，特别是对于有多种医学合并症和颅面异常的患者[39]。

3.4　其他治疗方法

夜间持续气道正压通气（continuous positive airway pressure，CPAP）是一种治疗OSAHS的高效疗法，至今仍然是降低OSAHS严重程度参数的最有效治疗方法。一项荟萃分析表明，CPAP和下颌前伸矫治器都能有效降低OSAHS患者的AHI，且接受CPAP治疗的患者AHI下降更多，但治疗前后Epworth量表的评分无显著差异。然而，CPAP疗法对患者具有较强刺激性，会导致皮肤刺激、噪音和幽闭恐怖症等不适，所以患者不一定能坚持治疗。部分OSAHS儿童炎症相关细胞因子和细胞增殖水平增高，引起扁桃体增殖肥大，加重气道堵塞，抗炎药物可能在OSAHS的管理中发挥作用[40]。目前，鼻内皮质类固醇和白三烯受体拮抗剂已被用于治疗轻度OSAHS（AHI < 5次/h）的儿童，以缩小扁桃体。但是，近来也有随机对照试验得出鼻内皮质类固醇治疗儿童OSAHS的疗效证据不足的结论，认为其可能会对轻度至中度OSAHS儿童的氧减指数和氧饱和度产生短期有益影响，但对AHI以及呼吸唤醒指数的益处确定性很低。同时，研究发现，孟鲁司特可以显著减少睡眠中呼吸暂停、低通气和呼吸觉醒的次数，对健康、非肥胖、未经手术治疗的儿童OSAHS具有短期有益的治疗效果，而且该药在所研究的儿童中具有良好的耐受性[41]。此外，维生素D的补充也在儿童OSAHS治疗中发挥着作用。OSAHS儿童普遍存在着维生素D缺乏，且由于睡眠时间长、缺氧、睡眠结构紊乱，常表现出更多的行为和心理问题。经补充维生素D的治疗后，患儿的行为问题、学习问题和多动指数有了显著改善，此现象与部分儿童在接受因慢性缺氧引起的行为问题的治疗后的变化是一致的[42]。因此，维生素D对缺氧引起的神经元损伤的改善与保护作用，也应被纳入在OSAHS儿童行为和认知障碍治疗的考虑之中。

4　总　结

目前对儿童OSAHS的研究较少。头颅侧位X线片、磁共振成像、计算机断层扫描等各种影像学技术虽已广泛应用，但这些方法作为儿童OSAHS诊断工具的有效性仍有待研究。基于生物信号处理和人工智能技术，一些便携血氧检测等设备为儿童OSAHS诊断提供了新方法，然而其监测标准及临床有效性并未得到充分的证实。作为治疗儿

童OSAHS方法的腺样体扁桃体切除术(普遍认为腺样体扁桃体切除术的成功率高于单独的腺样体切除术或扁桃体切除术[39]),虽然疗效较为显著,但术后OSAHS持续存在的发生率高,提示对现有治疗方法的改进仍很有必要。另外,针对伴有错𬌗畸形的OSAHS患儿,目前尚缺乏完善的多学科治疗的研究。

儿童OSAHS的发病与上气道、软组织和面部骨骼三者不同程度阻塞有相关性。鉴于部分患者伴有错𬌗畸形且常就诊于儿童口腔科及正畸科,因此,正畸医生和儿童口腔科医生应提高儿童OSAHS的鉴别能力,与耳鼻喉科、呼吸科、睡眠科等医生合作,对具有危险发病因素的患者适时干预,预防错𬌗畸形的发生,已发生错𬌗畸形的患者进行相应治疗,真正实现多学科诊疗及研究,以望进一步阐明OSAHS的发病机制作,对各种疗法的疗效进行研究,使患者得到更加精确有效的诊断和治疗。

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