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【文献综述】

近视与调节力关系的研究进展△

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【摘要】 随着近视患病率的越来越高，视力健康问题日益成为社会关注的焦点。研究表明，近视的发生发展与调节力密切相关。长时间近距离用眼会使睫状肌痉挛，引起调节力下降，改变调节参数，影响神经传导通路和晶状体，导致远视时失焦，诱发假性近视和轴性近视。目前研究发现，阿托品和角膜塑形镜通过改善调节力治疗近视有很好的效果。本文就近视与调节力的关系及治疗方法展开综述。

【关键词】 近视；调节参数；神经传导；睫状肌-晶状体机制；治疗
【中图分类号】 R778.1

近年来，近视患病率逐年增高，已成为影响青少年视力健康的重大问题。到2050年世界范围内近视的发生率将增加至50%，高度近视将增加至约10%[1]。高度近视常引发致盲性疾病，如白内障、青光眼、视网膜脱离和黄斑变性等[2]，近视的发生发展与调节力有密切联系，当近视发生时，其调节参数发生改变，表现在调节幅度（accommodative amplitude，AA）、调节灵活度（accommodative facility，AF）和调节反应（accommodative aeactive，AR）下降以及调节性集合与调节的比值（accommodation convergence/accommodation，AC/A）升高。在近距离工作时，视网膜离焦诱导自主神经冲动，其中副交感神经支配占主导地位，通过释放神经递质乙酰胆碱增加作用在睫状体平滑肌上的毒蕈碱（M3）受体使睫状肌收缩；交感神经神经递质去甲肾上腺素作用在睫状体平滑肌B2受体抑制睫状肌收缩。睫状肌收缩时带状纤维延伸到晶状体上皮，使晶状体变凸产生调节。长时间近距离工作睫状肌持续收缩引起痉挛，在远距离用眼时晶状体不能及时复原，视网膜处于持续离焦状态[3-4]，诱发假性近视和轴性近视[5]。研究发现，阿托品[6]和角膜塑形镜[7]可以通过改善调节力延缓近视的发展。

1 调节力与近视发生发展的关系

调节力下降是近视发生发展的重要因素。在儿童和成人近视研究中均表明，调节力下降会刺激近视的发展，其中儿童调节力下降在近视发生前1 a可被检测到[8]，故调节力下降可作为近视的预测指标。有研究通过测量正视者与近视患者对模糊的感知阈值发现，近视者对视网膜离焦的感知远不如正视者敏感，这样由视网膜离焦驱动的调节反应就会低于正视者。AR异常表现为调节滞后和调节超前增加。在对成人的临床研究表明，与正视者相比，近视患者在看近处（33 cm）目标时双眼调节滞后增加，它是与近视度数相关的唯一调节力参数[9]，调节滞后越大近视度数越大，但是此相关性主要体现在成人近视患者中，在儿童中不明显[10]。调节力下降时也偶有调节超前的出现，也有诱导眼轴拉长的趋势，但其机制研究尚不充分。低AF是调节力下降的标志。AF测量通过记录正透镜和负透镜所用的时间分别记为负反应时间和正反应时间。在对18～27岁学生的远距（6 m）测试中发现，单眼远距AF明显低于正视者，AR时间明显长且主要表现在放松调节时间（负反应时间）上，但在近距下AR没有显著差异[10]。而在6～7岁近视儿童流行病学研究中发现，正负反应时间均比正视者长；与早发性近视相比，晚发性近视在近处单眼AF调节反应时间更长[10]。此外，在一个对成人的流行病学研究中，对英国某一高校AF下降的非近视学生的12个月随访调查中发现，有58%学生出现屈光不正，因此，AF是预测近视进展的一个因子，可以预测近视的发展[9]。AA定义了视觉系统所能激发的最大调节量，是眼科检查中常用的视觉功能评估之一。近视患者的AA明显低于正视者，且随着AA的下降近视度数随之加深[9]。此外，有研究表示对测量AA常用的Hofstetter公式［平均调节幅度（average of accommodation，AOA）=18.5－0.3×年龄］存在异议。平均AOA受年龄和种族差异影响[11]，研究发现，加纳儿童平均AOA高于欧洲和亚洲儿童[9]。中国人AOA较其他国家偏低，与其较高的近视患病率的现状相吻合，推测AOA不足是近

视发生发展的重要因素[12]。所以,在诊断不同国家儿童的AA时,有必要酌情分析。与正常视力儿童相比,近视儿童的AC/A比值偏高,高AC/A值反映了晶状体和睫状肌的状态异常,常常引起睫状肌麻痹诱发假性近视。研究发现,AC/A比值升高至少出现在近视发病前2 a[13],于发病年份达到高峰,在发病后呈稳定状态。在一个对儿童为期2 a的流行病学研究中显示,AC/A比值升高促进近视的快速发展[14]。因此,AC/A值升高是近视发生的早期迹象,促进近视的形成发展,也可以预测近视的发生。调节力下降随着时间的推移,引起的假性近视超过一个临界水平,使眼睛的结构重塑即轴向伸长,诱发轴性近视。调节参数能预测和评价近视的发展进程,为干预性防治近视提供了依据。

2 调节时眼的神经调控与晶状体变化

2.1 自主神经调控 调节力下降时视网膜上的模糊像诱导神经冲动。调节的产生受自主神经调控,包括副交感神经和交感神经。而在近距离工作中,副交感神经支配占主导地位。副交感神经的动眼神经副核(edinger-westphal nucleus,EW)根据细胞的大小和形态,分为内侧和外侧。内侧的细胞向支配脉络膜血管的睫状神经节神经元投射,外侧的细胞向支配虹膜括约肌和睫状体的睫状神经节神经元投射,使睫状肌的环形纤维(Müller肌)收缩。此外,副交感神经通过神经递质乙酰胆碱,增加睫状体平滑肌突触后毒蕈碱(M3)受体的表达,使睫状肌收缩产生调节,调节范围可达20 D[15]。在看远处物体时,交感神经所支配的睫状肌中的纵状Brucke肌纤维收缩,此纵状纤维和环形肌在调节过程中,既对抗又协调地共同完成调节作用。交感神经系统通过神经递质去甲肾上腺素作用在睫状体平滑肌B2受体的介导下起抑制睫状肌收缩的作用,诱导的调节很小,约1.5 D[16]。此外,在调节期间,副交感神经也加强对脉络膜非血管平滑肌细胞的调控,导致这些细胞收缩使脉络膜变薄[17],说明在持续近距离工作过程中,副交感神经支配的增加会使睫状肌持续收缩,诱发假性近视,促进近视的发展。

2.2 睫状肌-晶状体调节机制 调节是睫状肌带状束的弹性与晶状体纤维层的可塑性之间的协调。在对7~11岁的成年猕猴实验中发现,由睫状突上皮细胞产生的带状纤维延伸到晶状体并系在晶状体囊上。纤维通过晶状体周围的细胞外基质(extracellular matrix,ECM)的成分(弹性蛋白、纤维连接蛋白、胶原蛋白和层黏连蛋白)与晶状体囊膜周围上皮细胞及细胞间隙的胶原蛋白结合,传递精确的收缩力,使晶状体变凸,晶状体前囊中央的最薄处向前鼓起更明显,产生调节[16]。在猕猴眼部实验中发现,随着晶状体增厚,前房压力增加,房水流向玻璃体内而使前玻璃体膜后弯,同时,随着晶状体后极部向后运动同样引起前玻璃体膜后弯松弛,加速眼轴增长[18]。从而得出结论,若长时间近距离工作,睫状肌持续收缩容易引起睫状肌痉挛,在看远距离物体时不能及时放松晶状体而模糊,且前玻璃体膜持续处于后弯松弛状态,对眼轴伸长起到促进作用。

3 通过改善调节力防治轴性近视的方法

3.1 低浓度阿托品 阿托品在24 h内对调节力有显著的临床效应[19],是控制近视进展的重要途径。目前研究发现其有剂量依赖性[20],认为0.1 g·L^{-1}的阿托品是最佳的质量浓度[7],它可以直接通过睫状肌麻痹使调节功能丧失发挥其功效[21]。有研究发现,在睫状肌麻痹和调节功能被阻断的情况下,可以降低副交感神经对睫状平滑肌细胞的调控,防止该细胞收缩导致的脉络膜变薄;阻断晶状体运动引起的前玻璃体膜后弯松弛;减少了巩膜突内的肌成纤维细胞随睫状肌收缩而产生的收缩,从而有效防止随调节增加而诱发的眼轴伸长。此外,研究发现,阿托品还可以通过以下作用来抑制眼轴生长:(1)阿托品作为毒蕈碱受体拮抗剂,通过作用于视网膜、脉络膜和巩膜上的毒蕈碱受体来抑制眼轴生长;(2)阿托品能抑制形态剥夺性近视豚鼠巩膜中G蛋白信号调节因子2表达,减少巩膜中肌钙蛋白受体表达和增加Ⅰ型胶原蛋白表达[22],抑制巩膜后极部变薄;(3)抑制巩膜软骨细胞DNA和糖胺聚糖的合成;(4)促进多巴胺的释放,进而控制眼睛的生长[23]。此外有研究发现,在使用阿托品的近视儿童中,发现有畏光(72%)、阅读困难(38%)和头痛(22%)[24]等不良反应,这些不良反应影响了阿托品的临床应用。

3.2 角膜塑形镜 角膜塑形镜(orthokeratology,OK镜)是一种通过改变角膜形态的光学治疗手法,白天可以在没有辅助的情况下拥有清晰的视力,改变周边视网膜离焦状态,进而起到延缓近视眼增长的作用。除了近视矫正效果,最近研究证实OK镜有通过影响调节力来减缓近视进展的潜力[25]且对儿童近视控制的效果更为显著[26]。配戴OK镜后AC/A降低、AA增加[27],调节滞后量减少,调节功能提高[28],从而抑制近视的进展。有研究发现,低、中度近视儿童戴OK镜1个月时AC/A值降低,3个月至1 a趋于稳定,能很好地降低异常的高AC/A值。此外,研究发现戴OK镜1 a后,用动态视网膜镜法测量单眼调节滞后值发现滞后时间明显减少[26]。在配戴2 a后的检测中发现AA为(16.12±2.41)D,较初始AA(13.68±2.65)D显著升高[29-30];眼轴长度降低40%~61%[29]。研究发现,配戴OK镜调节力改善的原因是可以平衡调节和集合的关系,此外OK镜在改变角膜形态的情况下,在视近时由于调节需求的增加,需要动用更多的调节储备,从而有效地锻炼和提高AA,有效改善调节功能[26]。此外,配戴OK镜引起近视儿童的球差增大,有利于提高调节散焦状态

下的准确性，进而改变调节指示，最终改善调节功能[30]，为OK镜通过影响调节力控制近视进一步提供依据。尽管有研究表示配戴者存在显著的个体差异[31-33]，但是其对延缓近视发展有极为显著的效果。

4 小结

调节力与近视的发生发展有着密切的联系。调节参数可以作为预测近视发展和评估进程的指标，为准确采取治疗方案提供依据。现有的治疗方式已经说明解除睫状肌痉挛恢复调节力是防控近视的有效手段，但其作用机制需进一步探索，且目前治疗方案存在缺陷，如阿托品的不良反应和OK镜的个体差异等限制了推广使用。寻找不良反应少的解除睫状肌痉挛以恢复调节力来防控近视的治疗方法现已成为迫切需要。

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Research progress of injectable hydrogel in eye diseases treatment

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【Abstract】 The complex of eye structure makes its treatment methods face various challenges. Hydrogel is a polymer material, with multidimensional potential application. This controllable mechanical and biological properties make hydrogel as a hotspot in the field of tissue engineering and biological engineering. Meanwhile, the transparency and great biocompatibility of hydrogel indicate its application in the prospect of eyes therapies. At present, it has been used as artificial tears, drug carrier, adhesive agents in ophthalmology. This review introduced the injectable hydrogel in the aspect of production, properties, and applications. The development of injectable hydrogel as ocular drug carrier, tissue adhesives, space filling agent and cell carrier face many challenges. This article explains the recent advances in various injectable hydrogel for corneal trauma, glaucoma, cataract, retinal detachment, age-related macular degeneration.

【Key words】 hydrogel; eye diseases; adhesives; ocular delivery; cell carrier; vitreous substitute

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Recent advance in the relationship between myopia and regulatory ability

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【Abstract】 With the increasing prevalence of myopia, the problem of vision health has increasingly become the focus of social concern. The research shows that the occurrence and development of myopia are closely related to regulatory ability. Eye using in close distance for a long time will make ciliary muscle spasm, cause the decline of the regulation, change the regulation parameters, affect the nerve conduction pathway and lens, and finally lead to hyperopia when out of focus, pseudomyopia and axial myopia. At present, atropine and keratoplasty have been found to be effective in the treatment of myopia by improving the regulatory ability. This article reviews the relationship between myopia and regulatory ability.

【Key words】 myopia; regulatory parameters; nerve conduction pathways; ciliary muscle-lens mechanism; treatment