四川大学学报（医学版） 2021，52（6）: 901－906
J Sichuan Univ（Med Sci） doi: 10.12182/20211160205

• 儿童眼视光与青少年眼保健论坛 •

‖ 文献综述 ‖

近视与光照的关系

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【摘要】 近视的发病率逐年上升且有低龄化趋势，减少近视发生、控制近视度数增长一直是近视防控领域的研究热点。有随机临床对照试验发现户外活动可以有效降低发病率，延缓近视度数加深；基础实验也证实光照与近视的发生发展存在一定的关系。本文对光照与近视的研究进展、局限性和未来发展方向进行了综述。从光照性质来看，增加光照强度能够减缓近视进展，减少实验性诱导近视的产生，但具体的作用机制尚不清楚。光照的明/暗周期节律性变化会造成褪黑素和多巴胺的分泌异常，眼压以及脉络膜厚度昼夜节律性的改变，从而对近视造成影响。此外，波长较长的红光成像在视网膜后，更易诱导近视产生，而中短波长的蓝光成像在视网膜之前，能够延缓近视进展。但不同物种对于不同波长光的反应不同，光波长与近视的关系还有待进一步研究。将来的研究可深入探索光照改变近视进展的作用机制，包括光照如何改变多巴胺的水平，引起下游信号通路的改变，从而控制眼轴长度的生长，以及视网膜感光细胞如何接收到不同波长光的信号，从而调节眼部屈光度，以设计合理的人工照明光照强度、组成成分和性质，并将其用于近视防控。

【关键词】 近视 光亮度 单色光 光照节律性 闪烁光 多巴胺

Relationship between Myopia and Light Exposure

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【Abstract】 Epidemiological studies found that the incidence of myopia was increasing year by year and the age of onset of myopia was showing a trend of affecting increasingly younger children. Reducing the occurrence of myopia and controlling the increase of myopia diopter have always been the focus of research on the prevention and control of myopia. Large randomized controlled clinical trials have found that outdoor activities can effectively reduce the incidence of myopia and delay the progression of myopia. Basic experiments also revealed that there were certain connections between light exposure and myopia. We herein review the research progress, limitations and future directions of research on light exposure and myopia. From the perspective of light properties, increasing the intensity of light can slow the progression of myopia and reduce the occurrence of experimentally induced myopia. However, the actual mechanism of action is still unclear. The rhythmic changes of light exposure caused by the light/dark cycle may cause abnormalities in the secretion of melatonin and dopamine, and changes in the circadian rhythm of intraocular pressure and choroidal thickness, thus affecting myopia. The red light, with relatively longer wavelength and forming images behind the retina, tends to induce myopia more easily, while the blue light, with medium and short wavelength and forming images before the retina, tends to delay myopia progression. However, different species respond differently to lights of different wavelengths, and the relationship between light wavelength and myopia needs further investigation. Future research can be done to further explore the mechanism of action of how light exposure changes the progression of myopia, including the following aspects: how light changes dopamine levels, causing changes in downstream signal pathways, and thus controlling the growth of the axial length of the eye; how retinal photoreceptor cells receive light signals of different wavelengths in order to adjust the refractive power of the eyes; and how to design artificial lighting of reasonable intensity, composition and properties, and apply the design in myopia prevention and control.

【Key words】 Myopia Luminance Monochromatic light Light exposure rhythm Flashing light Dopamine

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在全球范围内,尤其是东亚地区,近视发病率不断升高,而且发病年龄越来越小[1]。据估算,到2050年可能会有接近50亿人(49.8%)发展为近视,约10亿人(9.8%)形成高度近视[2-3]。一项天津的流行病学研究结果表明78.2%中小学生患有近视[4]。美国与欧洲近视的发病率虽然没有东亚地区高,但近几十年也呈现较大幅度的增长[5]。高度近视极有可能引起严重的眼底病变,包括脉络膜新生血管、黄斑变性、视网膜脱离等一系列不可逆的致盲性眼病,不仅加重了个人和国家的经济负担,也严重影响人们的生活质量[2-3]。

目前近视病因仍不明确,且尚无有效的治疗方法。Meta分析和系统评价的结果表明户外活动能控制近视[6-7]。延长课间户外活动时间能够有效逆转台湾学龄儿童视力下降的趋势[8]。每天额外增加户外活动时间能有效地降低近视发病率[9],每天户外慢跑30 min可延缓近视增长速度[10]。本文对光照强度、闪光频率、光波长以及光照其他性质与近视的关系进行综述,总结光照与近视的关系,以及可能的相关作用机制。

1 光照强度与近视

晴朗天气户外日间光强约130 000 Lux,阴天户外光强约15 000 Lux,明显强于室内人工照明光(约100～500 Lux)[11-12]。户外环境中的高强度光照,能够降低近视发生率[9, 13-14],这一结论得到正午户外活动时间与近视度数之间显著相关性[15]的支持。此外,户外活动还可预防近视的发生,控制近视增长[16-17]。每天增加20 min的户外活动时间,能降低4.8%的近视发病率,每周超过11 h的户外活动有近视保护作用[18]。利用新型的结膜紫外线自发荧光监测发现[19],在澳洲,青年人屈光不正的度数与眼部的光照水平呈反比。这些实验结果均指出户外光照强度与近视相关,而且增加户外活动时间,能有效地预防近视的发生以及控制近视进展。然而,近期回顾性实验表明,增加户外活动虽然有控制近视的作用,但光照水平与控制近视的效果无显著相关[20]。另有研究指出,近距离工作、光照强度与近视有关,但具体的因果关系以及剂量效应还有待进一步研究[21]。这提示光照强度与近视的关系尚无统一定论。

关于高强度光照可以减少近视发生、控制近视增长原因的学说有很多[11]。在强光照射下,瞳孔会缩小,景深会增加,可以适当改善视网膜上成像的清晰度,从而起到保护作用。但是在负镜诱导模型中,高强度光照并不能改变最终近视的形成,说明强光使瞳孔缩小并没有阻碍近视发生的作用。临床研究发现户外活动的生物标志物之一血清内维生素D含量与成年人(20～＜30岁)近视情况密切相关[22]。有学说猜测光照强度增加可促进维生素D的合成,从而改变巩膜基质重塑等新陈代谢的过程,与近视的形成有一定的关系[23]。

动物实验证实在一定范围内增加光照强度,能降低实验诱导性近视的发生率以及延缓近视进展[11]。雏鸡形觉剥夺诱导近视模型中发现[24],增强周围环境的光照亮度,能有效延缓眼轴增长,而且控制近视效果与光照强度呈正相关。高强度的光照可减缓雏鸡负镜诱导近视速率[25]。提高光照水平可使形觉剥夺模型猕猴近视度数降低[26],也可降低树鼩形觉剥夺性近视和负镜诱导性近视[11]。周围环境较低水平的光照虽然不一定会直接导致恒河猴近视,但会影响其视觉信号相关的正视化过程[27]。在鸡、猴子实验诱导性近视的过程中,视网膜多巴胺含量减少,玻璃体腔内二羟苯乙酸含量也降低[11, 28]。既往研究表明光照时间延长或光照强度增加会引起视网膜多巴胺含量的增加[29],也会使其在玻璃体腔的代谢产物二羟苯乙酸含量的增加[30],多巴胺是调控眼发育的重要视网膜神经递质之一,其合成和分泌受光刺激调控[29]。提高光照水平,可以激发与多巴胺能神经元突触相连接的视网膜光敏感性神经节细胞,从而促进多巴胺的合成与分泌[31]。光照水平的变化也会改变多巴胺受体活性,影响多巴胺的功能。利用大鼠视网膜R28前体细胞进行的体外实验发现,D1和D5受体通过转录生成的mRNA含量随着光照强度的增加而增加[32]。小鼠动物实验结果显示增强光照强度,可以通过增强视觉增强刺激信号传递通路中双极细胞内的D1受体活性,减缓近视度数的加深,延缓眼轴的增长[33]。

2 光照节律性与近视

包括眼轴长度、脉络膜厚度、眼压在内的一些眼部生理参数存在昼夜节律变化[34],光照周期改变,会影响人体生物钟、生长发育节律、激素分泌等。多巴胺的新陈代谢(合成、分泌与利用)也具有昼夜节律性,白天比夜晚更为活跃。光照节律性的改变,会导致多巴胺和褪黑素等神经调质分泌异常,从而影响眼部发育[35]。2岁儿童的入睡时间以及睡眠长度与近视相关,较晚入睡会增加儿童近视的风险[36],提示延长夜晚人工光照使用时间可能更易造成近视。澳洲的研究显示:夏季和冬季不同光照时长也与儿童眼轴长度、屈光度改变相关[37]。研究发现,虽然儿童在夏季户外活动的时间最长,但是在调整基线眼轴长度、年龄、性别、父母近视程度等因素之后,光照对眼轴长度的改变并没有显著的影响[38]。因此,季节性

的光照改变和近视的关系还需进一步研究。芬兰应征入伍者中,居住在极昼极夜北极圈内的人近视发病率高于其他地区,提示光照的明/暗周期对眼部发育会产生一定的影响[39]。

雏鸡诱导性近视实验中,与未剥夺的对侧眼相比,形觉剥夺眼视网膜与视网膜色素上皮细胞(RPE)复合体以及脉络膜内和生物钟、昼夜节律相关的基因都有一定程度的改变[40]。更多基础实验认为存在最佳光照周期,可以促进正常的视觉发育,减少近视发生,延缓度数增长。在保持日间12 h总光照亮度基本不变的情况下,雏鸡连续12 h暴露在更高光照环境中,比间歇性诱导的形觉剥夺性近视度数更低[41]。而且,夜晚黑暗环境中额外增加光照,会打破雏鸡眼部生长节律性,导致眼部发育异常和屈光不正[42]。将小鼠饲养在不同的明/暗周期环境中,发现长时间光照易诱导小鼠形成近视[43]。此外,视网膜特异性敲除与生物钟相关的基因*Bmal*1会导致在自然饲养环境中的小鼠形成近视[44]。

以上实验表明: 光照的节律性与眼压以及眼轴密切相关,儿童在夏季与冬季的眼轴长度改变量存在一定的差异。但具体的光照节律性的改变与近视发展的关系尚不清楚,例如: 眼压与近视的关系、脉络膜厚度与眼轴长度的改变相关机制也还有待进一步研究。多巴胺与褪黑素等生物分子如何调控眼轴生长也还需探索。

3　光波长与近视

视网膜可以感知纵向色差(即不同波长的光经过光学系统后聚焦在不同的位置),并以此作为离焦信号,诱导完成正视化过程[45-46]。窄光带照明环境不能维持正常视觉发育过程[47],自然光波长大致范围是380 ~ 760 nm。卤素灯亦为连续波长,范围大约是350 ~ 1 050 nm,但与太阳光相比,主要缺乏紫外线B(UVB)的部分。荧光素灯泡所发的光并不连续,而是有间断的波峰,在蓝、绿、红光处有峰值,比太阳光少了紫外和红外部分。研究发现通过佩戴透过紫外线(波长< 400 nm)的角膜接触镜可以抑制儿童近视进展[48]。有关青少年的调查研究发现,增加户外UVB接触时间,可以延缓近视度数的增加[49]。临床回顾性病例分析实验结果显示,高度近视患者置换滤过紫外线人工晶体组的患者,比置换透过紫外线人工晶体组的患者近视屈光度增加2倍,眼轴增长4倍[50]。

目前关于单色光与近视发生发展的关系尚无统一定论,不同波长的单色光对于动物屈光发育、眼部生长有不同的影响[46]。雏鸡依靠波长离焦信号诱导正视化的过程[51],将出生1 d的雏鸡分别于红光、蓝光的环境中饲养发现[52]: 红光照明更易诱导雏鸡发展形成近视,而蓝光会诱导逐渐形成远视。小鼠过度暴露在绿光环境中会形成近视[53],相反,短波长光能延缓小鼠近视进展[54]。蓝光可以延缓虹鳟鱼的眼轴增长[55],类似的实验结果在豚鼠近视模型中也得到验证[56-57]。此外,饲养在红光环境中的恒河猴与蓝光环境中的恒河猴屈光度差值大于红光组和自然光组的差值[58]。但也有文章报道暴露在长单色光中的树鼩比自然光照组的远视度数更高[59]。说明目前关于单色光线索与眼部发育、屈光状态的关系认识还不充分,值得进一步深入探讨[60]。

有学说推测由于视网膜上不同种类视锥细胞[60-61]——L-型、M-型以及S-型视锥细胞——对不同波长的光敏感度不一样,在不同的单色光照明条件下,三种视锥细胞的受激程度不一样,按照不同的比例组成的视觉信号传导至视皮质,一方面会形成不同的色觉,另一方面会对眼球的生长发育发挥不同的作用。红光、蓝光和紫外线均可刺激视网膜多巴胺的释放,且不同波长的光对多巴胺的分泌和代谢有不同的影响[53]。短波长的紫外光也可能是通过刺激小鼠紫外敏感的神经节细胞抑制实验性近视的产生[62]。眼部的生长发育以及代谢依靠于光照调节,增加混合白光中的蓝色光组分能够改变细胞能量合成、增殖、胶原蛋白周转以及一氧化氮代谢相关的深层脂质重塑[63]。

目前尚无统一结论阐释不同波长的单色光对眼部屈光发育的作用,是因为不同单色光动物实验得到的实验结果不具有一致性。一方面可能是因为不同种属的动物眼部,尤其是眼底结构不同(例如豚鼠和小鼠眼底无黄斑中心凹),而且灵长类动物与非灵长类动物眼部感光细胞组成成分也有所不同;另一方面也可能是不同课题组选用的单色光照明条件不同,单色光的光照来源、光照强度以及闪光频率有所差异。

4　光照其它性质与近视

光照对近视的控制作用同时也取决于给光的频率、间歇时长。1 min亮∶1 min暗和7 min亮∶7 min暗的给光方式可以增强光照的保护效果,防止近视形成[64]。日间12 h给予0.5 Hz的光照,可诱导豚鼠形成近视[65]。将豚鼠分别饲养在闪光频率为0.5 Hz、5 Hz的光照环境中,前者近视度数增加明显高于后者[66]。自然光照13 d后树鼩屈光发育按照正视化过程,远视度数逐渐降低;闪烁蓝光组屈光状态更为近视;闪烁红光组仍保持轻度远视状态[60]。推测正视化过程可能会被不同的闪光频率打断,形成屈光不正,但具体作用机制尚不清楚。

闪光刺激豚鼠近视模型中,近视眼玻璃体,视网膜以及RPE中的血清素以及其受体表达增加[65]。绿色闪光诱导豚鼠形成近视,且近视眼视网膜和巩膜组织中毒蕈碱1类受体mRNA含量降低[67]。闪光频率也会影响眼部的正常电生理过程,改变其生长发育情况,从而导致屈光不正。闪烁光还可能影响前房和玻璃体腔内液体流动状态,改变眼内新陈代谢过程,影响正视化的过程[68]。

然而受医学伦理约束,此部分的临床试验并未展开,观察和结论均来自动物实验,其外推性有待商榷。

5 总结

以上引用的有关光照与近视的临床研究中,涵盖儿童、青少年以及成年人,但存在一定的区别。增加户外活动可预防儿童青少年近视、幼龄儿童入睡越晚越易形成近视、以及配戴透过紫外线的角膜塑形镜能预防儿童近视属于前瞻性的临床试验,而成年人(20～<30岁)血清维生素D含量与近视密切相关等实验属于横断面研究,应进行类似的儿童相关研究,以利于启发未来关于光照与近视的可能作用机制的探索。

无论是动物实验还是临床研究,都发现光照与眼球生长发育、近视发生发展存在一定的联系,但具体作用机制还有待进一步研究,比如:高强度的光照相较于低强度的光照对视力的保护作用,到底是通过哪些神经递质以及信号通路发挥作用?在这些过程中,光照强度的改变是怎样影响多巴胺的含量、生物活性以及与受体的结合情况?除此之外,光照节律性、闪光频率、不同波长的单色光、纵向色差在近视形成过程中的作用均需进一步探讨。

在保证光照不损伤眼部健康的情况下,探索可以减少近视发生、阻止近视发展的光照强度、光谱的组成性质,并将其运用到实际生活中,提供合适的照明,确实还有很长一段路要走。但是,这些都是在近视防控领域非常有前景的研究方向,值得深入研究,做到真正将科研运用于社会实践,改善人们的生活质量。

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利益冲突 所有作者均声明不存在利益冲突

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(2021 – 07 – 31收稿, 2021 – 11 – 02修回)

编辑 吕 熙