

tDCS治疗ADHD的原理与临床进展

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摘要

注意缺陷多动障碍(ADHD)是儿童和青少年精神医学领域常见的神经发育障碍之一,以注意力缺陷和(或)多动-冲动为主要临床特征,ADHD还常伴随学习障碍、社交和情绪等问题,给个体的成长带来阻碍。经路直流电刺激(tDCS)是一种通过正、负电极片发出直流电透过骨层调控神经元状态的治疗方法,可以诱发神经元的去极化和超级化。tDCS在焦虑、抑郁等精神医学中已被广泛应用,其也表现出对多动-冲动的抑制效果,可以作为ADHD的辅助治疗策略。因此,本文综合分析ADHD的神经生物学基础,阐述tDCS的原理和干预ADHD的机制,并综述tDCS在ADHD治疗中的临床应用进展。

关键词

注意缺陷多动障碍, 神经生物学基础, 经颅直流电, 临床应用

Principle and Clinical Progress of tDCS in the Treatment of ADHD

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Abstract

Attention deficit hyperactivity disorder (ADHD) is one of the common neurodevelopmental disorders in children and adolescents in the field of psychiatry. It is characterized by attention deficit and/or hyperactivity impulsivity. ADHD is often accompanied by learning disabilities, social and emotional problems, which hinders the growth of individuals. Path direct current stimulation (tDCS) is a treatment method that can induce depolarization and hyperpolarization of neurons if direct current is sent through the bone layer to regulate the state of neurons. TDCS has been widely used in psychiatry such as anxiety and depression. It also shows the inhibitory effect on hyperactivity

impulsivity, and can be used as an adjuvant treatment strategy for ADHD. Therefore, this article comprehensively analyzes the neurobiological basis of ADHD, expounds the principle of TDCS and the mechanism of intervention in ADHD, and summarizes the clinical application progress of TDCS in the treatment of ADHD.

Keywords

Attention Deficit Hyperactivity Disorder, Basis of Neurobiology, Transcranial Direct Current, Clinical Application

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1. 引言

注意缺陷多动障碍(Attention Deficit Hyperactivity Disorder, ADHD)是儿童及青少年精神医学领域常见的神经发育障碍之一,根据《精神障碍诊断与统计手册(第五版)》(DSM-5)的定义,其主要临床表现为持续的注意力不集中和(或)多动与冲动,全球患病率约为 7.2%,我国约为 6.26% [1]。除核心症状外,ADHD 还常伴随学习障碍、社交障碍或情绪问题,且有部分患者的症状和功能损害会延续到成年期,严重影响其生活质量[2]。

ADHD 目前仍以药物治疗为主要方案,但药物长期使用可能伴随不良反应、滥用或药物依从性等问题[3]。而目前行为训练等非药物方案也有着操作复杂和长期效益不确定等问题[4]。近年来,基于无创脑刺激技术(Non-invasive Brain Stimulation, NIBS)的治疗方案得到了众多临床医生与学者的关注,其中经颅直流电刺激(Transcranial Direct Current Stimulation, tDCS)以其出色的安全性、良好的耐受性以及低廉且便携的技术特征,相较于重复经颅磁刺激(rTMS)表现出了更强的儿科适应潜力,成为具有应用潜能的辅助治疗手段或替代疗法或辅助调控手段[5]。

2. ADHD 神经生物学基础

ADHD 的神经生物学基础存在异常障碍,其核心症状主要在于大脑内部特定神经网络(特别是额叶 - 纹状体 - 小脑回路)的结构与功能完整性异常。磁共振成像(Magnetic Resonance Imaging, MRI)的大数据分析显示,相比正常群体,ADHD 患者整个脑体积与皮层容积存在普遍性的减小,特别是在基底节区域各亚区显现出明显的灰质损伤[6]。结构形态学研究进一步表明,ADHD 患者基底节区中的壳核、苍白球及尾状核体积在发育期存在异常,而这部分结构的异常与多动及冲动临床表现存在重合,且随着年龄的改变而发生形态自适应恢复,可部分解释为何部分患者的多动、冲动症状会随着发育成熟而自行缓和[7]。

除了深部脑核团的发育异常外,大脑皮质的发育指标同样检测到异常变化,ADHD 患者在前额叶(PFC)、扣带回及颞叶等关键注意维持区展现出显著狭小的皮层表面积[8]。儿童患者的梭状回和颞极处的皮质普遍变薄,作为神经元突触退化、细胞构筑畸变和骨架突起髓鞘化延迟的代偿表征,这种变薄倾向多数能见于未成年患儿中[9] [10]。大脑半球对称性异常也是常见问题,研究发现 ADHD 患者右半球的特异性脑形变比左半球更为显著,右侧前额皮质区兴奋性局限下降导致了对多动、冲动抑制功能的缺乏[11] [12]。

在脑结构层面,白质的微结构完整性异常主要影响了脑网络连接功能的缺损。研究指出,患者全脑

白质容积显著偏低,局部纤维完整度在胼胝体结构区、右前扣带回等神经网络交汇处均有减弱,导致了跨脑区大尺度功能连接(FC)的深度重组[13]。在功能影像(fMRI)表现中,ADHD 患者的大脑在面对认知负荷及反应选择时,右下额叶(rIFG)、背外侧前额叶(DLPFC)以及前扣带皮层(ACC)未能产生充足水平的激活动态,且此处灌注的不足水平和临床缺陷评定呈现明确的负性相关[14]。这条通路的功能整合依赖脑内去甲肾上腺素、多巴胺等关键神经递质系统的动态平衡,奖赏预测误差(RPEs)的信号中断与受体转运异常是导致底层认知网络激活异常的关键化学根源[15]。

3. tDCS 治疗 ADHD

3.1. tDCS 治疗 ADHD 原理

经颅直流电刺激(tDCS)能够有效调控局部皮层神经网络的激活状态,是一种神经精神障碍治疗中的前沿技术路径[16]。tDCS 配备一正(阳极)一负(阴极)两枚柔性接触式电极片,工作状态下弱直流电导入头皮后透过骨层传导,作用于深浅皮层,主要通过诱导神经元静息膜电位完成跨膜状态调节来改变局部细胞激活态,而这种神经调控行为本身并不直接激发新的神经动作电位[17]。一般情况下,阳极刺激下诱发神经元的去极化,从而提高皮层的兴奋性;阴极刺激下诱发神经元的超极化,降低其兴奋性[18]。

tDCS 治疗 ADHD 的长期调控机制并非单纯停留在即时激活层面,而是依赖突触水平的调控变化。通过高频刺激可引发 GABA 与谷氨酸介导的突触可塑性变化,即生长时程增强(LTP)生理机制[15]。长效突触增益可以在局部调控之外激活处于断联状态的皮层-下丘脑-纹状体深层回路,从而诱发整个认知处理网络发生神经重塑(Neuroplasticity) [17]。而阳极刺激被认为可能间接提升去甲肾上腺素系统的释放速率,并强化 DLPFC 区域的多巴胺循环,以修复 ADHD 患者在认知控制测试中出现的神经元激活不足现象[19]。

3.2. tDCS 治疗应用与安全性研究

tDCS 治疗的主要设置参数包括输入电流参数、刺激时间长度、电极尺寸规范以及贴片设置靶区。以往研究中使用的输出电流流量多控制在 0.1 mA 至 4 mA 之间,正常人体所适应的基本参数规格常设定在 1 至 2 mA,儿童颅腔小且颅骨层较薄,脑脊液阻抗比成年群体低,常规的儿科电流极限通常限制在 1 mA 以下[20]。近年来的一些系统安全测试表明,对 ADHD 实施高达 2 mA 强度的阳极连续干预也并未发现明显的临床器质毒害或全身严重不良事故,因此 0.5 至 2 mA 区间往往被多中心研究接纳并确立为临床安全性研究的基本输入常态,干预阶段以单次 10 至 30 分钟居多[21] [22]。常规成人多覆盖 35 cm² 面积的敷贴,而儿童靶刺激中常换成 25 cm² 微缩电极,以便在头围有限的情况下提升集聚电流密度[17]。在定位靶区的设计上,背外侧前额皮质(DLPFC)是该疗法的常用靶区,近年来也有研究关注右侧额部额下回(rIFG)的特异作用[23]。

系统性综述研究表明,tDCS 技术在 ADHD 干预中的安全性具有令人满意,没有观察到伴随干预实施产生的脑部不可逆局部软化变性或永久受损[22] [23]。大多数受试者的不良反应多位于表皮,如电极板边缘区域感觉刺痒、局部表皮红斑、偶发头痛、饮食下降等情况,少数的特异不良反应在绝大部分情况下几小时内即可消退,在规范操控情况下未表现严重并发症[24] [25]。

4. tDCS 治疗 ADHD 的临床应用

研究表明对 ADHD 患者大脑的左侧背外侧前额叶(L-DLPFC)进行 tDCS 阳极刺激,常能带来注意集中度的好转,以及视觉空间表标定处理误差的显著改善[26]。Anna 等人等采用静息态网络成像工具评估,在为期多次的 DLPFC 刺激干预后,ADHD 患儿前额网络与其对应的额纹状体通路表现出显著的连接重

构以及多维协调强化[27]。Cornelia 等人等对 14 名 ADHD 青少年的对照刺激实验也发现,相较于假刺激,经过单阶段多疗程规律刺激后,患者注意力的自我评价改善与量化客观都有改善,表明针对前额区阳极强化能在一定周期内改善临床症状[28]。

对不同刺激靶点的比较研究发现,相较于 DLPFC 对于整体认知速度与工作记忆容量的重振,将局部阳极靶点置于右侧额下回(rIFG)变现出更明显的反应抑制优势[21]。Soltaninejad 等人等分析了不同电极阵列对于主动抑制功能的影响,研究表明 DLPFC 以及右侧额下通路的电性变化会对个体的冲动、多动抑制具有明显效果[29]。目前 tDCS 治疗 ADHD 仍以联合药物或其他康复预策略共同实施,研究表明, tDCS 的联合注意力或工作记忆认知训练任务,能够借助微电流激发出的“神经元兴奋突触窗口”,优化皮层可塑性以延长单项康复课程的有效期[30]。

近年来,部分衍生无创神经干预技术也正成为研究热点。经颅随机噪声刺激(tRNS)被广泛测试可在特定随机共振阈下诱使前额系统更快建立重塑期,且其伴随的刺痛、瘙痒不良事件概率明显低于 tDCS 技术[31]。由 FDA 核准的经皮三叉神经刺激技术(TNS),在研究中已表现出对儿童 ADHD 核心症状的改善效果已接近非兴奋剂药物的药效[32]。

5. 小结与展望

经颅直流电刺激(tDCS)作为一个兼具安全与有效性的非药物治疗选择,在 ADHD 症状干预中具有独特优势。tDCS 通过增强前额叶特定网络的兴奋性,促进皮层结构的突触重塑,成为改善 ADHD 临床症状的重要工具。

目前, tDCS 治疗的临床试验样本规模较小,未来研究可以开展多中心、大样本的双盲随机对照试验,提供高质量的临床证据和治疗参数。在 ADHD 临床治疗上,未来也可积极探索 tDCS 联合常规药物或康复干预等其他方案的疗效,提供 ADHD 临床症状和功能障碍改善情况以及延长疗效时长。

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