· 抑郁症专题 ·

基于认知任务的近红外光谱成像技术在抑郁症中的研究进展

张福旭 张天宏 刘晓华
200030 上海交通大学医学院附属精神卫生中心精神科
通信作者：刘晓华，Email：drliuxiaohua@gmail.com
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【摘要】 抑郁症确切的病理生理学机制尚不清楚，近红外光谱脑功能成像技术是近年来新兴的一种基于血流动力学原理的非侵入式功能神经影像学技术，广泛应用于精神科，具有辅助诊断抑郁症的临床价值。此外，近红外光谱成像可以与其他神经调控物理治疗结合以检测大脑皮层的血流动力学及氧合状态变化，有望为相关技术参数设定及疗效预后提供有利指导。
【关键词】 抑郁症； 功能近红外光谱成像； 认知任务； 神经调控治疗； 综述

The progress on the study of near-infrared spectral imaging technology based on cognitive tasks in depressive disorder *Zhang Fuxu, Zhang Tianhong, Liu Xiaohua*
Department of Psychiatry, Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China
Corresponding author: Liu Xiaohua, Email: drliuxiaohua@gmail.com
【Abstract】 The pathophysiological mechanism of depressive disorder is still unclear.Functional near-infrared spectroscopy (fNIRS) is a useful neuroimaging technique based on hemodynamic principles for the non-invasive investigation of brain in motion. It is widely used in psychiatry and considered to be a potential auxiliary diagnostic method based on the current evidence. In addition, fNIRS can be combined with other neuromodulation therapies to detect changes in hemodynamics and oxygenation status of the cerebral cortex, providing valuable advices for setting related technical parameters and prognosis.
【Key words】 Depressive disorder; Functional near-infrared spectroscopy; Cognitive task; Neuromodulation therapy; Review

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抑郁症是慢性致残性精神疾病，在中国人群中的终身患病率和年患病率分别为3.4%和2.1%，是心境障碍中患病率最高的疾病[1]。功能近红外光谱成像(functional near-infrared spectroscopy，fNIRS)可以监测大脑皮层的血流动力学及血红蛋白氧合状态，近些年国内外有大量针对抑郁症基于认知任务的fNIRS研究，结果表明fNIRS对抑郁症的诊断具有潜在价值[2]。抑郁症患者存在认知功能损害[3]，且这种认知损害在缓解期仍然存在[4]，但认知功能与大脑血流动力学之间的关系尚不明确，现对抑郁症患者基于认知任务下的fNIRS相关研究进展做一综述。

一、fNIRS的基本原理

fNIRS是一种光学成像技术，它利用可以透过生物组织的波长为700～900 nm的近红外光来测量大脑皮层的血流动力学。大脑的活动与一系列生理活动相关，神经活动依赖葡萄糖的代谢，因此当神经活动时局部毛细血管床的葡萄糖和氧气消耗量会增加，局部葡萄糖和氧气的减少会刺激脑局部小动脉扩张，导致局部大脑血流量增加，这种现象被称作神经血管耦合。几秒钟之后，增加的血流为神经活动增强的大脑皮层带来了葡萄糖和氧气，这些运输的氧气超过了神经活动的消耗量，导致神经活动大脑区域的氧合过剩。氧气以氧合血红蛋白(oxygenated hemoglobin)形式运输，当与血红蛋白分离参与葡萄糖代谢时形成脱氧血红蛋白(deoxygenated hemoglobin)。由于氧合血红蛋白和脱氧血红蛋白在可见光和近红外光谱具有特征性光学特征，因此可以通过光学方法测定它们浓度的变化。NIRS根据朗伯比尔定律测量695 nm和830 nm两个红外光波长处的氧合血红蛋白和脱氧血红蛋白的变化[5]。fNIRS设备包括光源和光检测器，在头皮处射入的光穿过大部分组织，并被氧合血红蛋白和脱氧血红蛋白吸收、散射或反射。光子循着香蕉形路径返回皮肤表面，可以使用光探测器进行测量。由于光进入组织后会发生散射，检测器与光源的距离为2～7 cm时可以收集到光信号[6]。与其他神经影像技术相比，fNIRS具有明显的优势，其时间分辨率优于功能磁共振成像(functional magnetic resonance imaging，fMRI)和正电子发射断层扫描(PET)，空间分辨率优于脑磁图(MEG)和脑电图(EEG)，但低于fMRI和PET。fNIRS的主要局限性之一是其成像深度较浅，这是光强度穿过头皮和颅骨然后穿透脑组织时光强度呈指数衰减的结果。由于光强度必须控制在安全水平，避免光产生的热量引起皮肤损害，并且光源和光探测器之间的距离应可以高效地发送和接收信号。因此，对于人类fNIRS的成像深度通常仅限于皮质表面[7]。

二、抑郁症患者认知任务下fNIRS相关研究

1. 词语流畅性测试：词语流畅性测试(verbal fluency task，VFT)是用于神经心理学或神经影像学的一种认知测试，可以反映人的认知能力、记忆与执行能力，是fNIRS研究中应用最多的激活任务。在做VFT任务时，大脑神经活动增加，皮层血流动力学会发生相应改变，由fNIRS检测到的血红蛋白氧化水平也会相应改变。目前研究结果比较一致的是，尽管抑郁症患者与健康对照的VFT任务表现大致相同，但患者在VFT任务下前额叶皮质区、颞区等大脑皮层的氧合血红蛋白增加水平显著低于健康对照[8-12]。此外，fNIRS信号在不同的抑郁症亚型之间也有差异，比如，忧郁型抑郁症患者在VFT任务下大脑皮层的激活程度较非忧郁型更低[13-14]。目前fNIRS信号在预测抑郁症症状方面的研究结果一致性较差[9-12, 14-17]。一项为期1.5年的纵向研究结果显示，84.6%抑郁症患者在症状缓解之后右下额回对应通道氧合血红蛋白反应水平有恢复趋势[18]。Pu等[10]和Tsujii等[19]研究发现伴有自杀意念及自杀行为的抑郁症患者VFT任务下氧合血红蛋白增加水平小于没有自杀意念及行为的抑郁症患者，提示fNIRS对于识别自杀风险具有潜在意义。综上所述，由VFT引起的大脑皮层血流动力学改变及氧合血红蛋白水平改变可以作为识别抑郁症的潜在生物学指标，加之fNIRS具有无创、成本低、对活动耐受度大等优点，在临床推广方面具有优势。由于目前缺少大规模针对抑郁症患者的fNIRS研究，仍需大样本及纵向的长程随访研究进一步探索fNIRS在抑郁症中的应用。

2. 工作记忆任务：N-back任务是评估工作记忆能力的一项持续操作任务经典范式，在认知神经科学中有广泛的应用，也可以作为fNIRS的激活任务。Zhu等[20]对35例抑郁症患者和36名健康受试者进行N-back任务激活下的fNIRS信号研究，结果显示抑郁组由N-back任务引起的氧合血红蛋白水平改变在左额叶皮质(CH18：Z=−2.358，P=0.018)、左下额回眼部及三角部(CH30：Z=−2.174，P=0.030)、右侧下额前回(CH34：Z=−1.990，P=0.047)的激活低于健康对照组，且氧合血红蛋白水平与汉密尔顿抑郁关系分值无关，这一结果与以往的研究一致[21-22]，表明抑郁症患者在N-back任务与VFT任务激活下

的fNIRS血红蛋白信号改变均比健康对照组小。但这与一些fMRI研究结果并不一致，有研究团队的fMRI研究发现在认知任务激活下抑郁症大脑皮质活动增加，可能由于两种影像学技术检测的大脑区域异质性、血管敏感性差异及个体差异性所致[23-25]。今后仍需要学者对fNIRS信号在抑郁症患者的应用进行更大规模的探索，与其他影像学技术相结合，发展出抑郁症的影像学相关生物指标。

三、与神经调控物理治疗结合

神经调控物理治疗在精神科领域的应用愈发广泛，如电休克治疗(electroconvulsive therapy，ECT)、重复经颅磁刺激(repetitive transcranial magnetic stimulation，rTMS)、经颅直流电刺激(transcranial direct current stimulation，tDCS)等。近些年也有许多研究者把fNIRS技术与物理治疗相结合，致力于研究在进行各种物理治疗时大脑的血流状态，探索区分临床亚型、预测治疗效果等的潜在生物学标志。

1. ECT与fNIRS相结合：ECT可用于治疗严重或难治性的抑郁症患者，有快速的抗抑郁作用，治疗后可引起大脑血流动力学变化，这些变化可能与ECT治疗后情绪的改善及短暂认知障碍有关[26]，但具体机制并不清楚。Hirano等[27]研究发现，抑郁症在接受ECT治疗后2周内VFT任务诱导下大脑皮层氧合血红蛋白改变量增加。随后，Downey等[28]对抑郁症ECT治疗后前额血流动力学反应研究，发现在4次ECT治疗结束后的2 d内，VFT任务诱导的氧合血红蛋白改变量比ECT治疗前降低，与情绪或认知变化无关。这两个结果看似矛盾实则不然，因为ECT的不良反应之一就是短暂的认知功能障碍[29]，这种短暂的认知障碍可能是由于大脑的血流量抑制所致[30]，在2周左右这种抑制作用消失，氧合血红蛋白水平恢复正常。利用fNIRS信号检测ECT治疗时的血流动力学及氧合模式不仅有助于理解ECT治疗抑郁症的作用机制，还可能有助于判断ECT的治疗效果及临床分型，但ECT治疗对大脑血流动力学及血液氧化状态的影响仍需与其他的影像学技术整合进行多维度验证，从而发展个体化治疗体系。

2. rTMS与fNIRS相结合：rTMS是用于治疗抑郁症的一种安全的、非侵入性的神经调控治疗。它的原理是利用磁场使大脑神经元去极化以调节与抑郁症状相关的神经环路从而调节情绪[31-32]。Aoyama等[33]对10名健康志愿者进行rTMS干预，然后用fNIRS进行检测，发现左侧前额叶皮质的平均氧合血红蛋白水平降低，脱氧血红蛋白轻微增加，结束刺激后氧合血红蛋白回到基线水平。由于目前对于fNIRS与rTMS相结合的研究较少，尚缺乏对抑郁症患者rTMS治疗的血流动力学或fNIRS研究，未来有望使用fNIRS监测rTMS诱导的脑功能变化，并为患者提供个体化的参数设定。

3. tDCS与fNIRS相结合：tDCS是一种无创的神经调控技术，治疗成本比rTMS低，且不会出现癫痫发作等不良反应。它通过在头皮上放置电极并通上微弱的直流电以诱导大脑皮层神经活动及兴奋性改变[34]。将电极放置在与情绪调节有关的脑区可以用于治疗抑郁症，电流的刺激会使大脑皮层兴奋性改变从而起到抗抑郁效果[35]。Li等[36]对26例脑卒中后抑郁患者进行tDCS治疗，在治疗的前后1 d分别用fNIRS检测大脑皮层信号，激活任务为情绪面部性别识别任务和1-back任务，结果显示在tDCS治疗后1-back任务激活的前额叶皮质区氧合血红蛋白 信号改变明显高于治疗前，该结果表明tDCS可以增强脑卒中后抑郁患者前额叶皮质的有氧代谢状态从而改善抑郁症状。

综上所述，fNIRS可以与多种物理神经调控治疗相结合来检测大脑皮层的血流动力学及氧合状态变化，进一步探索治疗效果与fNIRS信号的关联，为神经调控治疗的技术参数设定及疗效预后提供有利的参考。

四、小结

fNIRS虽然存在一些局限性，比如只能检测大脑皮层浅部的信号，时间分辨率不如脑电图，空间分辨率不如fMRI，但其可移动性大、低成本、非侵入性、对被试者的限制较小、可与其他影像学技术同时进行，这些优点使其更容易推广应用于精神疾病患者，也可以根据疾病的可能病理机制和临床特点发展出不同的范式来测定相应的fNIRS信号。在相关研究中，抑郁症患者认知任务下fNIRS信号的异常存在于多个大脑皮层区域，提示抑郁症的大脑血流动力学及氧合状态改变并不局限于某个特定脑区。与其他影像学技术结合可以从不同维度探索抑郁症患者的脑功能变化，与fMRI相比，fNIRS具有较高的时间分辨率，探索fNIRS特定通道或大脑区域在抑郁症的特征性改变，同时也可弥补fMRI在抑郁症神经影像学研究不足之一。在多种认知激活任务下fNIRS与fMRI信号具有较高相关性，在有的通道两者信号相关性高达0.87[37]。但fNIRS-fMRI关联研究结果表明二者相关性与不同大脑区域、个体头皮-脑间距差异等因素有关，不同通道之间的相

关性存在较大差异[37]。fNIRS的信号检测深度及信号稳定性均劣于fMRI,这也是fNIRS应用于临床的瓶颈之一。国内外研究对于fNIRS判别抑郁症的准确度在51.5%~74%[38-39],表明fNIRS可以作为抑郁症潜在的辅助诊断技术。由于当前研究的样本量相对较小,多为横断面研究。未来的研究可以聚焦于纵向研究、扩大样本量,以克服目前研究设计的局限性,得出更加科学可信的结果。

利益冲突 文章所有作者共同认可文章无相关利益冲突

作者贡献声明 论文撰写为张福旭,论文修订为刘晓华、张天宏,刘晓华审校

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