

首发抑郁症患者词语流畅性任务脑激活特征

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【摘要】 目的 初步探讨首发抑郁症患者执行词语流畅性任务时前额叶和双侧颞叶脑激活特征。**方法** 纳入 2021 年 1-3 月上海交通大学医学院附属瑞金医院收治的 40 例首发抑郁症患者以及性别、年龄、受教育程度相匹配的正常对照者,采用 Zung 氏抑郁自评量表(SDS)评估抑郁症状严重程度,功能性近红外光谱成像(fNIRS)技术检测执行词语流畅性任务期间前额叶和双侧颞叶脑区激活特征。Pearson 相关分析探讨抑郁症患者前额叶和双侧颞叶氧合血红蛋白积分值与 SDS 评分的相关性。**结果** 抑郁症患者 SDS 评分高于正常对照者(68.38 ± 12.91 对 35.98 ± 6.83 ; $t = 11.832, P = 0.000$)。执行词语流畅性任务时,抑郁症患者前额叶[(35.25 ± 41.74) mmol·mm 对 (149.91 ± 54.88) mmol·mm; $t = -8.140, P = 0.000$]和双侧颞叶[(84.05 ± 59.23) mmol·mm 对 (211.01 ± 81.27) mmol·mm; $t = -6.250, P = 0.000$]氧合血红蛋白积分值低于正常对照者,组词数组间差异无统计学意义[(11.27 ± 4.35) 个对 (11.92 ± 5.55) 个; $t = -0.450, P = 0.665$]。Pearson 相关分析结果显示,抑郁症患者双侧颞叶氧合血红蛋白积分值与 SDS 评分呈负相关($r = -0.330, P = 0.039$),而前额叶积分值与 SDS 评分无相关性($r = -0.210, P = 0.184$)。**结论** 首发抑郁症患者执行词语流畅性任务时,前额叶和双侧颞叶脑区激活下降,双侧颞叶氧合血红蛋白积分值与抑郁程度呈负相关。

【关键词】 抑郁症; 认知障碍; 谱学,近红外线; 神经心理学测验

Spatial pattern of brain activation during a Verbal Fluency Test in first-episode depressive disorder patients: a functional near-infrared spectroscopy study

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【Abstract】 Objective To investigate the spatial pattern of the activation of the prefrontal and bilateral temporal cortex in first-episode depressive disorder patients during Verbal Fluency Test (VFT). **Methods** Forty first-episode patients who met the diagnostic criteria of Diagnostic and Statistical Manual of Mental Disorders Fifth Edition (DSM-5) depressive disorder and 14 normal controls were both measured of spatial pattern in the prefrontal and bilateral temporal cortex by functional near-infrared spectroscopy (fNIRS) during VFT, at the same time, the number of words produced during VFT was recorded. The severity of depressive symptoms was assessed by Zung's Self-Rating Depression Scale (SDS). The spatial pattern of brain activation during VFT was compared between 2 groups, and the correlation between the oxyhemoglobin (HbO₂) integral value of prefrontal or bilateral temporal lobes and SDS score were explored by Pearson correlation analysis in depressive disorder group. **Results** SDS score of the depressive disorder patients was higher than that of control group (68.38 ± 12.91 vs. 35.98 ± 6.83 ; $t = 11.832, P = 0.000$). Compared with the control group, the scores of prefrontal and bilateral temporal lobes in depression group were significantly lower during VFT [(35.25 ± 41.74) mmol·mm vs. (149.91 ± 54.88) mmol·mm, $t = -8.140, P = 0.000$; (84.05 ± 59.23) mmol·mm vs. (211.01 ± 81.27) mmol·mm, $t = -6.250, P = 0.000$]. There was no significant difference in the number of words between 2 groups (11.27 ± 4.35 vs. 11.92 ± 5.55 ; $t = -0.450, P =$

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0.665). There was a negative correlation between the HbO₂ integral value of bilateral temporal lobes and SDS score in patients with depressive disorder ($r = -0.330, P = 0.039$), and there was no significant correlation between the HbO₂ integral value of prefrontal lobe and SDS score ($r = -0.210, P = 0.184$).

Conclusions During the VFT, the decrease of prefrontal and bilateal temporal lobes activation and the bilateral temporal lobes HbO₂ integral value is negatively correlated with the degree of depression.

【Key words】 Depression disorder; Cognition disorders; Spectroscopy, near - infrared; Neuropsychological tests

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抑郁症是常见的精神障碍,以情绪低落、思维迟缓、认知损害为主要临床特征^[1-2],以注意力下降和执行功能障碍为主要表现的认知功能障碍^[3]是导致患者社会功能障碍的主要原因之一,但其相关机制尚不明确,临床缺乏客观的生物学指标^[4-5]。功能性近红外光谱成像(fNIRS)技术是一种非侵入性、功能性脑成像技术,通过检测神经活动过程中脑血流动力学变化,评估脑激活情况,近年逐渐应用于抑郁症的临床研究^[6]。词语流畅性测验(VFT)主要涉及记忆信息的提取速度和注意能量,可以有效激活额颞叶皮质,广泛应用于包括抑郁症在内的精神病认知功能障碍的临床研究^[7-8]。本研究采用fNIRS技术检测抑郁症患者执行认知任务时额颞叶皮质激活特征,初步探讨抑郁症患者认知功能障碍的可能机制。

资料与方法

一、临床资料

1. 纳入标准 (1)抑郁症的诊断标准参照美国精神障碍诊断与统计手册第5版(DSM-5)^[9],由至少1位主任医师确诊为首发抑郁症。(2)右利手。(3)年龄14~60岁。(4)小学及以上受教育程度。(5)头部MRI未见异常。

2. 排除标准 (1)严重神经系统疾病或器质性精神障碍。(2)严重躯体疾病或颅脑创伤。(3)双相情感障碍(BAD)。(4)交流困难。(5)左利手。(6)妊娠期或哺乳期女性。(7)药物或精神活性物质依赖或酒精成瘾。(8)因严重认知功能障碍无法完成fNIRS检查。

3. 一般资料 (1)抑郁症组:根据上述纳入与排除标准,选择2021年1-3月在上海交通大学医学院附属瑞金医院临床心理科门诊就诊的抑郁症患者

共40例,男性9例,女性31例;年龄13~56岁,中位年龄28.50(17.00,34.25)岁;受教育程度7~19年,中位值15.50(11.50,16.75)年。(2)正常对照组:同期招募临床心理科实习医师和就诊的排除精神病的志愿者共14例,男性6例,女性8例;年龄15~59岁,中位年龄29.50(19.75,52.25)岁;受教育程度为7~19年,中位值为16(12,16)年。两组受试者一般资料比较,差异无统计学意义(均 $P > 0.05$,表1),均衡可比。

二、研究方法

1. 抑郁症状评估 采用Zung氏抑郁自评量表(SDS)评估受试者抑郁症状严重程度,包含4组共20项条目,每项条目分为没有或很少时间、小部分时间、相当多时间、绝大部分或全部时间共4级,正向评分题依次评分为粗分1~4、反向评分题依次评分为粗分4~1,总评分为80,并计算标准分,标准分=(总评分/80)×100,结果取整数部分,其范围为25~100,评分<53为无抑郁、53~62为轻度抑郁、63~72为中度抑郁、>72为重度抑郁。

2. 词语流畅性测验 检查室内保持安静无嘈杂,受试者坐在有日光灯照明的房间内,目视前方,集中注意力,头部和身体保持不动,测试前以统一的指导语向受试者说明测试流程。测试过程分4个阶段,共计160s,第1阶段为预扫描期,共10s,受试者集中注意力,静候测试的开始;第2阶段为重复计数期,共30s,受试者重复计数数字1~5;第3阶段为组词任务期,共60s,机器语音提示3个简单汉字(大、天、白),受试者分别以这3个字组词,每个字20s;第4阶段为重复计数期,共70s,受试者仍重复计数数字1~5^[10]。第3阶段组词数为词语流畅性测验结果。

3. fNIRS数据采集 采用日本Hitachi公司生产

的 ETG4100 型近红外光谱成像仪评估脑激活情况,共 17 个发射光极和 16 个接收光极,任何一对相邻的发射光极和接收光极组成 1 个通道,共 52 个通道,光极间距为 3 cm,采样率为 10 Hz,选择 3×11 光极排列方式,参照国际 10-20 系统安置光极板,光极板覆盖前额叶和双侧颞叶,其中,检测通道 CH 1-3、CH 11-14、CH 22-24、CH 32-35、CH 43-45 覆盖右侧颞叶,CH 8-10、CH 18-21、CH 29-31、CH 39-42、CH 50-52 覆盖左侧颞叶,CH 4-7、CH 15-17、CH 25-28、CH 36-38、CH 46-49 覆盖前额叶。测试过程嘱受试者保持头部固定,避免频繁眨眼、咀嚼、过大张嘴等动作,发射光极发射波长为 695 和 830 nm 的近红外光,接收光极根据 Lambert-Beer 定律将光信号转换为电信号,再通过成像系统处理即可获得受试者执行词语流畅性任务时的大脑皮质氧合血红蛋白(HbO₂)、脱氧血红蛋白和总血红蛋白表达变化。绘制氧合血红蛋白浓度曲线并计算执行词语流畅性任务组词任务期曲线下面积(AUC),即为积分值(mmol·mm),积分值越高、氧合血红蛋白含量越高、认知任务相关神经活动越活跃。

4. 统计分析方法 采用 SPSS 22.0 统计软件进行数据处理与分析。计数资料以相对数构成比(%)或率(%)表示,采用 χ^2 检验。正态性检验采用 Shapiro-Wilk 检验,呈正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,采用两独立样本的 *t* 检验;呈非正态分布的计量资料以中位数和四分位数间距[*M*(*P*₂₅,*P*₇₅)]表示,采用 Mann-Whitney *U* 检验。抑郁症患者前额叶和双侧颞叶氧合血红蛋白积分值与 SDS 评分的相关性采用 Pearson 相关分析。以 *P* ≤ 0.05 为差异具有统计学意义。

结 果

抑郁症状评估,抑郁组患者 SDS 评分平均为 68.38 ± 12.91,正常对照组为 35.98 ± 6.83,组间差异有统计学意义(*P* = 0.000,表 2)。执行词语流畅性任务时,抑郁组患者平均组词数(11.27 ± 4.35)个,正常对照组为(11.92 ± 5.55)个,组间差异无统计学意义(*P* = 0.655);进一步计算氧合血红蛋白积分值,抑郁组患者前额叶(*P* = 0.000)和双侧颞叶(*P* = 0.000)积分值均低于正常对照组且差异有统计学意义(表 2)。

Pearson 相关分析结果显示,抑郁患者 SDS 评分与双侧颞叶氧合血红蛋白积分值呈负相关关系

表 1 抑郁症组与正常对照组受试者一般资料的比较

Table 1. Comparison of clinical characteristics between depressive disorder group and control group

观察指标	正常对照组 (n = 14)	抑郁症组 (n = 40)	χ^2 或 Z 值	P 值
性别[例(%)]			1.248	0.264
男性	6/14	9(22.50)		
女性	8/14	31(77.50)		
年龄 [<i>M</i> (<i>P</i> ₂₅ , <i>P</i> ₇₅),岁]	29.50 (19.75,52.25)	28.50 (17.00,34.25)	-1.166	0.244
受教育程度 [<i>M</i> (<i>P</i> ₂₅ , <i>P</i> ₇₅),年]	16.00 (12.00,16.00)	15.50 (11.50,16.75)	-0.143	0.886

Adjusted χ^2 test for comparison of sex, and Mann-Whitney *U* test for comparison of age and education,性别的比较采用校正 χ^2 检验,年龄和受教育程度的比较采用 Mann-Whitney *U* 检验

表 2 抑郁症组与正常对照组受试者 SDS 评分、组词数、前额叶和双侧颞叶积分值的比较($\bar{x} \pm s$)

Table 2. Comparison of the SDS score, words number and the integral value of frontal lobe and bilateral temporal lobe between 2 groups ($\bar{x} \pm s$)

组别	例数	SDS 评分	组词数(个)
正常对照组	14	35.98 ± 6.83	11.92 ± 5.55
抑郁症组	40	68.38 ± 12.91	11.27 ± 4.35
<i>t</i> 值		11.832	-0.450
<i>P</i> 值		0.000	0.655

组别	例数	前额叶积分值 (mmol·mm)	双侧颞叶积分值 (mmol·mm)
正常对照组	14	149.91 ± 54.88	211.01 ± 81.27
抑郁症组	40	35.25 ± 41.74	84.05 ± 59.23
<i>t</i> 值		-8.140	-6.250
<i>P</i> 值		0.000	0.000

SDS,Zung's Self-Rating Depression Scale,Zung 氏抑郁自评量表

表 3 抑郁患者 SDS 评分与前额叶和双侧颞叶氧合血红蛋白积分值的 Pearson 相关分析

Table 3. Correlation analysis for SDS score and HbO₂ integral value of prefrontal lobe or bilateral temporal lobes in depressive disorder patients

观察指标	<i>r</i> 值	<i>P</i> 值
前额叶积分值	-0.210	0.184
双侧颞叶积分值	-0.330	0.039

(*r* = -0.330, *P* = 0.039),而与前额叶积分值无相关性(*P* = 0.184,表 3)。

讨 论

认知功能障碍是抑郁患者的主要临床特征之一^[11],与额颞叶等脑区功能异常有关^[12],相关脑区血流动力学改变可以反映认知功能的变化。词语流畅性测验作为一种认知激活范式,是 fNIRS 检查中常用的脑激活任务,中文版、日文版和英文版

均证实其在抑郁症的辅助诊断中具有较高的敏感性和特异性^[13-15]。fNIRS 技术可以检测受试者执行词语流畅性任务时额颞叶皮质血流动力学变化,即脑激活情况,额颞叶代表空间位置,氧合血红蛋白积分值描述空间信息特征,重心值描述时间信息特征^[6,16]。与 fMRI 相比较,fNIRS 技术具有高生态效度、低噪音、高时间分辨率、对运动干扰不敏感等优势^[16]。有研究者认为,执行认知任务期间,相关脑区血红蛋白表达变化可能是抑郁症辅助诊断的潜在生物学标记^[17]。

本研究采用 52 通道 fNIRS 技术探讨首发抑郁症患者执行词语流畅性任务时前额叶和双侧颞叶脑血流动力学变化及脑激活特征,结果显示,执行词语流畅性任务期间,抑郁症患者前额叶和双侧颞叶脑激活程度明显低于正常对照者,提示抑郁症患者额颞叶功能下降,与既往研究结果相一致^[7-8,18-19],推测这可能是抑郁症患者认知功能障碍的神经病理学基础。Ho 等^[20]在 2020 年发表的系统综述共纳入 64 项临床研究,发现与正常对照者相比,抑郁症患者执行认知任务期间大脑皮质血流动力学变化减弱。Husain 等^[21]对抑郁症和边缘型人格障碍(BPD)患者的研究显示,与正常对照者相比,抑郁症和边缘型人格障碍患者认知功能下降的同时,额颞顶叶皮质血流动力学变化明显减弱,且抑郁症患者的皮质功能损害更广泛。

在本研究中,抑郁症患者执行词语流畅性任务时组词数与正常对照者无明显差异,与既往研究结果相一致^[18,22],反映出抑郁症患者认知活动与脑激活非同步的现象。脑激活程度与认知需求有关,组词等简单的认知活动对脑激活的需求较低,因此推测,抑郁症患者进行不同难度的认知活动,其相关脑区呈现出不同的血流动力学改变,这一结论尚待进一步验证。

本研究结果还显示,执行词语流畅性任务期间,抑郁症患者额颞叶皮质血流动力学变化即脑激活程度与抑郁程度具有相关性,SDS 评分与双侧颞叶氧合血红蛋白积分值呈负相关,提示抑郁程度越严重、双侧颞叶氧合血红蛋白含量越低、脑激活程度越低,可能与抑郁症患者认知功能障碍相关;而 SDS 评分与前额叶氧合血红蛋白积分值无明显相关性,与既往研究结果不符。Kawano 等^[23]的研究显示,包括抑郁症、精神分裂症、双相情感障碍、强迫症和惊恐障碍在内的精神障碍患者执行词语流畅

性任务时,额叶皮质激活程度与抑郁程度呈负相关。Noda 等^[24]也认为,抑郁症患者执行词语流畅性任务时,右侧额颞叶激活程度与抑郁程度相关。上述研究结果不一致可能是由于抑郁症患者存在症状异质性,不同症候群影响皮质激活的区域不同,涉及多个脑区^[18,25];大多数研究并未进行抑郁症状的维度划分,亦未对额颞叶皮质进行更精细的功能分区,均可能导致研究结果不一致,进一步研究应考虑抑郁症状的复杂性。

本研究是对首发抑郁症患者执行认知任务时脑激活特征的初步探讨,鉴于临床应用的便捷性,仅基于国际 10-20 系统进行定位,受受试者头围大小的影响,每个通道所对应的皮质位置可能存在差异,进而影响研究结果的一致性,后续研究将采用更精确的导航定位系统,将目标脑区缩小至更精确的功能分区,以探讨不同认知域损害时脑激活特征。本研究采用的 SDS 量表为自评量表,具有一定的局限性,如主观性较强,受教育程度较低者无法自评等,但既往研究显示,SDS 量表评估抑郁程度具有较好的信度和效度,适用于综合医院抑郁症患者的自评^[26-27],因此本研究仍具有科学价值,后续研究将引进他评量表的评估。本研究样本量相对较少,仅呈现氧合血红蛋白积分值这一空间特征,并未对描述时间特征的重心值进行分析,也是局限性所在。本研究采用的词语流畅性任务是参照日本多中心临床试验采取的任务范式^[8],仅涉及认知功能中的执行功能,无法反应抑郁症患者的认知功能全貌。抑郁症是异质性精神病,其认知功能障碍的评估方法和内容一直存有较大分歧,迄今尚无公认的评估量表,理想状态是进行多维度认知功能评估。后续尚待进一步扩大样本量,完善评估量表及空间和时间特征评估指标,为抑郁症认知功能障碍研究提供更强有力的证据。

利益冲突 无

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