·神经心理学研究·

抑郁障碍对颅脑创伤患者反应抑制功能的影响

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【摘要】 **目的**　初步探讨抑郁障碍对颅脑创伤患者反应抑制功能的影响。**方法**　采用Glasgow昏迷量表、汉密尔顿抑郁量表17项(HAMD-17)和日常生活活动能力量表(ADL)评价104例颅脑创伤患者(伴抑郁障碍54例、不伴抑郁障碍50例)颅脑创伤和抑郁障碍严重程度,刺激-反应相容性试验记录反应抑制任务反应时间。**结果**　颅脑创伤伴抑郁障碍组HAMD-17(P = 0.000, 0.000)和ADL(P = 0.000, 0.000)评分高于颅脑创伤不伴抑郁障碍组和对照组,颅脑创伤不伴抑郁障碍组HAMD-17(P = 0.000)和ADL(P = 0.000)评分亦高于对照组。无论执行相容性还是不相容性任务,颅脑创伤伴或不伴抑郁障碍组患者反应时间均长于对照组(P = 0.000, 0.000),颅脑创伤伴抑郁障碍组患者反应时间亦长于颅脑创伤不伴抑郁障碍组(P = 0.000)。**结论**　颅脑创伤后可发生认知功能障碍,且在伤后6个月或更长时间仍存在。颅脑创伤伴抑郁障碍可以加重患者认知功能障碍,应早期识别并及时干预。

【关键词】 颅脑损伤;　抑郁;　反应抑制;　神经心理学测验

Effect of depression on response inhibition of patients after traumatic brain injury

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【**Abstract**】 **Objective**　To investigate the effect of depression on response inhibition of patients after traumatic brain injury (TBI). **Methods**　Glasgow Coma Scale (GCS), Hamilton Depression Rating Scale-17 Items (HAMD-17) and Activities of Daily Living (ADL) were used to assess the severity of trauma, depression and activities of daily living in 104 TBI patients (54 with depression and 50 without depression). Besides, 51 normal controls with matched age, sex and education were enrolled. Stimulus - Response Compatibility (SRC) task was employed to record the reaction time (RT) of response inhibition of the subjects in 3 groups. **Results**　Both HAMD - 17 and ADL scores in TBI with depression group were significantly higher than those in TBI without depression group (P = 0.000, 0.000) and normal control group (P = 0.000, 0.000). Besides, HAMD-17 and ADL scores in TBI without depression group were significantly higher than those in normal control group (P = 0.000, 0.000). Compared with normal control group, no matter in compatible or incompatible condition, RT was significantly longer in both TBI groups (P = 0.000, 0.000). RT was much longer in TBI with depression group than that in TBI without depression group (P = 0.000). **Conclusions**　Cognitive dysfunction is a common symptom after TBI, which may exist 6 months after injury or even longer. TBI combined with depression could aggravate the impaired cognitive function, so early identification and timely intervention is very important.

【**Key words**】 Craniocerebral trauma;　Depression;　Reactive inhibition;　Neuropsychological tests

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颅脑创伤(TBI)指头部受到外力如跌落、交通事故、战争、击打等原因造成的损伤,可能直接造成脑组织损伤,也可能间接导致脑组织损伤、肿胀、炎症和颅内出血[1]。最初对颅脑创伤患者的治疗主要关注降低病死率和恢复肢体功能,后逐渐发现,颅脑创伤后生存患者,尤其是能够生活自理甚至恢复工作的患者,仍遗留认知功能障碍、情感障碍、行为改变、躯体和社会心理改变等神经精神症状,其中以认知功能障碍和情感障碍最为常见[2-3],此类患者躯体疾病似乎恢复,但难以融入家庭和社会,常被认为是"可行走的伤员",严重影响患者生活质量和重返工作岗位能力[4]。因此,越来越多的学者开始关注颅脑创伤患者认知功能障碍和情感障碍[5-6]。目前,国内相关研究较少见诸报道。本研究初步探讨抑郁障碍对颅脑创伤患者反应抑制功能的影响,以期有助于颅脑创伤患者改善预后、提高生活质量和恢复社会功能。

资料与方法

一、临床资料

1. 纳入标准 (1)抑郁障碍的诊断符合简明国际神经精神访谈(MINI)中文版标准[7]。(2)年龄为18~50岁。(3)受教育程度为初中或以上。(4)均于颅脑创伤后6个月进行认知功能和抑郁症状评价,创伤后遗忘(PTA)均已恢复,能够配合完成神经心理学测验。(5)本研究经复旦大学附属华山医院道德伦理委员会审核批准,所有受试者知情同意并签署知情同意书。

2. 排除标准 合并其他神经精神疾病;既往有抑郁障碍,以及严重心脏、肝脏、肾脏疾病病史;药物成瘾史或依赖史;妊娠期或哺乳期女性。

3. 一般资料 选择2012年7月–2014年12月在复旦大学附属华山医院神经外科和康复医学科门诊和住院治疗的104例颅脑创伤患者,男性72例,女性32例;年龄18~50岁,平均(30.44±8.67)岁;受教育程度8~20年,平均(13.53±3.61)年;发病至入院时间0.50~9.00 h,平均为(4.33±1.65) h;致伤原因为交通事故伤50例(48.08%)、跌落伤19例(18.27%)、运动损伤11例(10.58%)和击打伤24例(23.08%);损伤部位分别位于额颞叶58例(55.77%)、额叶21例(20.19%)、颞叶20例(19.23%)及其他部位5例(4.81%);入院时Glasgow昏迷量表(GCS)评分6~15分,平均(9.29±2.69)分;汉密尔顿抑郁量表17项(HAMD-17)评分4~31分,平均(14.15±6.91)分;日常生活活动能力量表(ADL)评分17~33分,平均(23.38±3.54)分。

二、研究方法

1. 颅脑创伤程度评价 采用GCS量表[8]评价颅脑创伤严重程度,包括睁眼、语言和运动反应3项内容,每项评分1~5分,总评分3~15分,评分越低、意识障碍越严重,其中评分≤8分为昏迷。

2. 抑郁程度评价 采用HAMD-17量表[9]评价抑郁障碍严重程度,包括抑郁情绪、负罪感、自杀倾向、入睡困难、睡眠浅、早醒、工作和兴趣、迟缓、激越、精神性焦虑、躯体性焦虑、胃肠道症状、全身症状、性症状、疑病、体重减轻和自知力共计17项内容,总评分越高、抑郁障碍越严重。其中,入睡困难、睡眠浅、早醒、胃肠道症状、全身症状、性症状、体重减轻和自知力项目评分为0~2分:0分,无抑郁;1分,轻至中度抑郁;2分,重度抑郁。其余项目评分为0~4分:0分,无抑郁;1分,轻度抑郁;2分,中度抑郁;3分,重度抑郁;4分,极重度抑郁。总评分<7分,无抑郁;>17分,轻至中度抑郁;>24分,重度抑郁。

3. 反应抑制功能评价 采用刺激-反应相容性(SRC)试验进行反应抑制任务[10]。通过美国PST公司生产的心理学E-prime 2.0软件在电脑上呈现刺激任务,即出现在黑色屏幕左侧或右侧的白色圆点,受试者按照刺激模块前出现的相容性提示模块进行反应,若出现相容性标志(compatible),则左侧出现刺激用左手反应,右侧出现刺激用右手反应;若出现不相容性标志(incompatible),则左侧出现刺激用右手反应,右侧出现刺激用左手反应,E-prime 2.0软件自动记录受试者对刺激的反应时间(RT)。

4. 日常生活活动能力评价　采用ADL量表评价日常生活活动能力[11]。包括两部分内容，即生活自理能力（共6项，包括上厕所、进食、穿衣、梳洗、行走和洗澡）和日常生活活动能力（共8项，包括打电话、购物、备餐、做家务、洗衣、使用交通工具、服药和自理经济）。评分＜16分，正常；16～21分，日常生活活动能力下降；≥22分，日常生活活动能力明显障碍。

5. 统计分析方法　采用SPSS 16.0统计软件进行数据处理与分析。计数资料以率（%）或相对数构成比（%）表示，采用χ^2检验；计量资料以均数±标准差（$\bar{x}\pm s$）表示，采用单因素方差分析，两两比较行LSD-t检验。以$P\leqslant 0.05$为差异具有统计学意义。

结　果

一、一般资料的比较

104例颅脑创伤患者根据是否伴发抑郁障碍分为颅脑创伤伴抑郁障碍组和颅脑创伤不伴抑郁障碍组。（1）颅脑创伤伴抑郁障碍组：54例患者，男性39例，女性15例；年龄18～50岁，平均（31.19±8.76）岁；受教育程度9～20年，平均为（13.57±3.58）年；颅脑创伤至入院时间2～8 h，平均（4.55±1.63）h；致伤原因分别为交通事故伤23例（42.59%）、跌落伤13例（24.07%）、运动损伤5例（9.26%）和击打伤13例（24.07%）；损伤部位位于额颞叶30例（55.56%）、额叶11例（20.37%）、颞叶11例（20.37%）及其他部位2例（3.70%）；首次入院时GCS评分为6～15分，平均（9.41±2.75）分；HAMD-17评分为17～31分，平均（20.41±2.88）分；ADL评分为18～33分，平均（24.72±3.67）分。（2）颅脑创伤不伴抑郁障碍组：50例患者，男性33例，女性17例；年龄18～50岁，平均（29.64±8.60）岁；受教育程度为8～20年，平均（13.48±3.68）年；颅脑创伤至入院时间0.50～9.00 h，平均（4.03±1.71）h；致伤原因分别为交通事故伤27例（54%）、跌落伤6例（12%）、运动损伤6例（12%）和击打伤11例（22%）；损伤部位位于额颞叶28例（56%）、额叶10例（20%）、颞叶9例（18%）及其他部位3例（6%）；入院时GCS评分为6～15分，平均为（9.16±2.64）分；HAMD-17评分为4～10分，平均（7.38±1.28）分；ADL评分17～19分，平均（21.94±2.77）分。（3）正常对照组（对照组）：选择同期在我院进行体格检查的健康志愿者共51例，男性36例，女性15例；年龄18～50岁，平均（30.18±9.21）岁；受教育程度8～19年，平均为（12.63±3.73）年；HAMD-17评分1～6分，平均为（3.55±1.43）分；ADL评分均为14分。3组受试者性别、年龄、受教育程度、颅脑创伤至入院时间、致伤原因、损伤部位、入院时GCS评分差异无统计学意义（均$P>0.05$）；而HAMD-17和ADL评分差异有统计学意义（$P=0.000, 0.000$），其中，颅脑创伤伴抑郁障碍组HAMD-17和ADL评分高于颅脑创伤不伴抑郁障碍组和对照组（HAMD-17评分：$P=0.000, 0.000$；ADL评分：$P=0.000, 0.000$），颅脑创伤不伴抑郁障碍组HAMD-17和ADL评分亦高于对照组（$P=0.000, 0.000$；表1）。

表1　3组受试者临床资料的比较

Table 1.　Comparison of clinical data among 3 groups

Item	Control (N = 51)	TBI without depression (N = 50)	TBI with depression (N = 54)	χ^2 or F value	P value
Sex [case (%)]				0.506	0.777
Male	36 (70.59)	33 (66.00)	39 (72.22)		
Female	15 (29.41)	17 (34.00)	15 (27.78)		
Age ($\bar{x}\pm s$, year)	30.18 ± 9.21	29.64 ± 8.60	31.19 ± 8.76	0.410	0.664
Education ($\bar{x}\pm s$, year)	12.63 ± 3.72	13.48 ± 3.68	13.57 ± 3.58	1.046	0.354
Duration ($\bar{x}\pm s$, year)	—	4.03 ± 1.71	4.55 ± 1.63	1.577	0.118
Cause of injury [case (%)]				3.007	0.391
Traffic accident	—	27 (54.00)	23 (42.59)		
Falling	—	6 (12.00)	13 (24.07)		
Sports injury	—	6 (12.00)	5 (9.26)		
Hitting	—	11 (22.00)	13 (24.07)		
Injury site [case (%)]				0.474	0.975
Fronto-temporal lobe	—	28 (56.00)	30 (55.56)		
Frontal lobe	—	10 (20.00)	11 (20.37)		
Temporal lobe	—	9 (18.00)	11 (20.37)		
Others	—	3 (6.00)	2 (3.70)		
GCS ($\bar{x}\pm s$, score)	—	9.16 ± 2.64	9.41 ± 2.75	0.218	0.642
HAMD-17 ($\bar{x}\pm s$, score)	3.55 ± 1.43	7.38 ± 1.28	20.41 ± 2.88	1008.626	0.000
ADL ($\bar{x}\pm s$, score)	14.00 ± 0.00	21.94 ± 2.77	24.72 ± 3.67	224.215	0.000

χ^2 test for comparison of sex, cause of injury and injury site, and one-way ANOVA for comparision of others。—，no data，此项无数据。TBI，traumatic brain injury，颅脑创伤；GCS，Glasgow Coma Scale，Glasgow昏迷量表；HAMD-17，Hamilton Depression Rating Scale-17 Items，汉密尔顿抑郁量表17项；ADL，Activities of Daily Living，日常生活活动能力量表

二、反应抑制功能的比较

刺激-反应相容性试验显示，无论执行相容性还是不相容性任务，颅脑创伤伴或不伴抑郁障碍组患

表2 3组受试者刺激-反应相容性试验反应时间的比较($\bar{x} \pm s$, ms)

Table 2. Comparison of RT in SRC task among 3 groups ($\bar{x} \pm s$, ms)

Group	N	Compatible	Incompatible
Control (1)	51	436.84 ± 50.71	450.66 ± 52.60
TBI without depression (2)	50	552.38 ± 81.01	588.49 ± 78.08
TBI with depression (3)	54	611.23 ± 97.84	645.67 ± 87.50
F value		65.112	94.247
P value		0.000	0.000

TBI, traumatic brain injury, 颅脑创伤

表3 3组受试者刺激-反应相容性试验反应时间的两两比较*

Table 3. Paired comparison of RT in SRC task among 3 groups*

Paired comparison	Compatible	Incompatible
(1):(2)	0.000	0.000
(1):(3)	0.000	0.000
(2):(3)	0.000	0.000

*P value

者反应时间均长于对照组($P = 0.000, 0.000$),颅脑创伤伴抑郁障碍组患者反应时间亦长于颅脑创伤不伴抑郁障碍组($P = 0.000$;表2,3)。

讨 论

MINI问卷是由Sheehan和Lecrubier教授设计,系美国精神障碍诊断与统计手册第4版(DSM-Ⅳ)以及国际疾病分类-10(ICD-10)中关于精神疾病的简短结构式访谈问卷,其中文版具有良好信度和效度[12]。本研究采用MINI问卷中文版评价颅脑创伤患者是否伴发抑郁障碍,实验心理学中的反应抑制任务评价患者认知功能。反应抑制任务可以反映注意力、记忆力、视空间信息处理能力和执行功能等[13]。刺激-反应相容性试验是一种选择性反应时间试验,能够较好揭示反应抑制情况[10]。

本研究纳入的颅脑创伤患者均为伤后6个月,与对照组相比,无论执行相容性还是不相容性任务,颅脑创伤伴或不伴抑郁障碍组患者反应时间均延长,表明颅脑创伤患者长期存在认知功能障碍,与国外研究结果相一致[14-15]。研究显示,这种认知功能障碍可以持续至伤后数月甚至数年[16],而且不仅与颅脑创伤急性期严重程度有关[17-18],还与伤后康复环境有关[19]。

在本研究中,颅脑创伤患者损伤部位主要位于额颞叶(55.77%),其次为额叶(20.19%)和颞叶(19.23%),与既往研究结果相符[20]。由于额叶和前颞叶参与执行功能、信息处理速度、人格改变和社会认知等多个认知域[21],该区域损伤是颅脑创伤后认知功能障碍的主要原因,因此也成为颅脑创伤患者康复治疗的靶点。近年来,多种治疗方法如有氧运动、目标管理训练(GMT)等均针对颅脑创伤患者额叶功能的改善[22-23]。

本研究结果显示,颅脑创伤伴抑郁障碍组患者执行反应抑制任务时反应时间长于颅脑创伤不伴抑郁障碍组和对照组,提示抑郁障碍可以加重颅脑创伤患者认知功能障碍,与国外研究结果相符[24]。尽管参照MINI问卷中文版颅脑创伤不伴抑郁障碍组患者并不符合抑郁障碍诊断标准,但其HAMD-17评分仍高于对照组,表明颅脑创伤后由于生物、心理和社会因素改变,增加抑郁障碍的易感风险[25]。颅脑创伤后抑郁障碍的发病机制尚不十分清楚,可能与下列两种因素有关:(1)颅脑创伤可以导致情绪调节通路即去甲肾上腺素能和5-羟色胺能神经元及其通路损伤,神经递质合成减少,从而导致抑郁[26]。(2)颅脑创伤后肢体灵活性下降,导致生活自理能力和社会适应能力下降,生活质量下降,从而导致抑郁[27-28]。一般认为,颅脑创伤后早期发生抑郁障碍可能与原发性损伤的关系更明显,而颅脑创伤后长期存在或晚发性抑郁障碍,则可能受社会和心理因素的影响较多。

本研究结果还显示,颅脑创伤伴抑郁障碍组患者日常生活活动能力低于颅脑创伤不伴抑郁障碍组,提示抑郁障碍对颅脑创伤患者的日常生活活动能力有一定影响。由于抑郁障碍的可治愈性,如果能够早期识别和及时干预,对患者认知功能和日常生活活动能力的恢复均具有重要意义,同时对患者康复计划的实施和提高康复的依从性也有积极作用。颅脑创伤增加罹患抑郁障碍的风险,抑郁障碍加重颅脑创伤患者认知功能和日常生活活动能力障碍。因此,应对颅脑创伤患者进行情绪障碍的动态筛查,以便及时根据临床情况进行积极干预。

本研究存在一定局限性:(1)未根据入院时GCS评分进一步分组,观察颅脑损伤程度与抑郁障碍的相关性。(2)仅为横断面研究,未按照不同随访时间进行纵向研究。希望在将来的研究中,进一步完善试验设计,并结合神经影像学进行深入探讨,从而

更加准确地发现相关神经生物学标志物,从而为临床提供有价值的理论依据。

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