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静息态功能磁共振在急性酒精中毒患者认知功能障碍评价分析*

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摘要 目的:探讨静息态功能磁共振在急性酒精中毒患者认知功能障碍影响。**方法:**随机选取我院 2018 年 4 月-2019 年 4 月收治治疗急性酒精中毒性脑病患者共 60 例,将患者作为研究组,另外选择健康实验成员 30 例作为对照组,对两组患者静息态功能磁共振检查结果及临床表现记录,有效观察和分析患者的认知功能障碍评分。**结果:**(1)研究组的模仿和回忆评分显著低于对照组($P<0.05$);(2)研究组的 Rey-Osterrieth 复杂图形测验(Complex figure test, CFT)测验结果异常比例为 43.3 % (26/60),对照组为 20.0 % (6/30),两组认知功能障碍差异对比有统计学意义($P<0.05$);(3)研究组简易智能量表测验(Mini-menta state examination, MMSE)、数符号转换测试(Symbol Digit Modality Test, SDMT)和言语流畅性测验(Verbal fluency test, VFT)评分结果相比于对照组均显著降低($P<0.05$);(4)与对照组相比,研究组的左颞上回、右颞中回、右楔前叶、左后扣带回等脑区的功能连接均显著增强($P<0.05$)。**结论:**急性酒精患者由于乙醇代谢产物对人体的神经系统造成不利影响,因此对患者的认知功能障碍存在着不利影响,静息态功能磁共振对急性酒精中毒患者检测可以促使患者的认知功能障碍的变化情况更好显示出来,静息态功能磁共振对该病诊断价值较为显著。过量摄入酒精容易造成默认网络关键脑区损害问题突出,使得人体大脑基本功能受损。

关键词:静息态功能磁共振;急性酒精中毒;认知功能障碍;评价

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Evaluation of Cognitive Dysfunction in Patients with Acute Alcoholism by Resting State Functional Magnetic Resonance Imaging*

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ABSTRACT Objective: To evaluate the evaluation of cognitive dysfunction in patients with acute alcoholism by Resting-State fMRI. **Methods:** A total of 60 patients with acute alcoholic encephalopathy were enrolled in our hospital from April 2018 to April 2019. The patients were selected as the study group, and 30 healthy members were selected as the control group. The rest of the two groups were rested. The results of functional magnetic resonance imaging and clinical manifestations are effective in observing and summarizing the cognitive dysfunction scores of patients. **Results:** (1) The imitation and recall scores of the study group patients were significantly lower than those of the control group ($P<0.05$). (2) The abnormal proportion of CFT test results in the study group was 43.3 % (26/60), and that in the control group was 20.0 % (6/30), the difference in cognitive dysfunction between the two groups is statistically significant($P>0.05$). (3) The MMSE, SDMT and VFT scores of the study group were significantly lower than those of the control group ($P<0.05$). (4) Compared with the control group, the functional connections of the left iliac crest, right iliac crest, right anterior cranial anterior lobes, and left posterior cingulate gyrus were significantly increased in the study group($P<0.05$). **Conclusion:** Acute alcohol patients have adverse effects on the patient's cognitive dysfunction due to the adverse effects of ethanol metabolites on the human nervous system, and resting-state functional magnetic resonance (MRI) can induce patients with acute alcoholism. Changes in cognitive dysfunction are better shown, and resting-state functional magnetic resonance imaging has significant diagnostic value for the disease. The default network damage caused by excessive intake of alcohol is obvious, which causes the basic function of the human brain to be impaired.

Key words: Resting state functional magnetic resonance; Acute alcoholism; Cognitive dysfunction; Evaluation

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前言

国外相关学者研究静息态功能磁共振在急性酒精中毒患者认知功能障碍评价时,多数应用静息态功能磁共振研究长期

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饮酒者的脑组织代谢,静息态功能磁共振基础扫描结果显示进行长期饮酒者前额叶背外侧皮质胆碱化合物(Choline,Cho)峰值明显升高,而在坚持戒酒4个月之后发生N-乙酰门冬氨酸(N-acetylaspartate,NAA)得以回升,充分说明静息态功能磁共振技术(Resting-State fMRI)通过检测酒精摄入后,致其脑内部的各种代谢物的变化现象,可以为酒精对脑部的作用机制提供相关依据。对我国而言,随着我国经济发展和人们生活质量的改善,饮酒人数也不断提升,饮酒消耗数量也呈现逐年攀升的趋势,同时酒精中毒发病率随之增高,该现象已成为严重的社会问题。长期饮酒造成大脑对酒精形成习惯性依赖,对大脑的功能造成损伤,影响人体脑区间的相关关系及相互协作功能。目前相关研究表明:静息态功能磁共振技术(resting state functional magnetic resonance imaging, Resting-State fMRI)是对人体脑网络功能连接研究的主要方式,该技术可直观地观察到急性酒精依赖患者相较于正常人其大脑功能连接的异常变化^[12]。本研究选取我院2018年4月-2019年4月收治治疗急性酒精中

毒性脑病患者,探讨静息态功能磁共振在急性酒精中毒患者认知功能障碍评价分析,现报告如下。

1 资料与方法

1.1 一般资料

选取我院2018年4月-2019年4月收治治疗急性酒精中毒性脑病患者共60例,将患者作为研究组,另外选择健康实验成员30例作为对照组,研究组都没有接受戒瘾治疗,男性44例,女性16例,年龄18-55岁,对照组男性21例,女性9例,年龄17-57岁。研究组排除^①标准:(1)合并其他原因造成的严重神经或精神疾病;(2)大脑曾发生过脑外伤或其他脑组织受损的情况;(3)短期内服用过精神类药物、毒品等具有依赖性的药物;(4)患者因其他原因具有静息态功能磁共振检查的禁忌。本研究经伦理委员会批准,所有受试者知情同意。两组一般资料对比无差异($P>0.05$),见表1。

表1 两组一般资料对比

Table 1 Comparison of two groups of general information

Groups	n	Sex (male/female)	Age (years)	Level of education		
				High school and below	Undergraduate course	Master or above
Study group	60	44/16	35.23± 2.35	23	32	5
Control group	30	21/9	36.01± 4.18	10	15	5

1.2 静息态功能磁共振方法

所有入组研究对象需要首先实施静息态功能磁共振扫描,从而对其他脑部病变情况有效排除处理,避免影响试验结果。

扫描参数^④:在患者保持静息状态下采集功能磁共振数据。轴位TSE T1WI序列,TR/TE显示为424.0/6.4 ms,层厚设置为6.0 mm,层距为0.9 mm,FOV=230 mm× 230 mm。轴位TSE T2WI序列,TR/TE主要为3600.0/95 ms,层厚设置为6.0 mm,层距设置为0.9 mm,FOV=230 mm× 230 mm。轴位FLAIR序列中,TR/TE 5000.0/81 ms,层厚设置为6.0 mm,层距为0.9 mm,FOV=230 mm× 230 mm。

脑功能网络分析:利用种子相关性分析的方法构建默认网络:选取种子点,随后扣带回为种子点,将皮层内球形区域半径设置为5 mm,中心坐标(Tailarach,0,-52,30)^⑤。随后从种子点中选择平均BOLD时间序列信息,实施种子点序列与其他区域体素中时间序列的时域相关性分析,以r代表时间序列的相关系数。通过Feisher r-to-z变换将相关系数进行处理,从而完成Z分数化过程,使数据满足正态分布。

1.3 认知功能障碍评价

1.3.1 认知功能评估 在患者出院后一周之内,需在安静的环境中对其认知功能进行评估:

(1)采用MMSE和CFT评估两组大脑的认知功能、视觉记忆功能和视觉空间结构功能;(2)采用SDMT评估两组患者的执行功能;(3)采用VFT的方式评估两组患者的语言功能。

1.3.2 评分标准^④ MMSE:根据受试者受教育程度:≤17分为文盲、≤20分为小学文化程度、≤24分判定为中学文化程度,将以上文化程度(即中学文化程度及以下)人员判定为具有认知功能障碍患者;CFT:视觉记忆和视觉空间结构能判定标准:正常者图形模仿>30分,延迟回忆>10分;SDMT:测试大脑记忆和反应速度判定,最高得分为90分;VFT:测试患者从记忆库中调用某类事物的能力。正常者>30分。

观察并记录MMSE、CFT、SDMT、VFT评分结果。

1.4 统计学处理

应用SPSS 18.00,计量数据以($\bar{x} \pm s$)表示,对比为t检验;计数数据以%表示,予以 χ^2 分析,检验水准均为双侧 $\alpha=0.05$, $P<0.05$ 有统计学意义。

2 结果

2.1 两组CFT测验异常结果对比

研究组的CFT测验结果异常比例为43.3%(26/60),对照组健康人员为20.0%(6/30),两组认知功能障碍对比差异有统计学意义($\chi^2=4.752$, $P=0.029$, $P<0.05$)。

2.2 两组CFT检测评分及MMSE、SDMT和VFT评分结果对比

研究组的模仿和回忆评分明显低于对照组,两组对比差异有统计学意义($P<0.05$);研究组MMSE、SDMT和VFT评分结果相比于对照组均显著降低,两组对比差异有统计学意义($P<0.05$)。见表2。

表 2 两组 CFT 检测评分结果对比($\bar{x} \pm s$)

Table 2 Comparison of CFT test scores between the two groups($\bar{x} \pm s$)

Groups	n	Imitate	Recall	MMSE	SDMT	VFT
Study group	60	29.3± 4.1*	11.5± 2.1*	24.5± 4.1*	30.7± 6.3*	30.4± 9.2*
Control group	30	34.2± 6.2	13.4± 2.4	28.5± 3.2	36.4± 7.8	37.4± 9.7

Note: Compared with the control group, * $P < 0.05$.

2.3 两组默认网络功能连接存在差异的脑区比较

与对照组相比,研究组的左颞上回、右颞中回、右楔前叶、

左后扣带回等脑区的功能连接均显著增强,两组对比差异有统计学意义($P < 0.05$),见表 3。

表 3 两组默认网络功能连接存在差异的脑区比较

Table 3 Comparison of brain regions with differences in default network functional connections between the two groups

Groups		Left superior temporal gyrus	Right middle temporal gyrus	Right anterior cuneiform lobe	Left posterior cingulate back
MNI coordinate	X	-57	62	21	-3
	Y	-47	-40	-63	-45
	Z	-14	-8	24	14
fALFF	Study group	1.42± 0.20*	1.31± 0.17*	1.81± 0.31*	1.49± 0.26*
	Control group	1.09± 0.12	1.10± 0.13	1.62± 0.27	1.23± 0.16

3 讨论

乙醇是酒水的主要成分,通常小剂量乙醇可以作为中枢神经系统的抑制剂,而大剂量则会对全身造成抑制效果,人体会发生昏迷等现象,严重者甚至会导致死亡,因此过量摄入酒精所造成的默认网络关键脑区损害现象明显,容易损害人体大脑基本功能^[6-8]。目前多数研究关注慢性酒精中毒对认知功能的损伤情况,而对短期内摄入大量乙醇患者的研究比较少^[9-11]。脑组织是人体组织中能量消耗最大的组织器官,在脑组织营养物质供应不足时也容易使得人体细胞代谢紊乱^[12-17],从而导致神经元正常的电生理活动也会存在着明显异常,不同脑区的受损也容易产生不同的功能发生障碍,利用静息态功能磁共振进行酒精中毒患者情况分析可以促使患者的变化情况和相关量表结果结合在一起分析,其能够更好的实施人体认识障碍判断^[18-24]。

本研究结果表明:急性酒精中毒患者的模仿和回忆评分明显低于对照组,表明急性酒精中毒导致患者大脑的模仿和回忆能力受到严重损伤;研究组患者 MMSE 和 SDMT 和 VFT 评分结果相比于对照组健康人员均显著降低,说明急性酒精中毒患者大脑相比于正常的受试者,其认知功能障碍程度加重,视觉记忆,视觉空间结构能力下降,大脑记忆和反应速度变得迟缓;短期饮酒可能对人大脑的认知障碍功能影响不明显,但对大脑认知功能仍具有一定程度损害,因此急性酒精中毒同样会影响患者大脑认知功能^[25-27]。分析该结果原因可能在于:乙醇代谢产物通常会抑制神经系统突触受体信号的传递和神经递质的释放,且容易对单个神经元的代谢活动造成不利影响,乙醇在抑制神经系统受体通道的时候会引发系列生化反应,从而引起内源性阿片受体和多巴胺神经递质兴奋。另外通过影响氨基丁酸递质基因的表达抑制谷氨酸能递质正常传递,从而损害人体中枢神经系统功能和大脑皮层功能,使得人体组织处于缺氧的危险状态,进而对人体认知功能造成不利影响^[28-30]。本研究中急

性酒精中毒患者的左颞上回、右颞中回、右楔前叶、左后扣带回等脑区的功能连接均显著增强。而这一结果表明酒精中毒发生的中枢神经机制可能会导致静息态脑默认网络功能连接的增强,从而使得急性酒精中毒患者的左颞上回和右颞中回及右楔前叶、左后扣带回等脑区的功能连接均出现明显增强。

综上所述,本研究探讨了急性酒精中毒患者由于乙醇代谢产物对人体的神经系统造成不利影响,在对患者实施磁共振检测的基础上可以得出两者的结果都说明酒精中毒对人体认知功能具有不利影响,而静息态功能磁共振对急性酒精中毒患者检测的时候能够准确显示出患者脑组织受到的影响,因此静息态功能磁共振对于急性酒精中毒患者认知功能障碍的影响具有显著的诊断价值,并为急性酒精中毒患者的治疗及预后的改善提供依据和新思路。本研究不足之处在于未能将急性酒精中毒与慢性酒精中毒在分子水平的作用机制异同进行探讨,由于本研究样本量较少,少部分结果可能存在偏倚性,将在后续展开进一步研究。

参考文献(References)

- [1] Wan QI, Shi M, Liu B, et al. Resting-state Functional Magnetic Resonance Imaging in Application of the Motor Function Rehabilitation in Patients with Acute Cerebral Infarction [J]. Rehabilitation Medicine, 2016, 26(5): e21
- [2] Keilholz S, Caballerogaudes C, Bandettini P, et al. Time-Resolved Resting-State Functional Magnetic Resonance Imaging Analysis: Current Status, Challenges, and New Directions[J]. Brain Connect, 2017, 7(8): 465-481
- [3] Zhu L, Wu G, Zhou X, et al. Altered Spontaneous Brain Activity in Patients with Acute Spinal Cord Injury Revealed by Resting-State Functional MRI[J]. Plos One, 2015, 10(3): e0118816
- [4] Hou J, Lin Y, Zhang W, et al. Abnormalities of Frontal-Parietal Resting-State Functional Connectivity Are Related to Disease Activity in Patients with Systemic Lupus Erythematosus[J]. Plos One, 2013, 8(9):

e74530

- [5] Peng CY, Chen YC, Cui Y, et al. Regional Coherence Alterations Revealed by Resting-State fMRI in Post-Stroke Patients with Cognitive Dysfunction[J]. Plos One, 2016, 11(7): e0159574
- [6] Monov SV, Rashkov R, Monova D, et al. SAT0208 Cognitive dysfunction and magnetic resonance imaging (MRI) measures in patients with neuropsychiatric systemic lupus erythematosus (NPSLE)[J]. Annals of the Rheumatic Diseases, 2013, 71(Suppl 3): 542-542
- [7] Pelletier S, Alarcon R, Ewert V, et al. Comparison of the MoCA and BEARNI tests for detection of cognitive impairment in in-patients with alcohol use disorders [J]. Drug and alcohol dependence, 2018, 187: 249-253
- [8] Parag Sawant, Preetee Gokhale, Zarine Ferzandi. Screening of Chronic Alcoholics for Cognitive Impairment Using Montreal Cognitive Assessment-Occupational Therapy Perspective[J]. J health management, 2017, 19(4): 634-648
- [9] Smirni D, Beadle JN, Paradiso S. An Initial Study of Alexithymia and Its Relationship with Cognitive Abilities Among Mild Cognitive Impairment, Mild Alzheimer's Disease, and Healthy Volunteers [J]. J Nervous Mental Disease, 2018, 206(8): 628-636
- [10] Le Berre AP, Fama R, Sullivan EV. Sullivan Executive Functions, Memory, and Social Cognitive Deficits and Recovery in Chronic Alcoholism: A Critical Review to Inform Future Research [J]. Alcohol Clin Exp Res, 2017, 41(8): 1432-1443
- [11] Rajesh V, Mridhulmohan M, Jayaseelan S, et al. Mefenamic Acid Attenuates Chronic Alcohol Induced Cognitive Impairment in Zebrafish: Possible Role of Cholinergic Pathway [J]. Neurochem Res, 2018, 43(7): 1392-1404
- [12] Koyanagi A, Lara E, Stubbs B, et al. Chronic Physical Conditions, Multimorbidity, and Mild Cognitive Impairment in Low-and Middle-Income Countries[J]. J Am Geriatr Soc, 2018, 66(4): 721-727
- [13] Qin HZhi, Jiang HB, Dai X, et al. Effects of aminooxyacetic acid on the learning and memory ability and its possible mechanism in rats with chronic alcoholism [J]. Zhongguo ying yong sheng li xue za zhi, 2018, 34(6): 485-489
- [14] Woods AJ, Porges EC, Bryant VE, et al. Current Heavy Alcohol Consumption is Associated with Greater Cognitive Impairment in Older Adults[J]. Alcohol Clin Exp Res, 2016, 40(11): 2435-2444
- [15] Sullivan EV. Contributions to Understanding the Neuropsychology of Alcoholism: An INS Legacy [J]. J Int Neuropsychol Soc, 2017, 23(9-10): 843-859
- [16] César KG, Brucki SM, Takada LT, et al. Prevalence of Cognitive Impairment Without Dementia and Dementia in Tremembé, Brazil[J]. Alzheimer Dis Assoc Disord, 2016, 30(3): 264-271
- [17] César KG, Brucki SM, Takada LT, et al. Prevalence of Cognitive Impairment Without Dementia and Dementia in Tremembé, Brazil[J]. Alzheimer Dis Assoc Disord, 2016, 30(3): 264-271
- [18] Fama R, Sullivan EV, Sassoon SA, et al. Impairments in Component Processes of Executive Function and Episodic Memory in Alcoholism, HIV Infection, and HIV Infection with Alcoholism Comorbidity[J]. Alcohol Clin Exp Res, 2016, 40(12): 2656-2666
- [19] Woods AJ, Porges EC, Bryant VE, et al. Current Heavy Alcohol Consumption is Associated with Greater Cognitive Impairment in Older Adults[J]. Alcohol Clin Exp Res, 2016, 40(11): 2435-2444
- [20] Peacock A, Cash C, Bruno R. Cognitive Impairment Following Consumption of Alcohol With and Without Energy Drinks [J]. Alcohol Clin Exp Res, 2015, 39(4): 733-742
- [21] Verster JC, Benson Sara, Johnson SJ, et al. Alcohol mixed with energy drink (AMED): A critical review and meta-analysis[J]. Hum Psychopharmacol, 2018, 33(38): e2650
- [22] Stavro K, Pelletier J, Potvin S. Widespread and sustained cognitive deficits in alcoholism: a meta-analysis [J]. Addict Biol, 2013, 18(2): 203-213
- [23] Kreinin A, Bawakny N, Ritsner MS. Adjunctive Pregnenolone Ameliorates the Cognitive Deficits in Recent-Onset Schizophrenia: An 8-Week, Randomized, Double-Blind, Placebo-Controlled Trial [J]. Clin Schizophr Relat Psychoses, 2017, 10(4): 201-210
- [24] Maurage P, Callot C, Philippot P, et al. Chemosensory event-related potentials in alcoholism: a specific impairment for olfactory function [J]. Biol Psychol, 2011, 88(1): 28-36
- [25] Hill TKeith, Colistra AL. Addiction-Related Cognitive Impairment in Substance Use Disorder Treatment: Behavioral Suggestions for Addictions Treatment Practitioners[J]. Alcoholism Treatment Quarterly, 2014, 32(1): 19-32
- [26] Wetherill RR, Rao H, Hager N, et al. Classifying and characterizing nicotine use disorder with high accuracy using machine learning and resting-state fMRI[J]. Addict Biol, 2019, 24(4): 811-821
- [27] Zhu X, Du X, Kerich M, et al. Random forest based classification of alcohol dependence patients and healthy controls using resting state MRI[J]. Neurosci Lett, 2018, 676: 27-33
- [28] Li G, Ji G, Hu Y, et al. Bariatric surgery in obese patients reduced resting connectivity of brain regions involved with self-referential processing[J]. Hum Brain Mapp, 2018, 39(12): 4755-4765
- [29] Fan J, Taylor PA, Jacobson SW, et al. Localized reductions in resting-state functional connectivity in children with prenatal alcohol exposure[J]. Hum Brain Mapp, 2017, 38(10): 5217-5233
- [30] Fein G, Camchong J, Cardenas VA, et al. Resting state synchrony in long-term abstinent alcoholics: Effects of a current major depressive disorder diagnosis[J]. Alcohol, 2017, 59: 17-25