[doi: 10.3969/j.issn.1006-7795.2022.02.014]

· 精神疾病神经调控和康复技术研究 ·

经颅交流电刺激联合抗抑郁药对抑郁发作的疗效及安全性

罗 炯[1,2] 孙丛丛[1,2] 潘伟刚[1,2] 王 丹[1,2] 史晓宁[1,2] 王 茜[1,2] 金文青[1,2] 梁立荣[3]
杨春林[1,2] 马 辛[1,2] 任艳萍[1,2*]

(1. 首都医科大学附属北京安定医院精神科 精神疾病诊断与治疗北京市重点实验室 & 国家精神心理疾病临床医学研究中心,北京 100088;2. 首都医科大学人脑保护高精尖创新中心,北京 100069;3. 首都医科大学附属北京朝阳医院 北京市呼吸疾病研究所临床流行病学研究室,北京 100020)

【摘要】 **目的** 探讨经颅交流电刺激(transcranial alternating-current stimulation, tACS)联合抗抑郁药对抑郁发作的治疗效果及安全性。**方法** 选择抑郁发作患者 62 例,分为治疗组和对照组,均服用抗抑郁药物,治疗组加用 tACS 真刺激治疗,对照组加用 tACS 伪刺激治疗。治疗次数两组均为 20 次。治疗部位为前额部、双侧乳 部, 为 77.5 Hz, 为 15 mA。 用 抑郁 -17 项(Hamilton Depression Scale-17 Item, HAMD-17), (Hamilton Anxiety Scale, HAMA) 患者治疗前 的临床 , , 安全性。 点为 ,治疗 (4), (8)。**结果** 用重 分 对治疗组和对照组 、治疗 4 、 8 HAMD-17 和 HAMA 的 分 行 , 两组 HAMD-17 分均 治疗及 的 (P <0.05),治疗组 大 对照组($P_{组}$ <0.05), 的 治疗的效 大($P_{交}$ <0.05)。两组 HAMA 分均 治疗及 的 (P <0.05), 两组 学 ($P_{组}$ >0.05)。治疗组和对照组第 4 HAMD-17 的 分 分 为 74.29% ±8.40% *vs* 32.54% ±13.30%;第 8 HAMD-17 的 分 分 为 81.00% ±10.68% *vs* 40.27% ±12.92%, 均 学 (P <0.001)。两组均 重 发 。**结论** 经颅交流电刺激联合抗抑郁药物治疗抑郁发作 治疗效果, 安全性高, 作为抑郁发作联合治疗的新选择。

【关键词】 经颅交流电刺激;抑郁发作;疗效;安全性
【中图分类号】 R749.4 【文献标识码】 A

Efficacy and safety of transcranial alternating-current stimulation combined with antidepressants in the treatment of depressive episode

Luo Jiong[1,2], Sun Congcong[1,2], an eigang[1,2], ang Dan[1,2], Shi iaoning[1,2], ang ian[1,2], Jin en-ing[1,2], Liang Lirong[3], ang Chunlin[1,2], Ma in[1,2], Ren anping[1,2*]

(1. *Department of Psychiatry, Beijing Anding Hospital, Capital Medical University, Beijing Key Laboratory of Mental Disorders & The National Clinical Research Center for Mental Disorders, Beijing* 100088, *China*; 2. *Advanced Innovation Center for Human Brain Protection, Capital Medical University, Beijing* 100069, *China*; 3. *Department of Clinical Epidemiology, Beijing Institute of Respiratory Medicine, Beijing Chaoyang Hospital, Capital Medical University, Beijing* 100020, *China*)

【**Abstract**】 **Objective** To investigate the efficacy and safety of transcranial alternating current stimulation (tACS) combined with antidepressants in the treatment of depression. **Methods** Sixty-two patients with depressive episode were randomly divided into treatment group and control group. Both groups took antidepressants. The patients in the treatment group received real tACS while the patients in the control group were treated with sham tACS. The treatment session was 20 times in both groups. The treatment site was prefrontal and bilateral mastoid, with a fre-uency of 77.5 Hz and intensity of 15 mA. Hamilton Depression Scale-17 Item (HAMD-17) and Hamilton Anxiety Scale (HAMA) were used to evaluate the clinical symptoms at baseline, the end of treatment (4 weeks), and follow-up (8 weeks). **Results** The scores of HAMD-17 and HAMA in the treatment and control groups at baseline, 4 weeks of treatment, and 8 weeks of follow-up were compared with repeated measurement analysis of variance. The total score of HAMD-17 in the two groups decreased gradually with the extension of treatment and follow-up time (P_{time} <0.05). The decrease in the treatment group was greater

基金项目:北京市科学技术委员会科技重大专项(D171100007017001)。This study was supported by Beijing Municipal Science & Technology Commission (D171100007017001).

* Corresponding author, E-mail: renyanping@ccmu.edu.cn

网络出版时间:2022-04-01 16:57 **网络出版地址**:https://kns.cnki.net/kcms/detail/11.3662.R.20220401.1504.006.html

than that in the control group ($P_{group} < 0.05$), and the effect of treatment increased with the extension of observation time ($P_{interaction} < 0.05$). The total score of HAMA in both groups decreased gradually with the extension of treatment and follow-up time ($P_{time} < 0.05$). However, there was no significant difference between the two groups ($P_{group} > 0.05$). The score reduction rates of HAMD-17 in the treatment and control groups at the end of the fourth week were 74.29% ± 8.40% *vs* 32.54% ± 13.30%, respectively. At the end of the 8th week, the score reduction rates of HAMD-17 were 81.00% ± 10.68% *vs* 40.27% ± 12.92%, respectively. The difference was statistically significant ($P < 0.001$). **Conclusion** tACS combined with antidepressants is effective and safe in the treatment of depressive episodes. It can be used as a new choice for the combined treatment of depressive episodes.

【Key words】 transcran s

疗效评估指标为 HAMD-17 分率，分率、（基线评分 治疗后评分）/基线评分 100%。

（2）安全性评估：采用副反应量表（Treatment Emergent Symptom Scale，TESS）及开放式记录收集反应。记录 反应时同时收集与 tACS 治疗的相关性、持续时间。

1.5 □□□□□

应用 S SS 26.0 统计软 对数据进行处理分析。计数资料计算率，采用 χ^2 检验或 isher 精确检验比较组间率差异。符合正态分布的连续变量采用均数 ± 标准差（$\bar{x} \pm s$）表示，采用独立样本 t 检验比较两组间均数的差异；采用重复测量的方差分析比较两组间 HAMD 及 HAMA 治疗前后的差异，采用 post-hoc 分析进行两两比较，Bonferroni 法校正 P 值。检验为双侧，以 $P<0.05$ 为差异 统计学 。

2 □□

2.1 □□□□□□□□□□□□□□□□□□□□□□□□

纳入 62 例患者，其中治疗组和对照组各 31 例。治疗组中，3 例患者自愿放弃未 完成治疗，共 28 例完成治疗；对照组中，2 例患者自愿放弃未 完成治疗，共 29 例完成治疗。治疗组和对照组 会人口学资料和临床特征比较，差异均无统计学 （$P>0.05$），详 表 1。

2.2 □□□□□□ HAMD-17 □ HAMA □□□□

采用重复测量方差分析对治疗组和对照组在基线、治疗 4 周末、随访 8 周末时 HAMD-17 和 HAMA 的评分进行比较。结果显示：两组 HAMD-17 总分均随治疗及随访时间的延长逐渐降低（$P_{时间}<0.05$），治疗组降低幅度大于对照组（$P_{组间}<0.05$），且随观察时间的延长治疗的效应增大（$P_{交互}<0.05$）。两组 HAMA 总分均随治疗及随访时间的延长逐渐降低（$P_{时间}<0.05$），但两组间差异无统计学 （$P_{组间}>0.05$），详 表 2。

2.3 □□□□□□ HAMD-17 □□□□□

治疗组和对照组第 4 周末 HAMD-17 的 分率分为 74.29% ± 8.40% *vs* 32.54% ± 13.30%，差异统计学 （$P<0.001$）；第 8 周末 HAMD-17 的 分率分 为 81.00% ± 10.68% *vs* 40.27% ± 12.92%，差异 统计学 （$P<0.001$），详 表 3。

2.4 □□□□

在治疗期间无死亡发 ，无神经系统并发症和其他 重 反应。 命体征无显著变化。试验组 2 例患者出现心慌，1 例患者出现耳鸣，均为轻度，休息后次日缓解，继续完成治疗。

□ 1 □□□□□□□□□□□□□□□□□□□□

Tab. 1 Comparison of demographic and clinical characteristic between the treatment and control groups $\bar{x} \pm s$

actor	Treatment group（n、28）	Control group（n、29）	χ^2/t	P
Age/a	39.11 ± 15.73	42.97 ± 13.88	0.983	0.330
ender			2.110	0.348
Male	3	7		
emale	25	22		
Diagnosis			4.472	0.941
Depression	24	25		
Bipolar disorder	4	4		
Course of illness	67.57 ± 78.60	70.45 ± 111.58	0.112	0.911
Dosage of antidepressant/（mg · d $^{-1}$）				
Escitalopram	16.00 ± 5.48	14.29 ± 6.07	0.501	0.627
luoxetine	20*	20*		
aroxetine	20*	20*		
Sertraline	78.85 ± 45.47	80.35 ± 36.92	0.095	0.925
Citalopram	16.67 ± 5.77	20*	0.500	0.667
HAMD-17	22.25 ± 2.73	22.21 ± 2.31	0.064	0.949
HAMA	24.82 ± 8.07	12.54 ± 6.10	0.415	0.679

* n、1；**HAMD-17**：Hamilton Depression Scale-17 Item；**HAMA**：Hamilton Anxiety Scale.

表 2　治疗组和对照组治疗前后 HAMD-17 和 HAMA 评分的重复测量方差分析

Tab. 2　Repeated measure analysis of variance of HAMD-17 and HAMA score between the treatment and control groups

($\bar{x} \pm s$)

Item	Baseline	eek 4	eek 8	*F*		
				Interaction effect	Time effect	roup effect
HAMD-17				73.983 **	574.354 **	120.955 **
Treatment group(n、28)	22.25 ±2.73	5.68 ±1.74△△	4.21 ±2.30△△			
Control group(n、29)	22.21 ±2.31	14.93 ±3.23	13.31 ±3.42			
HAMA				0.451	99.456 **	0.273
Treatment group(n、28)	24.82 ±8.07	12.54 ±6.1	7.71 ±4.74			
Control group(n、29)						

ganization, 2017: 1 24.

[3] Smith K. Mental health: a world of depression [J]. Nature, 2014, 515(7526): 181.

[4] Fava M. Diagnosis and definition of treatment-resistant depression [J]. Biol Psychiatry, 2003, 53(8): 649 659.

[5] Antal A, Paulus W. Transcranial alternating current stimulation (tACS) [J]. Front Hum Neurosci, 2013, 7: 317.

[6] 王红星, 王坤, 孙志超, 等. 经颅交流电刺激干预从未药物治疗的抑郁症患者的疗效初探[J]. 中华医学杂志, 2020, 100(3): 197 201.

[7] Wilkening A, Kurzeck A, Dechantsreiter E, et al. Transcranial alternating current stimulation for the treatment of major depression during pregnancy [J]. Psychiatry Res, 2019, 279: 399 400.

[8] Haller N, Senner F, Brunoni A R, et al. Gamma transcranial alternating current stimulation improves mood and cognition in patients with major depression [J]. J Psychiatr Res, 2020, 130: 31 34.

[9] American Psychiatric Association. Diagnostic and statistical manual for mental disorders[M]. 5th ed. Washington DC: American Psychiatric Association, 2013.

[10] Bergfeld I O, Mantione M, Figee M, et al. Treatment-resistant depression and suicidality [J]. J Affect Disord, 2018, 235: 362 367.

[11] Lebedev V P, Malygin A V, Kovalevski A V, et al. Devices for noninvasive transcranial electrostimulation of the brain endorphinergic system: application for improvement of human psycho-physiological status [J]. Artif Organs, 2002, 26(3): 248 251.

[12] Avirapetov L N, Zaichik A M, Trukhmanov M S, et al. Changes in the beta-endorphin levels in the brain and cerebrospinal fluid during transcranial electroanalgesia [J]. Fiziol Zh SSSR Im I M Sechenova, 1985, 71(1): 56 64.

[13] Lande R G, Gragnani C. Efficacy of cranial electric stimulation for the treatment of insomnia: a randomized pilot study [J]. Complement Ther Med, 2013, 21(1): 8 13.

[14] Matsumoto H, Ugawa Y. Adverse events of tDCS and tACS: a review [J]. Clin Neurophysiol Pract, 2017, 2: 19 25.

[15] Fertonani A, Ferrari C, Miniussi C. What do you feel if I apply transcranial electric stimulation? Safety, sensations and secondary induced effects [J]. Clin Neurophysiol, 2015, 126(11): 2181 2188.

(收稿日期:2021-11-10)

编辑 孙超渊