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电针联合归脾汤对产后抑郁大鼠抑郁症状的影响及机制分析 *

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摘要 目的:探讨电针联合归脾汤对产后抑郁大鼠抑郁症状的影响及机制。**方法:**选择雌性 SD 大鼠 36 只,将 36 只大鼠随机分为正常组、模型组、盐酸氟西汀组、归脾汤组、电针组、归脾汤联合电针组,每组 6 只大鼠。空白组大鼠不进行任何处理。盐酸氟西汀组给予 0.233 g/L 盐酸氟西汀。归脾汤组给予 1.72 g/mL 归脾汤。电针组选择百会、印堂、气海、关元进行电针刺激。归脾汤联合电针组归脾汤用药方法同归脾汤组,电针方法同电针组。正常组及模型组子均给予等量的双蒸水。每组分别在造模后 1 周、2 周时结束给药。对比糖水消耗水平、旷场实验评分及垂直评分、游泳实验不动时间、挣扎时间及游泳时间、血清 HPA 轴相关激素水平及大鼠脑组织中的 5-HT 含量。**结果:**与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第 1 周、第 2 周时的糖水消耗水平、旷场实验评分、垂直评分、海马、额叶皮质中的 5-HT 水平较低,游泳实验不动时间、挣扎时间、游泳时间、促肾上腺皮质激素、促肾上腺皮质激素释放激素及皮质醇较高;与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠呈相同趋势,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组呈相同趋势($P<0.05$)。盐酸氟西汀组、归脾汤组与电针组所有指标组间对比无差异($P>0.05$)。**结论:**电针联合归脾汤可明显改善产后抑郁大鼠抑郁症状,可能与其可调节产后抑郁大鼠的 HPA 轴相关激素及 5-HT 水平有关。

关键词:电针;归脾汤;产后抑郁

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Effect and Mechanism Analysis of Electroacupuncture Combined with Guipi Decoction on Depressive Symptoms in Postpartum Depression Rats*

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ABSTRACT Objective: To investigate the effect and mechanism of electroacupuncture combined with Guipi decoction on depressive symptoms in postpartum depression rats. **Methods:** 36 female SD rats were selected, and 36 rats were randomly assigned into normal, sham, model, fluoxetine hydrochloride, spleen soup, electroacupuncture, and 6 rats in each group. Blank group rats were treated without any treatment. The fluoxetine hydrochloride group was given 0.233 g/L of fluoxetine hydrochloride. The group was given 1.72 g/mL. Electroacupuncture group selected Baihui, Yintang, Qi hai and Guan Yuan for electroacupuncture stimulation. The method of the same spleen soup group and the same electric needle group. Equal amount of double steaming was given to the normal and model groups. Each group ended drug administration at 1 and 2 weeks after mold making. The sugar-water consumption level, absenteeism experiment score and vertical score, swimming experiment hyperactivity time, struggle time and swimming time, serum HPA axis-related hormone levels, and the 5-HT content in rat brain tissue were compared. **Results:** Compared with the model group, the sugar water consumption level, open field test score, vertical score, 5-HT levels in hippocampus and frontal cortex of rats in the control group, fluoxetine hydrochloride group, Guipi Decoction group and Electroacupuncture group were lower at week 1 and week 2. The immobilization time, struggle time, swimming time, adrenocorticotropic hormone, adrenocorticotropin-releasing hormone and cortisol were higher in swimming experiment. Compared with the control group, the fluoxetine hydrochloride group, Guipi decoction group and Electroacupuncture group showed the same trend, and compared with the fluoxetine hydrochloride group, Guipi decoction group and Electroacupuncture group, the Guipi decoction combined with Electroacupuncture group showed the same trend($P<0.05$). There was no difference in all indexes between flu-

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oxetine hydrochloride group, Guipi Decoction group and Electroacupuncture group ($P>0.05$). **Conclusion:** EA combined with Guipi decoction can significantly improve the depressive symptoms of postpartum depression rats, which may be related to the regulation of HPA axis-related hormone and 5-HT levels in postpartum depression rats.

Key words: Electric acupuncture; Spleen-invigorating soup; Postpartum depression

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前言

产后抑郁是产妇产褥期间出现的一种抑郁症状，在产后4~6周症状会逐渐明显，持续6~8周，甚至长达数年时间^[1,2]。分娩后产妇心理及自身角色的变化会对产后抑郁的发生产生巨大影响，导致产后抑郁发病率大幅度增加，其不仅会对产妇的家庭和谐、身心健康产生影响，疾病严重者甚至会出现杀婴、自杀的情况，也会对婴儿心理、生长发育产生影响，因此临幊上需给予积极干预及治疗^[3,4]。有研究表明^[5]，产后抑郁的生物学基础是分娩前后女性机体内的激素水平剧烈波动。同时产后抑郁并非单一系统紊乱引起，其与机体生殖、内分泌、免疫多个系统均与产后抑郁发生、发展密切相关，其中神经递质、激素水平、相关受体功能、某些肽类物质含量改变均有相关性^[6-8]。因产后抑郁的发病机制复杂，疾病发幊症状多样，目前常见的西医抗抑郁药存在价格昂贵、起效缓慢及用药副作用加大、影响产后哺乳等问题，使得多数患者及其家属不能接受，中医药具有整体调节、理法方药灵活、用药安全等优点，此外不影响产妇母乳喂养，疗效较好；电针也是中医常用的治疗方法，其不良反应较低^[9-11]。因此本文分析了电针联合归脾汤对产后抑郁大鼠抑郁症状的影响，并探讨了其作用机制，以期为临幊中提高产后抑郁的临床疗效提供依据。

1 材料与方法

1.1 实验动物

雌性SD大鼠，SPF级，3月龄，大鼠的平均体重为 200 ± 20 g，进行适应性喂养一周，期间自由饮水、摄食，术前禁食。饲养环境：温度20~22℃、相对湿度60%~80%，光照节律(12 h 光照，12 h 黑，其中6:00~18:00 光照)。

1.2 实验仪器

大鼠强迫游泳水缸(高度为60 cm、直径为25 cm、水深35 cm)，上海科华生物工程股份有限公司生产的ST360酶标仪，苏州医疗用品有限公司生产的Sdz-r电针仪，北京天宇恒科技有限公司生产的针灸针。

1.3 实验试剂

造模用激素使用天津金耀氨基酸有限公司生产的苯甲酸雌二醇注射液，上海通用药液股份有限公司生产的黄体酮注射液；免疫组化试剂兔抗5-HT1AR购自北京博奥森生物科技有限公司，二氨基联苯胺显色试剂盒、即用型免疫组化试剂盒均购自福州迈新生物科技有限公司；高效液相色谱试剂：羟苯甲酸及5-HT均购自美国Sigma公司。归脾汤方剂组成：生牡蛎、龙骨30 g、黄芪15 g、茯苓、党参、白术、当归、酸枣仁、龙眼肉、远志12 g、枳壳9 g、甘草6 g，根据灌胃剂量浓缩，使得生药浓度为1.72 g/mL，置于4℃备用，用药前进行加热。盐酸氟西汀购

自Patheon France公司，根据成人用量7倍，计算大鼠的给药量，确定为2.33 mg/kg·d，溶于蒸馏水中，浓度为0.233 g/L。

1.4 实验流程及动物分组

适应性喂养大鼠1周后，测定所有大鼠的旷野试验基线，选择其中评分相近的36只大鼠，将36只大鼠随机分为正常组、模型组、盐酸氟西汀组、归脾汤组、电针组、归脾汤联合电针组，每组6只大鼠。

1.5 造模方法

所有妊娠雌鼠在妊娠第1~14天皮下注射生理盐水以排除注射影响，妊娠第15~23天模型组和治疗组小鼠皮下注射0.2 mg/kg/d地塞米松磷酸钠以诱导产后抑郁，对照组小鼠注射等量的生理盐水^[12]。

1.6 干预方法

四组在造模结束后给药，灌胃体积为1 mL/100 g体重。盐酸氟西汀组：给予0.233 g/L盐酸氟西汀灌胃给药。归脾汤组：给予1.72 g/mL归脾汤进行灌胃给药。电针组：根据全国针灸学会动物针灸穴位图谱，选择相当于人体解剖部位的百会、印堂、气海、关元，用Sdz-r电针仪平刺进针，四个穴位的进针深度均为0.5~1 cm，频率设置为2 Hz，电流强度设置为0.6 mA，以大鼠的头部微颤为宜，实验期间需保持安静，轻柔操作，以免导致动物不适，每天1次，每次30 min。归脾汤联合电针组：归脾汤用药方法同归脾汤组，电针方法同电针组。正常组及模型组子均给予等量的双蒸水进行灌胃处理。每组分别在造模后1周、2周时结束给药。

1.7 实验方法

(1)糖水消耗实验^[13]：每组给药后1周及2周时对大鼠进行测试，测前24 h禁水，之后各组大鼠自由饮用1%蔗糖水，时间为1 h，计算每只大鼠的蔗糖水消耗情况。

(2)旷场实验^[14]：每组给药后1周及2周时对大鼠进行测试，以动物穿越方格数作为水平活动得分，直立次数为垂直活动得分，每只动物一次，每次3 min，敞箱内保持干净且隔音。

(3)强迫游泳测试^[15]：将大鼠置圆柱形透明容器中进行15 min前游泳，之后将大鼠取出，烘干，之后给予大鼠药物治疗或干预，干预后放回笼中进行饲养，前游泳24 h后，再次置于泳池中进行5 min测试游泳，记录游泳时间、挣扎时间、不动时间。

(4)大鼠血清HPA轴相关激素含量测定^[16]：每组大鼠分别在干预第1周及第2周时，腹腔注射10%水合氯醛将大鼠麻醉，取5 mL腹主动脉血，使用放射免疫法测量其促肾上腺皮质激素、促肾上腺皮质激素释放激素、皮质醇水平。

(5)脑组织5-HT含量测定^[17]：取血后，断头处死大鼠，冰上迅速剥离大鼠的前额、海马叶皮质称重，将组织置入0.1 mL/L高氯酸中进行匀浆，在低温下进行离心，上清转至另一离心管中，再次低温离心后收集上清液，用高效液相色谱的电化学法

测量 5-HT 水平。

1.8 统计学方法

SPSS23.0 软件, 计量资料 $\bar{x} \pm s$ 表示, t 检验、方差检验分析, SNK 法进行两两比较, $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 对比糖水消耗水平、旷场实验评分及垂直评分

表 1 对比糖水消耗水平、旷场实验评分及垂直评分($\bar{x} \pm s$)

Table 1 The sugar water consumption level, open field test score and vertical score were compared($\bar{x} \pm s$)

Groups	Sugar water consumption level(g)		Open field test score(score)		Vertical score(score)	
	1week(n=3)	2week(n=3)	1week(n=3)	2week(n=3)	1week(n=3)	2week(n=3)
Control Group	16.05± 3.15	17.05± 4.12	74.15± 14.25	81.52± 15.23	17.75± 3.15	20.02± 3.12
Model group	8.46± 2.14*	6.12± 1.23*	31.45± 10.25*	40.31± 8.15*	8.12± 1.86*	10.41± 1.89*
Fluoxetine hydrochloride group	12.02± 2.05**	12.15± 3.45**	59.14± 12.15**	65.14± 10.25**	13.23± 1.74**	14.23± 2.15**
Guipi decoction group	12.56± 1.85**	12.99± 2.89**	59.12± 11.43**	64.89± 9.89**	13.54± 2.05**	14.89± 2.45**
Electroacupuncture group	12.74± 1.65**	12.75± 2.42**	59.25± 11.25**	65.10± 10.56**	13.85± 2.15**	14.11± 2.78**
Guipi decoction combined with Electroacupuncture group	14.56± 1.98**^	15.45± 3.45**^	64.41± 10.25**^	74.23± 13.25**^	16.10± 3.25**^	17.45± 3.56**^
F	10.264	11.589	15.120	8.569	12.785	11.555
P	<0.001	<0.001	<0.001	0.002	<0.001	<0.001

Note: Compared with control group and model group, * $P < 0.05$; Compared with the model group, ** $P < 0.05$; Compared with fluoxetine hydrochloride group, Guipi Decoction group and EA group, ^ $P < 0.05$, the same as below.

2.2 对比游泳实验不动时间、挣扎时间及游泳时间

与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第 1 周、第 2 周时的游泳实验不动时间、挣扎时间及游泳时间较高,与对照组相比,盐酸氟西汀组、归脾汤组、电针组

与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第 1 周、第 2 周时的糖水消耗水平、旷场实验评分、垂直评分较低,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠较低,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组较低($P < 0.05$),盐酸氟西汀组、归脾汤组与电针组间对比无差异($P > 0.05$)。

大鼠较高,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组较高($P < 0.05$)。盐酸氟西汀组、归脾汤组与电针组间对比无差异($P > 0.05$)。

表 2 对比游泳实验不动时间、挣扎时间及游泳时间($\bar{x} \pm s$, s)

Table 2 Compares the motionless time, struggle time and swimming time($\bar{x} \pm s$, s)

Groups	Fixed time(g)		Struggling time(score)		The swimming time(score)	
	1week(n=3)	2week(n=3)	1week(n=3)	2week(n=3)	1week(n=3)	2week(n=3)
Control Group	63.71± 10.23	69.10± 11.52	138.52± 20.15	142.18± 25.89	99.02± 10.25	89.70± 11.25
Model group	150.44± 25.75*	154.85± 30.85*	74.15± 10.25*	80.52± 10.25*	77.25± 8.58*	66.10± 8.25*
Fluoxetine hydrochloride group	118.52± 15.42**	124.10± 20.45**	90.25± 11.54**	100.42± 16.89**	85.10± 9.23**	75.10± 8.23**
Guipi decoction group	117.52± 14.89**	124.89± 21.75**	90.78± 12.10**	100.78± 17.25**	85.45± 10.25**	74.89± 9.12**
Electroacupuncture group	118.25± 16.52**	124.42± 19.89**	90.10± 11.02**	100.10± 16.25**	85.88± 11.25**	75.25± 9.58**
Guipi decoction combined with Electroacupuncture group	90.41± 9.58**^	100.42± 15.74**^	110.42± 18.45**^	125.42± 18.58**^	92.00± 12.52**^	83.98± 10.25**^
F	12.589	13.114	14.258	15.102	16.125	10.258
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

2.3 对比血清 HPA 轴相关激素水平

与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第 1 周、第 2 周时的促肾上腺皮质激素、促肾上腺皮质激素释放激素及皮质醇较高,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠较高,与盐酸氟西汀组、归脾汤组、电针组

相比,归脾汤联合电针组较高($P < 0.05$)。盐酸氟西汀组、归脾汤组与电针组间对比无差异($P > 0.05$)。

2.4 对比脑组织中的 5-HT 含量

与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第 1 周、第 2 周时的海马、额叶皮质中的 5-HT 水平较

低,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠水平较低,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电

针组水平较低($P<0.05$)。盐酸氟西汀组、归脾汤组与电针组组间对比无差异($P>0.05$)。

表3 对比血清 HPA 轴相关激素水平($\bar{x}\pm s$)Table 3 Serum HPA axis-related hormone levels were compared($\bar{x}\pm s$)

Groups	Adrenocorticotropic hormone (ng/mL)		Adrenocorticotropin releasing hormone(pg/mL)		Cortisol(ng/mL)	
	1 week(n=3)	2 week(n=3)	1 week(n=3)	2 week(n=3)	1 week(n=3)	2 week(n=3)
Control Group	41.89± 8.56	39.02± 6.23	58.02± 8.25	52.42± 8.26	18.75± 3.56	22.40± 4.25
Model group	56.45± 12.45*	55.42± 8.25*	76.45± 12.52*	78.99± 12.25*	28.75± 5.62*	35.89± 8.56*
Fluoxetine hydrochloride group	50.85± 13.25**#	51.69± 8.96**#	66.12± 10.25**#	70.15± 11.78**#	24.10± 4.58**#	28.42± 7.89**#
Guipi decoction group	50.42± 12.75**#	51.10± 9.12**#	66.45± 10.78**#	70.25± 11.25**#	24.85± 5.12**#	28.75± 7.99**#
Electroacupuncture group	50.12± 11.78**#	51.02± 8.25**#	66.89± 11.75**#	70.45± 11.89**#	24.95± 5.43**#	28.76± 8.25**#
Guipi decoction combined with Electroacupuncture group	45.42± 10.25**#^	45.10± 9.25**#^	62.10± 14.23**#^	60.10± 10.75**#^	21.02± 4.22**#^	26.10± 6.23**#^
F	18.526	16.254	14.263	13.789	14.258	10.222
P	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

表4 对比脑组织中的 5-HT 含量($\bar{x}\pm s$)Table 4 Contrasts the 5-HT content in the brain tissue($\bar{x}\pm s$)

Groups	The hippocampus		The frontal cortex	
	1 week(n=3)	2 week(n=3)	1 week(n=3)	2 week(n=3)
Control Group	184.52± 35.23	194.56± 36.12	199.24± 35.62	195.10± 36.45
Model group	120.40± 25.89*	65.10± 10.25*	135.40± 26.89*	71.02± 12.52*
Fluoxetine hydrochloride group	140.89± 28.89**#	120.45± 30.25**#	152.02± 27.82**#	134.23± 26.53**#
Guipi decoction group	140.42± 29.52**#	121.89± 31.25**#	152.45± 29.63**#	134.99± 30.45**#
Electroacupuncture	140.10± 27.52**#	122.45± 32.58**#	152.85± 25.46**#	135.10± 31.25**#
Guipi decoction combined with Electroacupuncture group	168.75± 30.23**#^	156.89± 33.56**#^	176.23± 29.66**#^	175.42± 39.15**#^
F	11.263	13.152	12.555	16.230
P	<0.001	<0.001	<0.001	<0.001

3 讨论

产后抑郁为产妇产后出现的以悲伤、罪恶感、情绪不稳、睡眠障碍、疲乏等为特征的神经症状性抑郁,是抑郁症的一种类型,中医将其归于郁症范畴,多是因肝气郁结、情志不遂引起的,在发病模式中表现出病理复杂性及生理特殊性,多因产后气血失和、精血亏虚、五脏失于濡养、阴阳失调等引起^[18-20]。近年来,现代中医对产后抑郁进一步进行了细化、研究,认为其与肝、心、肾、脾相关,其中归脾汤具有健脾养心、益气补血的功效,电针是常用的中医治疗方法,应用较安全^[21-23],本文发现电针联合归脾汤对产后抑郁大鼠抑郁症状的改善效果显著。

本文结果表明,与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的糖水消耗水平、旷场实验评分、垂直评分较低,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时以上指标较低,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组的在第1周、第2周时的以上指标较高;与模型组相比,对照组、盐酸氟西

汀组、归脾汤组、电针组大鼠在第1周、第2周时的游泳实验不动时间、挣扎时间及游泳时间较高,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的以上指标较高,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组的在第1周、第2周时的以上指标较高。其中糖水消耗实验可以反映大鼠对奖赏的快感反应情况,垂直活动表明大鼠兴趣高低,旷场实验反应大鼠运动活动性水平^[24-25],本文结果表明单独应用电针或归脾汤时,其对产后抑郁大鼠的症状改善效果与盐酸氟西汀相当,在给予电针联合归脾汤后,其显著改善了产后抑郁大鼠产后抑郁的行为学状态,主要是由于归脾汤中的生牡蛎具有潜阳补阴、重镇安神、收敛固涩、软坚散之效,龙骨具有敛汗固精、重镇安神、镇惊安神、生肌敛疮、止血涩肠之效,黄芪、白术、党参具有益气补充之效,当归具有活血、润肠之效,酸枣仁具有宁心敛汗之效,龙眼肉具有养血补心之效,茯苓具有利水之效,远志具有除邪、止惊、消肿、安神之效,枳壳具有行痰、破气、消积之效,甘草具有补脾益气、清热解毒、镇咳祛痰之效果。现代药理研究表明,龙骨可镇静、催眠、抗惊厥,黄芪可以

增强患者的心肌功能,酸枣仁可镇静催眠,可修复缺血心肌;龙眼肉具有镇静作用,当归具有抗血栓,增强造血功能,抑菌利尿的作用,白术具有抗菌、保肝、抗凝血、抗氧化、镇静作用,茯苓具有防止肝损伤的作用,诸药共用,提高疗效^[26,27]。电针具较普通针刺的刺激强度较强,通过刺激相当于人体的百会、印堂穴等情感穴位^[28],从而进一步改善大鼠的产后抑郁行为状态。

与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的促肾上腺皮质激素、促肾上腺皮质激素释放激素及皮质醇较高,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的以上指标较高,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组的在第1周、第2周时的以上指标较高。与模型组相比,对照组、盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的海马、额叶皮质中的5-HT水平较低,与对照组相比,盐酸氟西汀组、归脾汤组、电针组大鼠在第1周、第2周时的以上指标较低,与盐酸氟西汀组、归脾汤组、电针组相比,归脾汤联合电针组的在第1周、第2周时的以上指标较低,本文结果表明在给予电针联合归脾汤后改善产后抑郁大鼠产后抑郁的行为学状态,可能与其可调整产后抑郁大鼠的HPA轴相关激素及5-HT水平有关。本文结果与张力旋等^[29]研究相似。当大鼠产后抑郁时,HPA轴功能出现紊乱,血清中的促肾上腺皮质激素、促肾上腺皮质激素释放激素及皮质醇分泌明显增多,因此产后抑郁的发生与HPA轴靶器官相对激素失衡密切相关,而给予电针联合归脾汤后,显著降低了产后抑郁大鼠的HPA相关激素水平;5-HT具有广泛生物活性,参与调节机体的体温、睡眠、情绪变化、精神活动等生理反应,在抑郁发生、发展中有重要作用,抑郁症状的发生与单胺类神经递质的降低明显相关^[30],给予电针联合归脾汤后,显著提高了大鼠海马、额叶皮质中的5-HT水平,因此电针联合归脾汤通过调整HPA相关激素水平及5-HT水平改善了产后抑郁大鼠的行为学特征。

综上所述,电针联合归脾汤可明显改善产后抑郁大鼠抑郁症状,可能与其可调节产后抑郁大鼠的HPA轴相关激素及5-HT水平有关。

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