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右正中神经电刺激联合高压氧对颅脑外伤促醒作用及认知功能与脑血流的影响

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【摘要】 **目的** 探索右正中神经电刺激联合高压氧对颅脑外伤促醒作用及认知功能与脑血流的影响。**方法** 前瞻性纳入南阳南石医院 2021-01—2021-07 收治的 122 例颅脑外伤患者,根据随机数字表法分为 2 组,对照组 61 例采用右正中神经电刺激治疗,观察组 61 例采用右正中神经电刺激联合高压氧治疗,均治疗 6 个疗程后,比较 2 组治疗效果。**结果** 观察组治疗后 6 个疗程的 rCBV(3.56±0.67)mL/100 g、rCBF(43.57±5.22)mL/100 g、Vm(55.42±5.42)cm/s、Vp(68.42±4.51)m/s 以及脑干血流灌注(8.88±1.44)mL/(min·100 g)、丘脑血流灌注(12.56±1.82)mL/(min·100 g)、皮层区域血流灌注(13.58±2.37)mL/(min·100 g)改善情况优于对照组($P<0.05$),治疗后 1 个疗程、3 个疗程、6 个疗程的疾病改善率分别为 50.82%、73.77%、95.08%均高于对照组($P<0.05$)。同时观察组治疗后 3 个疗程和 6 个疗程的 GCS 评分、MMSE 评分也高于对照组($P<0.05$)。**结论** 对颅脑外伤患者实施右正中神经电刺激联合高压氧治疗,能够提高脑血流量,改善认知功能。

【关键词】 颅脑外伤;正中神经电刺激;高压氧;促醒;认知功能;脑血流
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Effect of right median nerve electrical stimulation combined with hyperbaric oxygen on the awakening, cognitive function and cerebral blood flow of craniocerebral injury

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【**Abstract**】 **Objective** To explore the effect of electrical stimulation of right median nerve combined with hyperbaric oxygen on awakening effects of traumatic brain injury, cognitive function and cerebral blood flow. **Methods** Prospectively enrolled 122 cases of craniocerebral trauma patients were admitted between January 2021 and July 2021. They were divided into two groups according to the random number table method. Sixty-one cases of the control group were treated with electrical stimulation of the right median nerve, and the observation group sixty-one patients were treated with right median nerve electrical stimulation combined with hyperbaric oxygen therapy. After 6 courses of treatment, the therapeutic effects of the two groups were compared. **Results** The observation group's rCBV (3.56±0.67) mL/100 g, rCBF (43.57±5.22) mL/100 g, Vm (55.42±5.42) cm/s, Vp (68.42±4.51) m/s and 6 courses after treatment in the observation group brainstem blood perfusion (8.88±1.44) mL/(min·100 g), thalamic blood perfusion (12.56±1.82) mL/(min·100 g), cortical area blood perfusion (13.58±2.37) mL/(min·100 g) improved better than In the control group ($P<0.05$), the disease improvement rates of 1 course, 3 courses, and 6 courses after treatment were 50.82%, 73.77%, and 95.08%, which were higher than those of the control group ($P<$

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0.05). At the same time, the GCS scores and MMSE scores of the observation group were higher than those of the control group for 3 courses and 6 courses after treatment ($P<0.05$). **Conclusion** Applying right median nerve electrical stimulation combined with hyperbaric oxygen therapy to patients with craniocerebral trauma can increase cerebral blood flow and improve cognitive function.

【Key words】 Craniocerebral trauma; Median nerve electrical stimulation; Hyperbaric oxygen; Awakening; Cognitive function; Cerebral blood flow

颅脑外伤具有病情变化迅速、病死率高、并发症多等特点，是神经外科较为严重的病症，由于患者长时间处于昏迷状态，可导致多脏器功能及电解质紊乱，降低新陈代谢水平，引发多种并发症，若治疗不及时，可对脑神经功能造成严重影响，危及患者生命安全[1]。由于颅脑外伤的致病机制尚未明确，使相关救治工作难以真正开展，但有研究表明，神经电刺激、高压氧等物理疗法对脑外伤术后催醒有较为理想效果[2]。正中神经电刺激通过低频电流刺激，能够诱导神经自身修复，增加皮质活动和脑血流量，重建大脑侧支循环，促进患者苏醒[3]；高压氧是国内外均较为推崇的治疗方法，可改善缺血半影区的缺氧状态，促使大脑内毛细血管血氧增加，增加氧弥散半径，使得神经细胞功能恢复[4]。虽然正中神经电刺激、高压氧在改善神经功能中具有一定疗效，但也存在各自局限性，因此有学者提议联合使用。现代康复理论认为，由于当颅脑损伤后可因颅内压升高，导致血流速度下降，引起脑内微循环障碍，出现明显认知功能障碍，故需注重治疗期间血运、脑神经功能恢复检测。当颅脑损伤后中枢神经系统在功能上仍具有一定可塑性和重新组织能力，故早期的康复能够加速脑侧支循环建立，促使神经细胞轴突再生发芽，促进健侧脑细胞重组或病灶周围组织代偿或重组，发挥脑可塑性，促使脑功能恢复。而将高压氧联合正中神经电刺激治疗能够从多方面发挥作用，如能够帮助恢复、重组神经元功能和活性，改善脑病灶局部血供，促进神经网络重建，在病灶局部血运改善中具有显著作用，同时还能够激活上行性网状结构系统，促进脑内5-羟色胺代谢，恢复神经功能，促进神经元活性和功能重组，在促醒方面具有显著作用。然而，临床关于联合疗效报道较少，效果仍处于探索阶段。本文进一步分析正中神经电刺激联合高压氧治疗优势，并以不同脑部血流灌注情况、脑血流量、认知功能、疾病改善率等指标作为预后评估指标，进一步探索联合治疗的作用性。

1　资料和方法

1.1　一般资料　前瞻性纳入南阳南石医院2021-01—2021-07收治的122例颅脑外伤患者作为研究对象。年龄(43.39±5.44)岁；男73例，女49例；受伤原因：高空坠落28例，暴力打击43例，交通意外51例；疾病类型：弥漫性轴索损伤17例，脑挫裂39例，颅脑内血肿66例。122例患者根据随机数字表法分为观察组和对照组，2组临床资料比较差异无统计学意义($P>0.05$)。见表1。纳入标准：(1)患者均因外伤所致颅内损伤；(2)循环系统、呼吸系统指标稳定；(3)明显创伤史；(4)签署书面知情同意书，且研究符合《赫尔辛基宣言》的伦理审查。排除标准：(1)既往有急性脑血管病史者；(2)中枢神经系统疾病者；(3)合并其他重要脏器损害者；(4)存在精神家族史者。

1.2　方法　2组均给予营养神经、改善微循环、对症支持等常规治疗，根据恢复情况进行相应康复训练。对照组运用右正中神经电刺激干预，采用神经肌肉刺激仪(Focus 300PV)进行低频电刺激治疗，在患者腕关节掌面腕横纹上右正中神经电放置电极，给予断续脉冲波，脉宽15～25 ms，电流强度5～20 mA，频率60～120 Hz，以手指轻微抽动为宜，1次/d，25 min/次。观察组在对照组基础上，再联合高压氧治疗，由美国EMPJ公司生产高压氧舱，以戴面罩的形式给予Ⅰ级供氧，表压值调整为0.1 MPa，进行20 min升压，

表1　2组一般资料比较　[例(%)]

Table 1　Comparison of general data between the two groups　[n(%)]

组别	n	年龄/岁	性别		受伤原因			疾病类型		
			男性	女性	高空坠落	暴力打击	交通意外	弥漫性轴索损伤	脑挫裂	颅脑内血肿
观察组	61	43.18±5.28	38(62.30)	23(37.70)	15(24.59)	21(34.43)	25(40.98)	10(16.39)	20(32.79)	31(50.82)
对照组	61	43.58±5.54	35(57.38)	26(42.62)	13(21.31)	22(36.07)	26(42.62)	7(11.48)	19(31.15)	35(57.38)
χ^2/t值		0.408	0.307		0.186			0.797		
P值		0.684	0.580		0.666			0.372		

60 min稳压吸氧，间隔5 min呼吸高压舱内部空气，再进行恒速减压20 min，供氧总时间为105 min，1次/d。2组均连续治疗6个疗程，1个疗程为10 d。

1.3 观察指标 （1）比较各项评分值：格拉斯哥昏迷量表（Glasgow coma scale，GCS）评分[5]：包括运动反应、言语反应、睁眼动作等三个维度，最高分15分，若分数越低，表示意识状态越严重；简易精神状态检查表（minimum mental state examination，MMSE）评分[6]：最高分30分，评估项目包括注意力、计算力、定向力、语言表达能力、记忆力等，若分数越高，表示认知功能越好。（2）比较脑血流动力学参数：使用DWL2000型号多普勒超声检查大脑中动脉平均血流速度（velocity maximumvelocity，Vm）、动脉峰流速（velocity peakvelocity，Vp），使用CT灌注成像检查局部脑血容量（reginal cerebral blood volume，rCBV）、局部脑血流量（reginal cerebral blood flow，rCBF）以及脑干、丘脑、皮层区域的血流灌注情况。

1.4 疗效判定 显效：生活可自理，神智恢复清楚，生命体征平稳；有效：神智清楚，但存在轻微运动障碍或精神障碍，需要他人照顾；无效：对各类反射及刺激无反应，生活无法自理。疾病改善率=显效率+有效率。

1.5 统计学处理 采用SPSS 21.0统计学软件处理，计量资料用均数±标准差（$\bar{x}\pm s$）表示，多时点对比运用重复测量方差分析，两两对比运用LSD-t检验，计数资料用（%）表示，行广义估计方程分析或χ^2检验，以$P<0.05$为差异有统计学意义。

2 结果

2.1 2组GCS、MMSE评分比较 经重复测量方差分析，GCS评分、MMSE评分以时间因素和分组的交互作用、时间因素差异均有统计学意义（$P<0.05$）。事后两两LSD-t成对比较，治疗前GCS评分、MMSE评分均差异无统计学意义（$P>0.05$），而观察组治疗后3个疗程和6个疗程的GCS评分、MMSE评分高于对照组（$P<0.05$）。如表2所示。

2.2 2组脑血流动力学比较 2组治疗前脑血流动力学参数比较差异无统计学意义（$P>0.05$），观察组治疗后6个疗程的rCBV、rCBF、Vm、Vp改善情况优于对照组（$P<0.05$）。见表3、图1~4。

2.3 2组血流灌注情况比较 2组治疗前脑干、丘脑、皮层的血流灌注情况比较差异无统计学意义（$P>0.05$），观察组治疗后6个疗程脑干、丘脑、皮层区域的血流灌注改善情况优于对照组（$P<0.05$）。见表4。

2.4 2组疾病改善率比较 广义估计方程分析结果

表2 2组GCS、MMSE评分比较 （分，$\bar{x}\pm s$）

Table 2 Comparison of GCS and MMSE scores between the two groups （scores，$\bar{x}\pm s$）

指标	组别	n	治疗前	治疗后3个疗程	治疗后6个疗程
GCS评分	观察组	61	5.69±0.15	8.95±1.55	12.11±0.55
	对照组	61	5.82±0.24	7.12±0.15	10.36±0.15
	F值		$F_{时点}$=13 830.694，$F_{交互}$=483.733，$F_{组间}$=186.212		
	P值		$P_{时点}<0.001$，$P_{交互}<0.001$，$P_{组间}<0.001$		
MMSE评分	观察组	61	18.75±1.56	22.36±1.11	25.44±1.35
	对照组	61	18.33±1.22	20.11±1.05	23.19±1.14
	F值		$F_{时点}$=2 557.904，$F_{交互}$=66.317，$F_{组间}$=77.039		
	P值		$P_{时点}<0.001$，$P_{交互}<0.001$，$P_{组间}<0.001$		

表3 2组脑血流动力学比较 （$\bar{x}\pm s$）

Table 3 Comparison of cerebral hemodynamics between the two groups （$\bar{x}\pm s$）

组别	n	时间	rCBV（mL/100 g）	rCBF（mL/100 g）	Vm（cm/s）	Vp（m/s）
观察组	61	治疗前	1.13±0.19	28.45±3.31	45.38±3.33	55.29±2.13
		治疗后6个疗程	3.56±0.67*	43.57±5.22*	55.42±5.42*	68.42±4.51*
		t值	27.252	19.106	12.327	20.560
		P值	<0.001	<0.001	<0.001	<0.001
对照组	61	治疗前	1.09±0.15	28.39±3.45	45.59±3.81	55.38±2.25
		治疗后6个疗程	2.43±0.33	36.63±4.69	51.27±4.63	62.11±3.83
		t值	28.872	11.054	7.399	11.833
		P值	<0.001	<0.001	<0.001	<0.001

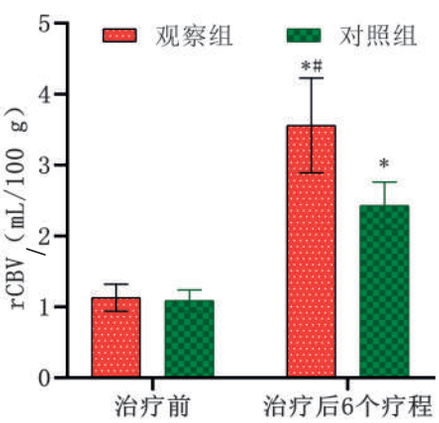
注：与对照组治疗后6个疗程比较，t=11.817、7.724、4.547、8.29，*$P<0.001$

表4　2组不同脑部位血流灌注情况比较　［mL/(min·100 g)，$\bar{x}\pm s$］

Table 4　Comparison of blood perfusion in different cerebral parts in two groups　［mL/(min·100 g)，$\bar{x}\pm s$］

组别	n	时间	脑干	丘脑	皮层
观察组	61	治疗前	7.95±1.36	9.12±1.65	10.39±1.11
		治疗后6个疗程	8.88±1.44$^{\triangle}$	12.56±1.82*	13.58±2.37*
		t值	3.667	10.937	9.520
		P值	<0.001	<0.001	<0.001
对照组	61	治疗前	8.11±1.58	9.33±1.43	10.42±1.29
		治疗后6个疗程	9.15±1.69	10.88±1.57	11.88±1.52
		t值	3.511	5.701	5.720
		P值	0.001	<0.001	<0.001

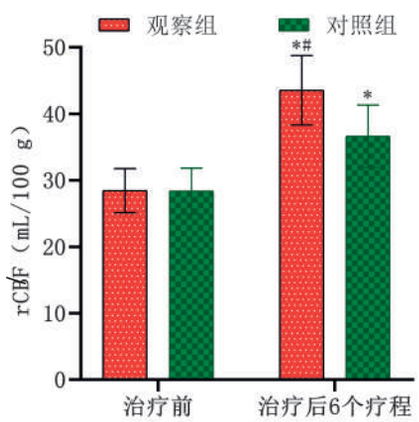
注：与对照组治疗后6个疗程比较，t=0.950，$^{\triangle}P$=0.344；t=5.459，$^{*}P<0.001$；t=4.716，$^{*}P<0.001$



注：与同组治疗前比较，$^{*}P<0.05$，与治疗6个疗程后对照组比较，$^{\#}P<0.005$

图1　2组治疗前后rCBV比较

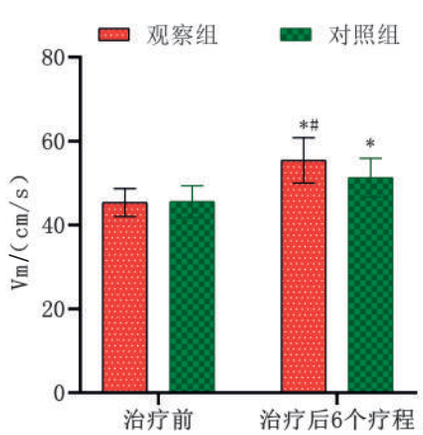
Figure 1　Comparison of rCBV before and after treatment between the two groups



注：与同组治疗前比较，$^{*}P<0.05$，与治疗6个疗程后对照组比较，$^{\#}P<0.005$

图2　2组治疗前后rCBF比较

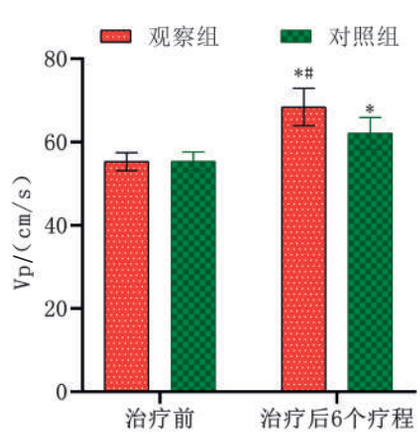
Figure 2　Comparison of rCBF before and after treatment between the two groups



注：与同组治疗前比较，$^{*}P<0.05$，与治疗6个疗程后对照组比较，$^{\#}P<0.005$

图3　2组治疗前后Vm比较

Figure 3　Comparison of Vm before and after treatment between the two groups



注：与同组治疗前比较，$^{*}P<0.05$，与治疗6个疗程后对照组比较，$^{\#}P<0.005$

图4　2组治疗前后Vp比较

Figure 4　Comparison of Vp before and after treatment between the two groups

显示：组间方面：Wald χ^2=6.729，P=0.009，OR=$e^{0.915}$=2.487，95%置信区间为($e^{0.3528}$，$e^{0.224}$)=(0.959，0.609)；时点方面：Wald χ^2=67.604，P<0.001。观察组治疗后1个疗程、3个疗程、6个疗程的疾病改善率均高于对照组(χ^2=4.077、4.346、9.385；P=0.043、0.037、0.002)。见表5、6及图5。

表5 2组疾病改善率比较 [n(%)]

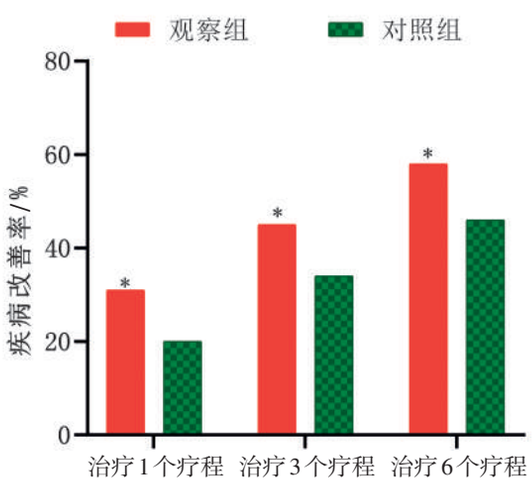
Table 5 Comparison of disease improvement rates between the two groups [n(%)]

组别	n	疾病改善率		
		治疗后1个疗程	治疗后3个疗程	治疗后6个疗程
观察组	61	31(50.82)	45(73.77)	58(95.08)
对照组	61	20(32.79)	34(55.74)	46(75.41)
χ^2值		Wald $\chi^2_{组别}$=8.226, Wald $\chi^2_{时点}$=74.751		
P值		$P_{组别}$=0.004, $P_{时点}$<0.001		

表6 2组广义方程参数估计值

Table 6 Estimated values of parameters for two groups of generalized equations

参数	β	标准误	95% 置信区间		假设检验		
			下限	上限	χ^2	自由度	P值
截距	1.355	0.3053	0.756	1.953	19.697	1	< 0.001
治疗后1个疗程	−2.184	0.2558	−2.686	−1.683	72.938	1	< 0.001
治疗后3个疗程	−1.192	0.2168	−1.617	−0.767	30.216	1	< 0.001
治疗后6个疗程	0[a]	—	—	—	—	—	—
观察组	0.959	0.3344	0.304	1.614	8.226	1	0.004
对照组	0	—	—	—	—	—	—



注:与对照组比较,*P < 0.05

图5 2组各个疗程段的疾病改善率比较

Figure 5 Comparison of disease improvement rates in each treatment period between the two groups

3 讨论

颅脑外伤是一种因头颅受伤而引起的病变,大多因跌伤、事故、车祸引起,当一侧脑组织与坚硬而凸起的颅骨发生碰撞时,可导致颅脑外伤牵拉,撕裂或扭曲脑内血管、神经[7-9]。而神经通路受到破坏,可引起水肿、出血,若得不到及时救治,可导致颅腔内容物增大,升高颅内压,破坏颅脑组织,严重威胁患者生命安全[10-12]。目前治疗方案包括物理疗法、手术治疗、药物保守治疗,虽能够达到一定促醒作用,但难以彻底满足临床需求[13-14]。随着治疗方案不断丰富,学者发现电刺激、高压氧在脑侧支循环重建中具有一定作用,可尽早恢复脑功能,降低致残率[15-16]。

分析本次结果,2组患者接受治疗后,GCS评分、MMSE评分均较同组治疗前有所升高,分析原因在于:右正中神经电刺激通过针对患者右腕内侧正中神经区域进行电刺激,能够激活皮层功能区传导通路,长期神经电刺激,还可持续传入脑桥薄束核和丘脑束核,继而传导内侧丘系和丘脑的腹后核,激活脑干网状觉醒系统,恢复患者意识,改善认知功能[17-20],但观察组GCS评分、MMSE评分更高于对照组,说明在神经电刺激基础上,配合高压氧治疗更好促进机体神经递质释放,为脑组织神经元自我修复提供营养物质和充足氧成分。高压氧作为国内外推崇的方法,不仅能够促进血管内皮细胞修复和再生,使得受损神经元获取养分和营养,还可改善脑组织缺血缺氧状态,促进侧支循环生成,对神经干细胞诱导、增殖定向分化具有一定促进作用[21-23]。同时,本次观察组各时间段疾病改善率也高于对照组,说明联合疗法在催醒中具有显著作用,利于尽早恢复脑功能,改善预后[24-25]。两者联合能够起到以下作用:(1)高压氧能够促进新的侧支循环建立,增加氧的有效弥散距离,提高机体组织、血液间的血氧含量和氧分压,改善缺血脑组织的氧供给微循环,联合正中神经电刺激能够重建颅脑神经网络,抑制神经递质分泌,调节局部血供,对神经元进行功能重组和活性恢复,改善预后[26-28];(2)高压氧能够防止脑细胞凋亡,抑制脑组织炎症反应,联合电刺激,更好激活上行性网状结构系统,提高脑内5-羟色胺代谢功能,促使神经功能恢复[29-30]。

随着现代检测技术的发展，可通过经颅超声检查获取脑动脉血流动力学参数，以便更好评估患者预后情况[25]。分析本次结果，观察组 rCBV、rCBF、Vm、Vp 水平以及脑干、丘脑、皮层区域的血流灌注改善情况均优于对照组，说明右正中神经电刺激联合高压氧有助于改善脑血流量和脑血流速度，改善神经营养功能，促进脑组织自我修复，利于意识恢复。分析原因在于：一方面右正中神经低频电刺激作为一种催化剂，能够通过兴奋效应扩展至尺神经，形成双重刺激效应，增加脑局部组织血液供应，恢复大脑中动脉血流灌注，利于网状结构功能恢复，活化神经细胞，利于脑组织修复[31-33]；另一方面高压氧能够在修复受损中枢神经系统，使神经细胞轴突再生发芽，建立脑侧支循环，促进健侧脑细胞或病灶周围组织重组代偿，发挥脑可塑性，促进脑功能恢复[34-35]。两者联合有效增强中枢神经系统功能，帮助恢复、重组神经元的活动和功能，促进脑功能恢复[36-37]。

右正中神经电刺激联合高压氧能够改善缺血脑组织氧供给，增加脑部血流灌注量，尽早恢复脑神经功能，运用于颅脑外伤患者中效果显著，可在临床进一步应用[38-47]。但本研究在治疗方案、时间、疗程等方面仍以各自经验为主，故很难对最佳治疗方案作出客观评价，对此需通过日后多中心、多样本研究进一步论证。

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