

重度抑郁症脑深部电刺激术治疗进展

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【摘要】 近 1/3 的重度抑郁症患者对正规抗抑郁治疗、心理治疗和认知行为疗法无效。脑深部电刺激术治疗重度抑郁症作为一种新的方法,仅在少数医学中心开展,病例数较少。其作用机制尚不明确,缺乏有效的靶点核团,刺激参数尚不统一,疗效仍存争议,尚处于临床试验阶段。本文拟对脑深部电刺激术治疗重度抑郁症的作用机制、适应证、刺激参数、手术疗效和并发症以及未来发展趋势进行综述。

【关键词】 抑郁症; 深部脑刺激法; 综述

Advance on treatment of major depression with deep brain stimulation

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【Abstract】 About 1/3 of patients with major depression cannot benefit from regular antidepressant therapy, psychotherapy and cognitive behavioral treatment (CBT). Currently, deep brain stimulation (DBS), as a new treatment, has been used to treat major depression. However, only a few medical centers have performed DBS in major depression, and the number of cases is limited. DBS for treating major depression is still in clinical trial stage due to unclear mechanism, lacking of effective stimulation targets, no uniform stimulation parameters, and controversial efficacy. This article reviews mechanism, indications, stimulation parameters, curative effect, complications and future trends of DBS in the treatment of major depression.

【Key words】 Depressive disorder; Deep brain stimulation; Review

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重度抑郁症是一种常见的、复杂的精神病,主要症状是情绪低落、绝望、焦虑、情感淡漠、自主神经系统症状、认知功能障碍以及某些情况下妄想和自杀意念,终身患病率约 16.2%^[1]。近 1/3 的抑郁症患者对正规抗抑郁治疗、心理治疗和认知行为疗法(CBT)无效,称为难治性抑郁症(TRD)^[2]。难治性抑郁症患者自杀率约为 15%^[3]。重度抑郁症的治疗除抗抑郁药、心理治疗、认知行为疗法外,还有电刺激,主要包括电休克疗法(ECT)、经颅直流电刺激(tDCS)、重复经颅磁刺激(rTMS)、迷走神经刺激术(VNS)、硬膜外前额皮质电刺激术(EpCS)和脑深部电刺激术(DBS)。1999 年, Nuttin 等^[4]首次将脑深部

电刺激术应用于精神外科,以某些神经核团电刺激术替代毁损术;此后经大量临床研究证实其治疗强迫症疗效肯定,并于 2009 年经美国食品与药品管理局(FDA)批准用于强迫症的治疗^[5]。迄今,尽管有脑深部电刺激术治疗重度抑郁症的文献报道,但病例数较少、缺乏有效靶点,且目前尚无重度抑郁症脑深部电刺激术的共识与指南,其作用机制、刺激参数、治疗效果、并发症等仍在探讨中。

一、脑深部电刺激术治疗重度抑郁症的作用机制

帕金森病(PD)和迟发性运动障碍性疾病患者行苍白球内侧部(GPi)脑深部电刺激术可以显著提高情绪反应^[6-7]。Benabid 等^[8]采用脑深部电刺激术治疗帕金森病,皮质下单一位点的神经调控即可引起整个脑网络改变。皮质-纹状体-苍白球-丘脑-皮质环路与边缘系统和中枢相互联系,边缘系统环路的关键节点包括伏隔核(NAc)外壳、杏仁核和胼胝体膝下扣带回(SCG),认知功能环路的关键节点包

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括中央纹状体和背外侧前额皮质(DLPFC)。脑深部电刺激术刺激这些关键节点中的 1 个或多个,可以改善皮质-纹状体-苍白球-丘脑-皮质环路功能,从而形成脑深部电刺激术治疗重度抑郁症的神经环路基础。PET 和 fMRI 研究显示,抑郁症发作期胼胝体膝下扣带回呈高代谢、背外侧前额皮质和纹状体呈低代谢,缓解期上述区域代谢恢复正常^[9-11]。胼胝体膝下扣带回脑深部电刺激术后,该区域脑血流量(CBF)减少,代谢恢复正常^[11];伏隔核脑深部电刺激术后即刻皮质和皮质下代谢改变^[12]。扩散张量纤维束示踪成像(DTT)研究也证实,脑深部电刺激术刺激节点与情感网络关键节点相重合^[13]。上述理论基础的确立、临床试验结果的发表、立体定向神经外科的迅速发展、神经核团解剖学的精确定位、结构和功能影像学新方法的出现,共同促使脑深部电刺激术治疗重度抑郁症成为可能。

二、脑深部电刺激术治疗重度抑郁症的适应证

通常病程较长、多种药物和方法治疗后症状仍控制欠佳的重度抑郁症患者选择脑深部电刺激术。脑深部电刺激术治疗重度抑郁症尚无统一标准,综合国外文献,应满足以下条件:(1)符合美国精神障碍诊断与统计手册第 4 版(DSM-IV)中的重度抑郁症诊断标准^[14]。(2)年龄 18~65 岁。(3)病程 > 2 年,汉密尔顿抑郁量表 24 项(HAMD-24)评分 ≥ 20 分^[15], Montgomery - Asberg 抑郁量表(MADRS)评分 > 21 分^[16],抗抑郁药治疗史记录表(ATHF)评分 ≥ 3 分。(4)至少 2 种不同类型第 2 代抗抑郁药治疗无效。(5)多个疗程心理治疗无效。(6)电休克疗法无效。

三、脑深部电刺激术治疗重度抑郁症的常用靶点核团

目前,脑深部电刺激术治疗重度抑郁症的刺激靶点仍在探讨中。有效靶点包括胼胝体膝下扣带回(Brodman 25 区)、伏隔核、腹侧内囊/腹侧纹状体(VC/VS)、内囊前肢腹侧(vALIC)、前脑内侧束(MFB)、外侧缰核(lateral habenular)、丘脑下脚(inferior thalamic peduncle)等,最常用的是胼胝体膝下扣带回,其次是腹侧内囊/腹侧纹状体,前脑内侧束和伏隔核较少,外侧缰核和丘脑下脚最少。

四、脑深部电刺激术治疗重度抑郁症的刺激参数

目前,尚未确定脑深部电刺激术治疗重度抑郁症的最佳刺激参数。根据靶点核团及其周围结构

的特点,脑深部电刺激术[包括丘脑底核(STN)脑深部电刺激术、丘脑腹中间核(Vim)脑深部电刺激术、苍白球内侧部脑深部电刺激术]治疗重度抑郁症的刺激参数普遍高于运动障碍性疾病,特别是刺激电流和电压方面。

Zhou 等^[17]进行的 Meta 分析显示,脑深部电刺激术治疗重度抑郁症的大多数靶点核团的刺激参数为:电压 3.50~5.00 V 或电流 4 mA,脉宽 90 μ s。为获得最佳疗效,不同个体或不同靶点核团的刺激参数差异较大,例如,同为胼胝体膝下扣带回脑深部电刺激术,Lozano 等^[18]的刺激参数相对稳定,术后即刻、6 个月和 12 个月平均电流为 4.20、4.90 和 5.20 mA,平均脉宽为 91、100.50 和 93.90 μ s,平均频率为 130 Hz;而 Merkl 等^[19]应用的最大刺激电压为 2.50~10.00 V,脉宽为 90 μ s,频率为 130 Hz。同样采用腹侧内囊/腹侧纹状体脑深部电刺激术,Dougherty 等^[20]应用的最大刺激电压为 8 V,脉宽为 90~210 μ s;Malone 等^[21]在平均 37 个月的随访中,刺激电压为 (6.70 ± 1.80) V,脉宽为 (113 ± 45) μ s,频率为 (127.00 ± 11.10) Hz,且由于刺激电压、脉宽和频率均较大,电池消耗十分明显,其使用寿命平均 10.60 个月。Bewernick 等^[22]采用的伏隔核脑深部电刺激术最初刺激参数为电压 2 V、脉宽 90 μ s、频率 130 Hz,最终刺激参数为电压 1.50~10.00 V、脉宽 60~210 μ s、频率 100~150 Hz。Fenoy 等^[23]和 Bewernick 等^[24]采用的前脑内侧束脑深部电刺激术刺激参数分别为电压 3 V、脉宽 60 μ s、频率 130 Hz 和电压 4 V、脉宽 90 μ s、频率 130 Hz。较小的刺激参数下,如果效果不明显,在无不良反应的前提下,可以逐渐增大刺激参数以获取更佳效果。目前,美国 Medtronic 公司和北京品驰医疗设备有限公司均已研制出成熟的可充电脉冲发生器,从而弥补脑深部电刺激术耗电量大、频繁更换电池的弊端,也为脑深部电刺激术治疗重度抑郁症的临床研究提供有利条件。

五、脑深部电刺激术治疗重度抑郁症的疗效分析

尽管大多数临床研究显示,脑深部电刺激术治疗重度抑郁症疗效肯定,但仍有少数文献报道其疗效并不理想^[18-36](表 1)。由于靶点核团较多,各靶点核团脑深部电刺激术的病例数较少,且缺乏合理的实验设计和病例选择(如研究对象症状较严重,甚至有自杀倾向,且药物治疗和心理治疗等长期无

表 1 重度抑郁症患者不同靶点脑深部电刺激术疗效

Table 1. The outcomes of DBS in different targets

Study	N	Target	Follow-up	Outcomes
Mayberg, et al ^[25] (2005)	6	SCG	6-12 months	4 patients showed a positive responder (HAMD-17 reduction $\geq 50\%$) and 3 patients were in remission (HAMD-17 < 8 score) at 6 months, 65% reduction in score on the HAMD-17 at 12 months
Lozano, et al ^[18] (2008)	20	SCG	12 months	60% of the patients were positive responders (HAMD-17 reduction $\geq 50\%$), 35% of the patients were in remission (HAMD-17 < 7 score)
Schlaepfer, et al ^[34] (2008)	3	NAC	5-25 weeks	3 patients showed a positive responder HAMD-24 reduction to 42% at one week, and MADRS reduced to 31%. All patients had improvement in symptoms of anhedonia
Malone, et al ^[21] (2009)	15	VC/VS	14-67 months	Responder rates with HAMD were 40% at 6 months and 53.33% at last follow-up. Remission rates were 20% at 6 months and 40% at last follow-up with the HAMD
Kennedy, et al ^[28] (2011)	20	SCG	3 years	The average response rates 1, 2 and 3 years after DBS implantation were 62.5%, 46.2%, and 75%, respectively. At the last follow-up visit (3-6 years), the average response rate was 64.3%
Puigdemont, et al ^[29] (2012)	8	SCG	1 year	62.5% of the patients were positive responders (HAMD-17 reduction $\geq 50\%$) at one year, 50% of the patients were in remission (HAMD-17 < 7 score). HAMD-17 reduced to 62%
Bewernick, et al ^[22] (2012)	11	NAC	1-4 years	5 of 11 patients were classified as responders after 12 months and remained sustained responders without worsening of symptoms until last follow-up after 4 years (HAMD-28 reduction $\geq 50\%$)
Holtzheimer, et al ^[27] (2012)	17	SCG	24 months	11 of 12 patients responded at 2 years (HAMD-17 reduction $\geq 50\%$), remission rate 58.33% (HAMD-17 < 8 score)
Lozano, et al ^[26] (2012)	21	SCG	12 months	The responder (HAMD-17 reduction $\geq 50\%$) was 57% at one month, 48% at 6 months, and 29% at 12 months; 62% of patients had 40% decrease in HAMD-17 or better at 12 months
Merkel, et al ^[19] (2013)	6	SCG	24-36 weeks	2 patients were in remission (HAMD-24 < 10 score), and 4 other patients were non-responders (HAMD-24 reduction < 50%)
Ramasubbu, et al ^[30] (2013)	4	SCG	6 months	2 patients were positive responders (HAMD-17 reduction $\geq 50\%$), one patient was a partial responder (HAMD-17 reduction 35%)
Schlaepfer, et al ^[36] (2013)	7	MFB	6 months	6 patients were positive responders (MADRS reduction $\geq 50\%$), 4 patients were in remission (MADRS < 10 score)
Millet, et al ^[35] (2014)	4	NAC	6 months	3 patients exhibited a significant response (HAMD-17 reduction $\geq 50\%$)
Dougherty, et al ^[20] (2015)	30	VC/VS	24 months	There was no significant difference in response rates between active and control groups at the end of 16-week controlled phase, however, the response rates at 12, 18 and 24 months during the open-label continuation phase were 20%, 26.67%, and 23.33%, respectively (MADRS reduction $\geq 50\%$)
Bergfeld, et al ^[33] (2016)	25	vALIC	51.60 weeks	10 patients (40%) were classified as responders and 15 individuals (60%) as non-responders. Sixteen patients entered the randomized crossover phase [9 responders (56.25%), 7 non-responders (43.75%)]. During active DBS, patients scored significantly lower on the HAMD-17 than during sham DBS ($P < 0.001$)
Accolla, et al ^[31] (2016)	5	SCG and BPGR	24 weeks	One patient showed an excellent clinical response after DBS of BPGR rather than the initially targeted SCG (Brodmann 25). The remaining 4 patients with DBS of SCG (Brodmann 25) were considered as non-responders
Fenoy, et al ^[23] (2016)	4	MFB	26 weeks	3 of 4 patients had $\geq 50\%$ decrease in MADRS scores at 7 d post-stimulation initiation relative to baseline. One patient withdrew from study participation. At 26 weeks, 2 of 3 patients continued to have $\geq 80\%$ decrease in MADRS scores
Bewernick, et al ^[24] (2017)	8	MFB	1-4 years	6 of 8 patients were positive responders at 12 months (MADRS reduction $\geq 50\%$), 4 patients were in remission (MADRS < 10 score); longterm results revealed a stable effect up to 4 years
Merkel, et al ^[32] (2018)	8	SCG	2-4 years	51% of patients were positive responders (HAMD-24 reduction $\geq 50\%$); 2 patients were in remission (HAMD-24 < 10 score)

SCG, subcallosal cingulate gyrus, 胼胝体膝下扣带回; NAC, nucleus accumbens, 伏隔核; VC/VS, ventral internal capsule/ventral corpus striatum, 腹侧内囊/腹侧纹状体; MFB, medial forebrain bundle, 前脑内侧束; vALIC, ventral anterior branch of the internal capsule, 内囊前肢腹侧; BPGR, bilateral posterior gyrus rectus, 双侧直回后部; HAMD, Hamilton Depression Rating Scale, 汉密尔顿抑郁量表; MADRS, Montgomery-Asberg Depression Rating Scale, Montgomery-Asberg 抑郁量表; DBS, deep brain stimulation, 脑深部电刺激术

效), 患者是否配合试验, 因试验设计的要求而中断正在受益的电刺激违背道德伦理等, 给疗效分析带来困难。

1. 胼胝体膝下扣带回脑深部电刺激术

Mayberg 等^[25]于 2005 年率先报告 6 例行胼胝体膝下扣带回脑深部电刺激术患者, 术后 6 个月 4 例(4/6)临床症状明显减轻[汉密尔顿抑郁量表 17 项(HAMD-17)评分减少 $\geq 50\%$], 3 例(3/6)临床症状基本消失(HAMD-17 评分 < 8 分); 术后 12 个月

HAMD-17 评分减少 65%; 进一步 PET 研究显示, 脑深部电刺激术可以逆转胼胝体膝下扣带回的高代谢。2008 年, Lozano 等^[18]对 20 例行胼胝体膝下扣带回脑深部电刺激术的患者进行 1 年的随访, 12 例(12/20)临床症状明显减轻(HAMD-17 评分减少 $\geq 50\%$), 7 例(7/20)临床症状基本消失(HAMD-17 评分 < 7 分); 术后 3~6 年平均有效率为 64.3%。Lozano 等^[26]于 2012 年的多中心临床研究对 21 例行胼胝体膝下扣带回脑深部电刺激术的患者进行随

访,术后 1、6 和 12 个月分别有 57%、48% 和 29% 患者临床症状明显减轻(HAMD-17 评分减少 $\geq 50\%$, 平均减少 41%);术后 12 个月有 62% 患者 HAMD-17 评分减少 40%。Holtzheimer 等^[27]对 17 例行胼胝体膝下扣带回脑深部电刺激术的患者进行单盲随访研究,随访 2 年时,失访 5 例,余 12 例患者中 11 例(11/12)临床症状明显减轻(HAMD-17 评分减少 $\geq 50\%$),7 例(7/12)临床症状基本消失(HAMD-17 评分 < 8 分)。

2. 腹侧内囊/腹侧纹状体脑深部电刺激术 腹侧内囊/腹侧纹状体这一靶点核团首先应用于强迫症脑深部电刺激术,研究显示,伴抑郁症状的重度强迫症患者行脑深部电刺激术后,抑郁症状减轻,从而促使该方法用于重度抑郁症的治疗^[37-39]。腹侧内囊/腹侧纹状体体积较大,需特制的 IES 3387 电极(美国 Medtronic 公司;每一触点长 3 mm,触点间距为 4 mm)^[21,40]。Malone 等^[21]的多中心临床研究纳入 15 例重度抑郁症患者,6 个月和最终随访时分别有 6 例(6/15)和 8 例(8/15)临床症状明显改善,3 例(3/15)和 6 例(6/15)临床症状基本消失。Taghva 等^[41]对 4 项临床研究进行系统综述,结果显示,腹侧内囊/腹侧纹状体脑深部电刺激术的有效率为 40%~70%。Bergfeld 等^[33]对 25 例重度抑郁症患者行内囊前肢腹侧脑深部电刺激术,至治疗最佳阶段(持续 51.60 周)时,HAMD-17 评分自 22.20 分降至 15.90 分($P=0.001$),MADRS 评分自 34 分降至 23.80 分($P=0.001$),抑郁症快速自评量表(QIDS-SR)评分自 49.30 分降至 38.80 分($P=0.005$);10 例(40%)临床症状明显减轻(HAMD-17 评分减少 $\geq 50\%$),15 例(60%)治疗无效(HAMD-17 评分减少 $< 50\%$);本组有 16 例进入随机交叉试验,9 例(9/16)治疗效果显著,7 例(7/16)治疗无效,且脑深部电刺激术组治疗效果优于假刺激组($P<0.001$)。

3. 伏隔核脑深部电刺激术 伏隔核与腹侧内囊/腹侧纹状体关系密切,解剖学上伏隔核位于腹侧内囊腹内侧部。Schlaepfer 等^[34]对 3 例重度抑郁症患者行伏隔核脑深部电刺激术,随访 5~25 周,治疗 1 周后 3 例临床症状均明显减轻,HAMD-24 评分下降 42%、MADRS 评分下降 31%,兴趣感均显著增加,PET 显像可见额叶-纹状体网络代谢改变。Bewernick 等^[22]对 11 例重度抑郁症患者行伏隔核脑深部电刺激术,治疗 1 年后 5 例(5/11)治疗效果良好,共随访 4 年,其治疗效果持续良好。Millet 等^[35]

对 6 例(实际开机刺激 4 例)重度抑郁症患者行伏隔核脑深部电刺激术,随访 6 个月,3 例(3/4)临床症状明显减轻(HAMD-17 评分减少 $\geq 50\%$);¹⁸F-脱氧葡萄糖(¹⁸F-FDG)PET 显像研究显示,右侧边缘叶扣带回后部(Brodmann 23 和 31 区)、左侧额上回(Brodmann 6 区)和额中回(Brodmann 8 区)、双侧小脑葡萄糖代谢降低,双侧额上回(Brodmann 9 区)、左侧额中回(Brodmann 10 区)、右侧边缘叶扣带回前部(Brodmann 32 区)葡萄糖代谢升高。Grubert 等^[42]的研究显示,伏隔核脑深部电刺激术治疗 1 年后,认知功能无明显改变但认识表现有改善趋势。

4. 前脑内侧束脑深部电刺激术 前脑内侧束脑深部电刺激术治疗重度抑郁症的机制与伏隔核脑深部电刺激术相同。重度抑郁症患者前脑内侧束和伏隔核均认为是病理状态的快感中枢,其中,前脑内侧束上外侧部与奖励寻求和欲望动机相关,且与其他靶点核团相互联系(如胼胝体膝下扣带回、伏隔核、腹侧内囊/腹侧纹状体)^[43]。Schlaepfer 等^[36]认为,前脑内侧束上外侧部脑深部电刺激术有显著的抗抑郁作用,他们采用前脑内侧束上外侧部脑深部电刺激术治疗 7 例重度抑郁症患者,随访 6 个月,6 例(6/7)临床症状明显减轻(MADRS 评分减少 $\geq 50\%$),4 例(4/7)临床症状基本消失(MADRS 评分减少 < 10 分),同时,欲望动机和情绪也显著增加;进一步的随访研究将病例增至 8 例,为期 1~4 年,随访 12 个月时 6 例(6/8)临床症状明显减轻(MADRS 评分减少 $\geq 50\%$),4 例(4/8)临床症状基本消失(MADRS 评分 < 10 分),治疗效果持续 4 年且对认知功能无明显影响^[24]。Fenoy 等^[23]对 4 例重度抑郁症患者行前脑内侧束上外侧部脑深部电刺激术,假刺激阶段无明显情绪变化,术后 7 天 3 例(3/4)临床症状明显减轻(MADRS 评分减少 $\geq 50\%$),1 例(1/4)退出试验;术后 26 周 3 例患者中 2 例(2/3)MADRS 评分减少 $\geq 80\%$ 。

尽管大多数研究证实脑深部电刺激术治疗重度抑郁症疗效肯定,但仍有两项临床研究未得出阳性结果。2015 年,Dougherty 等^[20]开展首个有明确对照的多中心腹侧内囊/腹侧纹状体脑深部电刺激术临床研究,如果该项研究获得阳性结果,有望促使美国食品与药品管理局同意将腹侧内囊/腹侧纹状体作为重度抑郁症的有效靶点,共纳入 30 例重度抑郁症患者,经过 16 周的盲法研究,脑深部电刺激术组与对照组患者 MADRS 评分差异无统计学意

义;在 12、18 和 24 个月的开放试验阶段,分别有 20% (6/30)、26.67% (8/30) 和 23.33% (7/30) 患者临床症状明显减轻 (MADRS 评分减少 $\geq 50\%$)。另一项为期 6 个月的前瞻性随机对照临床试验将 90 例重度抑郁症患者随机分为胼胝体膝下扣带回脑深部电刺激术组 (60 例) 和假刺激组 (对照组, 30 例), 两组主要疗效指标或治愈指标差异无统计学意义, 试验结束后继续治疗, 随访 24 个月时 48.72% (38/78) 治疗有效 (较基线抑郁严重程度降低 $\geq 40\%$), 25.64% (20/78) 治愈;同时, 该项研究声明其阴性结果不能简单概括为胼胝体膝下扣带回脑深部电刺激术治疗重度抑郁症失败^[44-45]。后续研究进一步分析原因, 是人群临床特征不同 (如极度慢性抑郁症) 还是电极位置欠佳? 目前尚无结论^[45]。Zhou 等^[17]对 14 项临床研究进行 Meta 分析总结常用的靶点核团, 结果显示, 从短期和长期疗效看, 电刺激胼胝体膝下扣带回 ($P=0.000$)、前脑内侧束 ($P=0.0001$)、腹侧内囊/腹侧纹状体 ($P=0.005$) 和伏隔核 ($P=0.003$) 均有明显抗抑郁作用, 随访 1、3、6 和 12 个月的治疗有效率分别为 37%、36%、50% 和 48%。

由此可见, 脑深部电刺激术治疗重度抑郁症的疗效并不优于运动障碍性疾病, 值得我们进一步研究, 应探寻新的靶点核团、设计科学的临床试验, 以解决脑深部电刺激术治疗重度抑郁症的相关问题。

六、脑深部电刺激术治疗重度抑郁症的并发症

脑深部电刺激术治疗重度抑郁症的并发症中颅内出血、术后感染、设备自身问题等不再赘述。目前, 有大量关于脑深部电刺激术治疗运动障碍性疾病的并发症的相关文献可供参考。与之相比, 脑深部电刺激术治疗重度抑郁症的精神症状相关并发症尚不明确。Zhou 等^[17]报告 156 例行脑深部电刺激术治疗的抑郁症患者, 主要并发症包括抑郁症状加重 (12 例, 7.69%)、自杀 (4 例, 2.56%)、有自杀想法 (7 例, 4.49%)、企图自杀 (10 例, 6.41%)、轻度躁狂 (6 例, 3.85%)、兴奋 (12 例, 7.69%)、焦虑 (9 例, 5.77%)、睡眠紊乱 (10 例, 6.41%)、失控 (8 例, 5.13%)、易激惹 (5 例, 3.21%)、幻觉 (1 例, 0.64%) 等, 其中自杀是最严重的并发症。某些研究为避免脑深部电刺激术后自杀, 选择患者时排除有自杀想法的患者, 但是由于采用该术式的患者均为重度抑郁症患者, 故完全避免术后自杀是不可能的。

大多数学者认为, 脑深部电刺激术与自杀并无关联性^[44]。自杀是一个很复杂的问题, 研究显示,

脑深部电刺激术后 1 年自杀风险最高, 可能与患者期望值较高但治疗效果不明显有关。此外, 也有学者根据帕金森病患者脑深部电刺激术后增加神经电生理方面相关冲动, 推断出慢性电刺激可以使重度抑郁症患者腹侧内囊/腹侧纹状体、胼胝体膝下扣带回和背外侧前额皮质之间的功能连接紊乱, 产生异常冲动, 从而导致自杀^[46]。

七、展望

脑深部电刺激术治疗重度抑郁症尚处于探索阶段, 尽管胼胝体膝下扣带回、腹侧内囊/腹侧纹状体、前脑内侧束和伏隔核等靶点核团有一定治疗作用, 但均未获得显著疗效。因此, 探寻新的靶点核团仍是脑深部电刺激术治疗重度抑郁症的关键。我们基于多年脑深部电刺激术治疗帕金森病的临床经验认为, 丘脑底核脑深部电刺激术电极位置较深时, 可以引起兴奋状态。我们研究团队对 1 例重度抑郁症患者行丘脑底核-黑质脑深部电刺激术和伏隔核脑深部电刺激术, 术后即刻 (尚未刺激时) 即显示较好疗效, 刺激后丘脑底核-黑质脑深部电刺激术疗效明显, 而伏隔核脑深部电刺激术无明显疗效, 术后 7 天埋置脉冲发生器, 电刺激丘脑底核-黑质, 疗效显著, 但仅持续 1 个月, 增加刺激参数后, 出现眼部不适的不良反应, 无法再增加刺激电压; 继而电刺激伏隔核, 短期无明显疗效, 患者拒绝继续配合研究, 宣布治疗失败。

相信随着抑郁症诊断与治疗过程的不断探索, 一定会发现新的抑郁症相关神经环路、神经功能改变和靶点核团, 为脑深部电刺激术治疗重度抑郁症取得良好疗效提供新的方法。

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中英文对照名词词汇(一)

- 白细胞介素-6 interleukin-6(IL-6)
- 背外侧前额皮质 dorsolateral prefrontal cortex(DLPFC)
- 表观扩散系数 apparent diffusion coefficient(ADC)
- 丙型肝炎病毒 hepatitis C virus(HCV)
- 苍白球内侧部 globus pallidus internus(GPi)
- 超敏C-反应蛋白
high-sensitivity C-reactive protein(hs-CRP)
- 重复经颅磁刺激
repetitive transcranial magnetic stimulation(rTMS)
- 重组组织型纤溶酶原激活物
recombinant tissue-type plasminogen activator(rt-PA)
- 磁共振黑血血栓成像
magnetic resonance black-blood thrombus imaging(MRBTI)
- 磁共振静脉血管造影术
magnetic resonance venography(MRV)
- 磁共振血管造影 magnetic resonance angiography(MRA)
- 雌二醇 estradiol(E₂)
- 催乳素 prolactin(PRL)
- 达峰时间 time to peak(TTP)
- 大脑后动脉 posterior cerebral artery(PCA)
- 大脑中动脉 middle cerebral artery(MCA)
- 大脑中动脉闭塞 middle cerebral artery occlusion(MCAO)
- 大脑中动脉远端闭塞
distal middle cerebral artery occlusion(dMCAO)
- 带状疱疹后神经痛 postherpetic neuralgia(PHN)
- S-100B 蛋白 S-100B protein(S-100B)
- 低密度脂蛋白胆固醇
low-density lipoprotein cholesterol(LDL-C)
- 电休克疗法 electroconvulsive therapy(ECT)
- 短暂性脑缺血发作 transient ischemic attack(TIA)
- C-反应蛋白 C-reactive protein(CRP)
- 非朗格汉斯细胞组织细胞增生症
non-Langerhans' cell histiocytosis(NLCH)
- 肺动-静脉瘘 pulmonary arteriovenous fistula(PAVF)