·专题综述·

脑深部电刺激术治疗耐药性癫痫研究进展

王梦莹 胡峰 舒凯 蔡宏斌 康慧聪

【摘要】 脑深部电刺激术作为神经调控疗法的重要形式，通过精准选择刺激靶点为耐药性癫痫患者提供新的治疗选择。其可以通过在特定靶点植入电极并发放电刺激，对癫痫发作过程中相关神经核团及神经回路兴奋性进行调控，从而发挥控制癫痫发作的功效。目前脑深部电刺激术治疗耐药性癫痫的调控机制、不同发作类型个体化刺激靶点选择、临床疗效与安全性等积累了一定的临床和实验室证据，本文拟就上述三方面进行阐述，以促进脑深部电刺激术在耐药性癫痫领域的应用。

【关键词】 耐药性癫痫； 深部脑刺激法； 综述

Research of deep brain stimulation in the treatment of drug-resistant epilepsy

WANG Meng-ying[1], HU Feng[2], SHU Kai[2], CAI Hong-bin[3], KANG Hui-cong[1]

[1]Department of Neurology, [2]Department of Neurosurgery, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, Hubei, China

[3]Department of Neurology, The Ninth Hospital of Wuhan, Wuhan 430081, Hubei, China

Corresponding author: KANG Hui-cong (Email: kanghuicong@163.com)

【Abstract】 Deep brain stimulation (DBS), an important form of neuromodulation therapy, provides a new treatment option for drug-resistant epilepsy (DRE) patients through precisely selections the stimulation target. By implanting electrodes at specific targets and releasing electrical stimulation, DBS can regulate the excitability of the relevant nuclei and neural circuits in the process of seizure, so as to exert the effect of controlling seizure. At present, some clinical and laboratory evidence has been accumulated on the regulatory mechanism of DBS in the treatment of DRE, the individualized selection of stimulation targets for different types of seizures, the curative effect and adverse events. This article will elaborate the above three aspects, in an effort to promote the application of DBS in DRE.

【Key words】 Drug resistant epilepsy; Deep brain stimulation; Review

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药物难治性癫痫(drug refractory epilepsy)也称耐药性癫痫(DRE)，是指经两种或两种以上足量足疗程抗癫痫发作药物(ASM)单药或联合治疗后仍无法有效控制发作的癫痫类型，占所有癫痫类型的30%～40%[1-2]。外科手术可使此类患者发作减少甚至完全缓解[1]，但仅有约20%致痫灶位于非功能区的局灶性癫痫患者符合手术适应证并可从中获益，其中仍有30%～40%患者无法达到预期疗效[1,3]。因此，对于存在手术禁忌证、致痫灶位于功能区或手术失败的耐药性癫痫患者，神经调控疗法不失为一种替代性选择。脑深部电刺激术(DBS)是神经调控疗法的重要形式，可以通过对脑内特定靶点施以电刺激，进而调节相应核团及神经回路兴奋性[4]，用

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作者单位:430030 武汉,华中科技大学同济医学院附属同济医院神经内科(王梦莹、康慧聪),神经外科(胡峰、舒凯);430081 湖北省武汉市第九医院神经内科(蔡宏斌)

通讯作者:康慧聪,Email:kanghuicong@163.com

于治疗特发性震颤、肌张力障碍、帕金森病和耐药性强迫症(OCD)等[5]疗效确切。对脑深部电刺激术治疗耐药性癫痫的初步探索始于1974年[6],时至今日,所积累的证据大多来自离体或动物实验,仅在为数不多的临床试验中获得疗效与安全性相关的初步证据[7-9],但是对其调控机制、刺激靶点选择等仍无一致性结论。本文拟就脑深部电刺激术治疗耐药性癫痫的调控机制、刺激靶点选择、临床疗效与安全性进行系统阐述,以期实现耐药性癫痫的精准治疗。

一、调控机制

脑深部电刺激术发挥治疗作用的基本原理是在脑深部结构或相邻脑区安置电极,并通过导线连接到位于胸壁皮下的脉冲发生器,由计算机按预设刺激模式经脉冲发生器向电极发出刺激指令[10]。由于参与癫痫发作的解剖结构和神经回路复杂多变,故很难据其发病机制预测电刺激对癫痫发作的影响或明确产生疗效的确切机制。目前主流假说"网络导向的神经调控"认为,其疗效主要与电刺激对各种神经回路的影响有关[11-12]。脑深部电刺激术大多以癫痫网络中关键"传播点"为靶点,刺激发出时可对其产生抑制作用,进而抑制致痫灶放电或阻断相应神经传导通路,达到抑制痫样放电扩散的效果[11,13]。边缘系统回路可在皮质及皮质下结构之间的痫样放电扩散中发挥重要作用[14],其中以颞叶癫痫发作相关性Papez回路最受关注[13],该回路由海马-穹隆-乳头体-乳头丘脑束-丘脑前核-扣带回-海马构成,脑深部电刺激术可能通过刺激Papez回路中某个节点,阻断其异常神经活动,并利用自身的输出替代原有神经回路的轴突输出[15]。例如,电刺激丘脑前核(ATN)可抑制局灶性发作向皮质扩散,从而阻断痫样放电扩散,电刺激海马则可阻断起源于颞叶内侧的异常电活动,而大多数局灶性起源伴知觉障碍发作者,致痫灶正是位于此[16]。目前尚无单一机制可以解释不同刺激靶点的脑深部电刺激术在不同疾病中的作用[12]。

研究表明,脑深部电刺激术对于单个神经纤维的影响是可以预测的,而当电刺激作用于神经组织时,通常只能对电刺激后产生的电流分布场进行估计,不能简单地将刺激对神经组织的影响分为兴奋性或抑制性;刺激在电极相邻区域产生的效应与在远隔部位的效应存在明显差异,甚至完全相反[10]。也有研究认为,对神经组织进行电刺激时,可通过抑制大脑抑制性途径、同步或去同步化参与癫痫网络而发挥作用[17];其中,高频电刺激主要通过抑制刺激电极相邻脑区的神经元电活动而抑制癫痫发作[5]。王乃东等[18]采用低能低频电刺激联合低剂量丙戊酸钠[γ-氨基丁酸(GABA)能系统增强药]或尼卡地平(钙通道阻滞药)治疗局灶性伴知觉障碍性发作模型大鼠(杏仁核电点燃模型),结果显示,低频电刺激与低剂量GABA增强药或钙通道阻滞药联合应用可产生协同作用,抑制大鼠杏仁核的点燃,提示低频电刺激抗癫痫发作机制可能与脑组织GABA系统和钙通道系统相关,但确切机制尚未阐明。低频电刺激对癫痫发作的抑制作用可能是通过提高痫样发作阈值实现的;也可能与激活脑组织癫痫发作相关递质系统有关,即低频电刺激激活GABA-苯二氮䓬类受体系统和内啡肽系统,促进GABA与苯二氮䓬类受体及内源性阿片肽与μ受体的结合,从而使大脑神经元兴奋性降低[19-20]。未来尚待开展更深入的基础研究以探究脑深部电刺激术治疗癫痫的确切机制。

二、刺激靶点选择

目前,实验室研究可通过刺激小脑、蓝斑、黑质、尾状核、海马、杏仁核、下丘脑、丘脑中央中核(CM)、丘脑前核、新皮质等[9]结构影响癫痫动物模型的发作特征。而临床往往根据耐药性癫痫发作类型选择脑深部电刺激术靶点,包括丘脑前核、丘脑中央中核、丘脑底核、海马和小脑[16]。(1)丘脑前核:丘脑前核为Papez回路组成部分[21],电刺激不仅可直接阻断痫样放电在Papez回路中的扩散[16],而且可使同侧海马背景电活动去同步化,减少发作间期尖波、高频振荡等病理性放电[22],从而达到控制癫痫发作之目的。丘脑前核电刺激术以耐药性局灶性癫痫患者为首选[23-25],尤其适用于颞叶或额叶起源的局灶性耐药性癫痫[21,26]。(2)丘脑中央中核:丘脑中央中核与大脑皮质及皮质下结构存在广泛性功能连接[27],且皮质-丘脑投射数目多于反向投射数目,故丘脑中央中核可以整合来自前岛叶、额盖以及其他丘脑核团和脑干的输入信号,并将特定信号投射至大脑皮质前运动皮质、运动皮质、初级躯体感觉皮质及皮质下结构[28]。在全面性癫痫发作期,丘脑中央中核较早被激活,诱导发作开始或促进痫样放电早期扩散[29-30],高频(60~130 Hz)电刺激丘脑中央中核可阻断异常电活动扩散至扣带回,控制癫痫发作[31]。据张檀等[21]对大量临床病例

的总结，丘脑中央中核脑深部电刺激术（CM-DBS）对全面性发作和失神发作疗效良好，而对局灶性伴知觉障碍性发作疗效欠佳。然而，CM-DBS用于治疗耐药性全面性癫痫和Lennox-Gastaut综合征尚未获得美国食品与药品管理局（FDA）批准[28,32]。（3）丘脑底核：丘脑底核脑深部电刺激术（STN-DBS）目前较多应用于帕金森病等锥体外系运动障碍性疾病的治疗且疗效确切[33-36]。局灶性与全面性发作小鼠模型研究证据表明，大脑皮质与丘脑底核之间存在神经传导通路，且丘脑底核神经元可传入黑质网状部（SNr）[37]，并与中脑背侧抗惊厥区（DMAZ）存在功能连接[38]，进而抑制癫痫发作。对局灶性继发全面性癫痫模型大鼠的观察发现，STN-DBS可以显著抑制癫痫发作，而SNr-DBS治疗无效，提示STN-DBS抗癫痫作用可能与皮质-丘脑底核通路被逆行激活有关[39]。临床研究显示，STN-DBS可以使耐药性局灶性肌阵挛癫痫发作患者5年随访中发作频率减少75%，发作严重程度、生活满意度显著改善[40]；高频STN-DBS可抑制异常电活动从运动皮质向同侧丘脑底核持续扩散，显著减少发作间期棘波[41]。上述研究提示，丘脑底核是局灶性运动性癫痫网络的重要节点，STN-DBS对起源于运动皮质的耐药性局灶性癫痫有一定疗效。（4）海马和小脑：海马在内侧颞叶癫痫（mTLE）的发生发展过程中发挥重要作用[42]。内侧颞叶癫痫的形成可能是由于海马齿状回颗粒细胞轴突（苔藓纤维）出芽形成正反馈癫痫发作神经回路，或存在损伤等导致海马体或颞叶内侧广泛性神经元丢失，从而诱导癫痫发作或海马硬化[43-45]。颞叶癫痫是最常见的与苔藓纤维出芽相关的癫痫类型[44]，以海马为刺激靶点的脑深部电刺激术可通过阻断异常电活动自致痫灶传播至癫痫维持相关脑区（如丘脑前核），从而控制痫样放电扩散[46]。以海马为刺激靶点的海马脑深部电刺激术（Hip-DBS）主要适用于伴或不伴内侧颞叶硬化的内侧颞叶癫痫[47-49]。此外，Cooper等[6]于1973年首次提出将慢性人脑电刺激应用于调控皮质兴奋性，并致力于对小脑皮质电刺激的研究，但是后续研究并未证实小脑电刺激对癫痫患者有效。

脑深部电刺激术需要综合癫痫发作类型、致痫灶部位和个体化等因素选择刺激靶点。目前的临床研究多以单中心、小样本研究为主，尚待深入开展多中心、大样本临床研究以获得可靠证据，为脑深部电刺激术刺激靶点的选择提供更准确可行的参考。

三、临床疗效与安全性

1.临床疗效　现有研究初步证实，不同刺激靶点的脑深部电刺激术对不同发作类型的耐药性癫痫均具有一定疗效。一项有关耐药性癫痫患者的回顾性研究根据发作类型分别选择丘脑前核、海马、丘脑中央中核、丘脑底核和杏仁核作为刺激靶点，术后随访1～8年，然后将患者近6个月的发作频率与术前比较，结果显示，ATN-DBS组20例局灶性发作或全面性强直性发作患者共治疗逾2年，75%（15/20）发作控制良好（发作频率减少＞50%）；Hip-DBS组4例患者均伴海马硬化，疗程超过3年，控制良好率为3/4；CM-DBS组1例全面性强直性发作伴失神发作患者，疗程1年8个月，发作频率减少＞80%；STN-DBS组入组5例呈运动性发作病例，经2年以上电刺激治疗均达到控制良好；余1例MRI提示杏仁核肿胀患者，施行相应部位脑深部电刺激术，刺激后发作即刻消失，3年9个月内无发作[50]。除对癫痫发作频率的改善，脑深部电刺激术对发作严重程度、患者生活质量，以及神经心理等方面均具有改善作用。对耐药性局灶性癫痫患者的长期随访可以发现，ATN-DBS术后5年，发作频率、主观“最严重”发作类型分别减少69%和75%，利物浦癫痫发作严重程度量表（LSSS）和成年癫痫患者生活质量问卷31（QOLIE-31）评分分别下降18.3分和提高6.1分，神经心理综合评分如注意力、执行功能、抑郁、紧张/焦虑、总情绪障碍和主观认知功能障碍等也有所改善[26]。一项研究对20例耐药性全面性癫痫患者CM-DBS术后的心理状态进行评价，评价工具为SNAP-Ⅳ评定量表（Swanson, Nolan, And Pelham-Ⅳ rating scales），入组患者平均随访时间为2.55年，对其注意力、多动-冲动和对立违抗症状评价显示，所有患者平均有4.8项获得改善，其中18例（90%）癫痫发作频率下降＞50%，且发作频率下降与注意力改善呈显著正相关（$P=0.033$）[51]，与于晓曼等[52]的研究结果相一致。提示耐药性癫痫患者经脑深部电刺激术治疗后癫痫发作频率、发作严重程度、生活质量以及神经心理状态均有不同程度改善，为脑深部电刺激术治疗耐药性癫痫的临床疗效提供有利依据。

2.安全性　虽然脑深部电刺激治疗耐药性癫痫已取得一定临床疗效，但是其存在的手术安全性亦不可忽视。例如，术中或术后并发症，诸如开机时

刺激发生器植入部位对侧手臂可出现数分钟刺痛感[53]或植入部位皮肤感觉异常(刺痛、震动感和双上肢震颤等)[54-55]。术后5年内约有12.7%患者发生植入部位感染、9.1%植入部位不适感、6.4%出现记忆障碍[54];其他不良反应包括短暂性失写、眩晕、术后植入部位疼痛、设备移位等[53-55]。此外,脑深部电刺激术治疗其他疾病时出现的不良反应也有一定参考价值,运动障碍性疾病患者脑深部电刺激术中可发生血管迷走神经反应[0.82%(6/728)]、低血压[0.27%(2/728)]或癫痫发作[0.27%(2/728)];术后可出现经影像学证实的无症状性脑室内出血[3.43%(25/728)]、无症状性脑出血[0.55%(4/728)]、症状性脑出血[1.10%(8/728)]或缺血性卒中[0.41%(3/728)][56]。其中手术并发症如出血、重要脑组织结构破坏、植入部位感染等较为常见,但手术对神经精神系统的影响则难以评估,需要密切关注[57]。其他少见不良反应还有轻度步态或语言障碍、情感障碍、抑郁恶化、癫痫发作程度加重、注意力难以集中以及头痛等症状与体征[26,56-57]。总之,相较癫痫外科手术,脑深部电刺激术治疗过程中不良事件发生率较低,但仍需临床医师术中谨慎对待,术后严密观察。

四、小结与展望

脑深部电刺激术对耐药性癫痫患者是一种有效且安全性较高的治疗方法,根据癫痫发作类型选择不同刺激靶点的脑深部电刺激术,可以使患者发作频率、发作严重程度、生活质量以及神经心理等方面均不同程度改善,为长期发作难以控制的癫痫患者带来希望。但目前脑深部电刺激术治疗耐药性癫痫的调控机制、适应证、个体化靶点选择的确切标准及治疗过程中不良反应的预防等尚无定论,未来尚待更多大样本、多中心随机对照临床试验进一步探究,以期积累更多临床证据,使更多癫痫患者受益。

利益冲突 无

参 考 文 献

[1] Rincon N, Barr D, Velez-Ruiz N. Neuromodulation in drug resistant epilepsy[J]. Aging Dis, 2021, 12:1070-1080.

[2] Perucca E, Brodie MJ, Kwan P, Tomson T. 30 years of second-generation antiseizure medications: impact and future perspectives [J]. Lancet Neurol, 2020, 19:544-556.

[3] Toffa DH, Touma L, El Meskine T, Bouthillier A, Nguyen DK. Learnings from 30 years of reported efficacy and safety of vagus nerve stimulation (VNS) for epilepsy treatment: a critical review[J]. Seizure, 2020, 83:104-123.

[4] Davis P, Gaitanis J. Neuromodulation for the treatment of epilepsy: a review of current approaches and future directions[J]. Clin Ther, 2020, 42:1140-1154.

[5] Wu YC, Liao YS, Yeh WH, Liang SF, Shaw FZ. Directions of deep brain stimulation for epilepsy and Parkinson's disease[J]. Front Neurosci, 2021, 15:680938.

[6] Cooper IS, Amin I, Gilman S. The effect of chronic cerebellar stimulation upon epilepsy in man[J]. Trans Am Neurol Assoc, 1973, 98:192-196.

[7] Ryvlin P, Jehi LE. Neuromodulation for refractory epilepsy[J]. Epilepsy Curr, 2021, 22:11-17.

[8] Ryvlin P, Rheims S, Hirsch LJ, Sokolov A, Jehi L. Neuromodulation in epilepsy: state-of-the-art approved therapies[J]. Lancet Neurol, 2021, 20:1038-1047.

[9] Graber KD, Fisher RS. Deep brain stimulation for epilepsy: animal models[M]//Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV. Jasper's basic mechanisms of the epilepsies. 4th ed. Bethesda (MD): National Center for Biotechnology Information (US), 2012.

[10] Fariba KA, Gupta V. Deep brain stimulation[M]. Treasure Island (FL): StatPearls Publishing, 2022.

[11] Piper RJ, Richardson RM, Worrell G, Carmichael DW, Baldeweg T, Litt B, Denison T, Tisdall MM. Towards network-guided neuromodulation for epilepsy[J]. Brain, 2022, 145:3347-3362.

[12] Perlmutter JS, Mink JW. Deep brain stimulation[J]. Annu Rev Neurosci, 2006, 29:229-257.

[13] Klinger NV, Mittal S. Clinical efficacy of deep brain stimulation for the treatment of medically refractory epilepsy[J]. Clin Neurol Neurosurg, 2016, 140:11-25.

[14] Chaitanya G, Toth E, Pizarro D, Iasemidis L, Murray TA, Riley K, Pati S. Acute modulation of the limbic network with low and high-frequency stimulation of the human fornix[J]. Epilepsy Behav Rep, 2020, 14:100363.

[15] Moreira-Holguín JC, Barahona-Morán DA, Hidalgo-Esmeraldas J, Guzmán-Rochina C. Neuromodulation of the anterior thalamic nucleus as a therapeutic option for difficult-to-control epilepsy[J]. Neurocirugia (Astur: Engl Ed), 2022, 33:182-189.

[16] Perez-Malagon CD, Lopez-Gonzalez MA. Epilepsy and deep brain stimulation of anterior thalamic nucleus[J]. Cureus, 2021, 13: e18199.

[17] Park EH, Barreto E, Gluckman BJ, Schiff SJ, So P. A model of the effects of applied electric fields on neuronal synchronization[J]. J Comput Neurosci, 2005, 19:53-70.

[18] Wang ND, Zhao YB, Chen YH, Guo DJ, Zhang F, Yue W. The inhibitive effect of low frequency electric brain stimulation on amygdala kindling in rats and its possible mechanisms[J]. Zhonghua Wu Li Yi Xue Yu Kang Fu Za Zhi, 2007, 29:296-299.[王乃东, 赵永波, 陈英辉, 闵登俊, 张芳, 岳旺. 低频脑深部电刺激对大鼠杏仁核点燃的抑制作用及其相关机制探讨[J]. 中华物理医学与康复杂志, 2007, 29:296-299.]

[19] Albensi BC, Ata G, Schmidt E, Waterman JD, Janigro D. Activation of long-term synaptic plasticity causes suppression of epileptiform activity in rat hippocampal slices[J]. Brain Res, 2004, 998:56-64.

[20] López-Meraz ML, Neri-Bazán L, Rocha L. Low frequency stimulation modifies receptor binding in rat brain[J]. Epilepsy Res, 2004, 59:95-105.

[21] Zhang T, Liu C, Zhang JG, Meng FG. Target selection of deep brain stimulation for epilepsy[J]. Zhonghua Shen Jing Wai Ke Za Zhi, 2013, 29:97-100.[张檀, 刘崇, 张建国, 孟凡刚. 脑深部电刺激治疗癫痫的靶点选择[J]. 中华神经外科杂志, 2013, 29:97-100.]

[22] Yu T, Wang X, Li Y, Zhang G, Worrell G, Chauvel P, Ni D, Qiao

L, Liu C, Li L, Ren L, Wang Y. High-frequency stimulation of anterior nucleus of thalamus desynchronizes epileptic network in humans[J]. Brain, 2018, 141:2631-2643.

[23] Tassigny D, Soler-Rico M, Delavallée M, Santos SF, El Tahry R, Raftopoulos C. Anterior thalamic nucleus deep brain stimulation for refractory epilepsy: preliminary results in our first 5 patients[J]. Neurochirurgie, 2020, 66:252-257.

[24] Fasano A, Eliashiv D, Herman ST, Lundstrom BN, Polnerow D, Henderson JM, Fisher RS. Experience and consensus on stimulation of the anterior nucleus of thalamus for epilepsy[J]. Epilepsia, 2021, 62:2883-2898.

[25] Zheng H, Chengcheng W, Bin J, Chaochao W, Hongying Z, Wenqiang G, Bin L, Hailong T, Zhigang W. Deep brain stimulation of anterior thalamic nucleus for treatment of patient with tuberous sclerosis-related refractory epilepsy[J]. World Neurosurg, 2020, 138:141-144.

[26] Salanova V, Witt T, Worth R, Henry TR, Gross RE, Nazzaro JM, Labar D, Sperling MR, Sharan A, Sandok E, Handforth A, Stern JM, Chung S, Henderson JM, French J, Baltuch G, Rosenfeld WE, Garcia P, Barbaro NM, Fountain NB, Elias WJ, Goodman RR, Pollard JR, Tröster AI, Irwin CP, Lambrecht K, Graves N, Fisher R; SANTE Study Group. Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy[J]. Neurology, 2015, 84:1017-1025.

[27] Velasco F, Saucedo-Alvarado PE, Reichrath A, Valdés-Quiroz H, Aguado-Carrillo G, Velasco AL. Centromedian nucleus and epilepsy [J]. J Clin Neurophysiol, 2021, 38:485-493.

[28] Zillgitt AJ, Haykal MA, Chehab A, Staudt MD. Centromedian thalamic neuromodulation for the treatment of idiopathic generalized epilepsy[J]. Front Hum Neurosci, 2022, 16:907716.

[29] Zhang Z, Zhou X, Liu J, Qin L, Ye W, Zheng J. Aberrant functional connectivity of the cingulate subregions in right-sided temporal lobe epilepsy[J]. Exp Ther Med, 2020, 19:2901-2912.

[30] Torres Diaz CV, González-Escamilla G, Ciolac D, Navas García M, Pulido Rivas P, Sola RG, Barbosa A, Pastor J, Vega-Zelaya L, Groppa S. Network substrates of centromedian nucleus deep brain stimulation in generalized pharmacoresistant epilepsy [J]. Neurotherapeutics, 2021, 18:1665-1677.

[31] Kim SH, Lim SC, Yang DW, Cho JH, Son BC, Kim J, Hong SB, Shon YM. Thalamo-cortical network underlying deep brain stimulation of centromedian thalamic nuclei in intractable epilepsy: a multimodal imaging analysis[J]. Neuropsychiatr Dis Treat, 2017, 13:2607-2619.

[32] Dalic LJ, Warren AEL, Bulluss KJ, Thevathasan W, Roten A, Churilov L, Archer JS. DBS of thalamic centromedian nucleus for Lennox-Gastaut syndrome (ESTEL Trial)[J]. Ann Neurol, 2022, 91: 253-267.

[33] Bove F, Mulas D, Cavallieri F, Castrioto A, Chabardès S, Meoni S, Schmitt E, Bichon A, Di Stasio E, Kistner A, Pélissier P, Chevrier E, Seigneuret E, Krack P, Fraix V, Moro E. Long-term outcomes (15 years) after subthalamic nucleus deep brain stimulation in patients with Parkinson disease[J]. Neurology, 2021.[Epub ahead of print]

[34] Kim A, Kim HJ, Kim A, Kim Y, Jang M, Paek SH, Jeon B. Bilateral subthalamic nucleus deep brain stimulation is an effective treatment for diphasic dyskinesia[J]. Eur J Neurol, 2021, 28:1574-1580.

[35] Mitchell KT, Younce JR, Norris SA, Tabbal SD, Dowling JL, Rich KM, Perlmutter JS, Ushe M. Bilateral subthalamic nucleus deep brain stimulation in elderly patients with Parkinson disease: a case-control study[J]. Oper Neurosurg (Hagerstown), 2020, 19:234-240.

[36] Shin HW, Kim MS, Kim SR, Jeon SR, Chung SJ. Long-term effects of bilateral subthalamic deep brain stimulation on postural instability and gait difficulty in patients with Parkinson's disease [J]. J Mov Disord, 2020, 13:127-132.

[37] Dinner DS, Neme S, Nair D, Montgomery EB Jr, Baker KB, Rezai A, Lüders HO. EEG and evoked potential recording from the subthalamic nucleus for deep brain stimulation of intractable epilepsy[J]. Clin Neurophysiol, 2002, 113:1391-1402.

[38] Elias GJB, Loh A, Gwun D, Pancholi A, Boutet A, Neudorfer C, Germann J, Namasivayam A, Gramer R, Paff M, Lozano AM. Deep brain stimulation of the brainstem[J]. Brain, 2021, 144: 712-723.

[39] Usui N, Maesawa S, Kajita Y, Endo O, Takebayashi S, Yoshida J. Suppression of secondary generalization of limbic seizures by stimulation of subthalamic nucleus in rats[J]. J Neurosurg, 2005, 102:1122-1129.

[40] Wang X, Du J, Wang D, Xu C, Ren Z, Wang Y, Li Y, Yu T, Ren L. Long-term outcome of unilateral deep brain stimulation of the subthalamic nucleus for a patient with drug-resistant focal myoclonic seizure[J]. Ann Transl Med, 2020, 8:18.

[41] Ren L, Yu T, Wang D, Wang X, Ni D, Zhang G, Bartolomei F, Wang Y, Li Y. Subthalamic nucleus stimulation modulates motor epileptic activity in humans[J]. Ann Neurol, 2020, 88:283-296.

[42] Foutz TJ, Wong M. Brain stimulation treatments in epilepsy: basic mechanisms and clinical advances[J]. Biomed J, 2022, 45:27-37.

[43] Secchi TL, Brondani R, Bragatti JA, Bizzi JWJ, Bianchin MM. Evaluating the association of calcified neurocysticercosis and mesial temporal lobe epilepsy with hippocampal sclerosis in a large cohort of patients with epilepsy[J]. Front Neurol, 2022, 12:769356.

[44] Buckmaster PS. Mossy fiber sprouting in the dentate gyrus[M]// Noebels JL, Avoli M, Rogawski MA, Olsen RW, Delgado-Escueta AV. Jasper's basic mechanisms of the epilepsies. 4th ed. Bethesda (MD): National Center for Biotechnology Information (US), 2012.

[45] Wu J, Wang L, Huang Y, Wu Q, Luo X, Li Y, Ren S, Wu G. Cognitive impairment and mossy fiber sprouting in a rat model of drug-resistant epilepsy induced by lithium-pilocarpine[J]. Curr Neurovasc Res, 2021, 18:374-380.

[46] Vetkas A, Germann J, Elias G, Loh A, Boutet A, Yamamoto K, Sarica C, Samuel N, Milano V, Fomenko A, Santyr B, Tasserie J, Gwun D, Jung HH, Valiante T, Ibrahim GM, Wennberg R, Kalia SK, Lozano AM. Identifying the neural network for neuromodulation in epilepsy through connectomics and graphs[J]. Brain Commun, 2022, 4:fcac092.

[47] Wang S, Zhao M, Li T, Zhang C, Zhou J, Wang M, Wang X, Ma K, Luan G, Guan Y. Long-term efficacy and cognitive effects of bilateral hippocampal deep brain stimulation in patients with drug-resistant temporal lobe epilepsy[J]. Neurol Sci, 2021, 42:225-233.

[48] Vetkas A, Fomenko A, Germann J, Sarica C, Iorio-Morin C, Samuel N, Yamamoto K, Milano V, Cheyuo C, Zemmar A, Elias G, Boutet A, Loh A, Santyr B, Gwun D, Tasserie J, Kalia SK, Lozano AM. Deep brain stimulation targets in epilepsy: systematic review and meta-analysis of anterior and centromedian thalamic nuclei and hippocampus[J]. Epilepsia, 2022, 63:513-524.

[49] Cukiert A, Cukiert CM, Burattini JA, Mariani PP. Long-term seizure outcome during continuous bipolar hippocampal deep brain stimulation in patients with temporal lobe epilepsy with or without mesial temporal sclerosis: an observational, open-label study[J]. Epilepsia, 2021, 62:190-197.

[50] Xu X, Ling ZP, Yu XG, Zhang JN, Xu BN, Cui ZQ, Mao ZQ, Pan LS, Zong R, Zhang LW, Zhang X, Wan M. Deep brain stimulation for intractable epilepsy: a long-term clinical comparison of five

different stimulating targets[J]. Lin Chuang Shen Jing Wai Ke Za Zhi, 2021, 18:404-408.[徐欣, 凌至培, 余新光, 张剑宁, 许百男, 崔志强, 毛之奇, 潘隆盛, 宗睿, 张利为, 张旭, 万明. 脑深部电刺激治疗药物难治性癫痫:5个不同刺激靶点的长期临床效果比较[J]. 临床神经外科杂志, 2021, 18:404-408.]
[51] Cukiert A, Cukiert CM, Burattini JA, Mariani PP. Seizure outcome during bilateral, continuous, thalamic centromedian nuclei deep brain stimulation in patients with generalized epilepsy: a prospective, open-label study[J]. Seizure, 2020, 81:304-309.
[52] Yu XM, Zhang SH, Ding P, Gao C, Li XX, Liang SL. Hippocampal stimulation in patients with temporal lobe epilepsy (5 cases report and literature review)[J]. Li Ti Ding Xiang He Gong Neng Xing Shen Jing Wai Ke Za Zhi, 2016, 29:330-335.[于晓曼, 张绍辉, 丁平, 高超, 李学秀, 梁树立. 海马电刺激治疗颞叶癫痫(附5例报道及文献复习)[J]. 立体定向和功能性神经外科杂志, 2016, 29:330-335.]
[53] Valentín A, García Navarrete E, Chelvarajah R, Torres C, Navas M, Vico L, Torres N, Pastor J, Selway R, Sola RG, Alarcon G. Deep brain stimulation of the centromedian thalamic nucleus for the treatment of generalized and frontal epilepsies[J]. Epilepsia, 2013, 54:1823-1833.
[54] Salanova V, Sperling MR, Gross RE, Irwin CP, Vollhaber JA, Giftakis JE, Fisher RS; SANTÉ Study Group. The SANTÉ study at 10 years of follow-up: effectiveness, safety, and sudden unexpected death in epilepsy[J]. Epilepsia, 2021, 62:1306-1317.
[55] Sobstyl M, Stapińska-Syniec A, Rylski M. Deep brain stimulation for the treatment of refractory and super-refractory status epilepticus [J]. Seizure, 2020, 81:58-62.
[56] Fenoy AJ, Simpson RK Jr. Risks of common complications in deep brain stimulation surgery: management and avoidance [J]. J Neurosurg, 2014, 120:132-139.
[57] Dougherty DD. Deep brain stimulation: clinical applications[J]. Psychiatr Clin North Am, 2018, 41:385-394.

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·小词典·

中英文对照名词词汇(二)

钙激活钾离子通道 calcium activated potassium(KCa)
干燥综合征 Sjögren syndrome(SS)
感兴趣体积 volume of interest(VOI)
高度同步化 hypersynchronous(HYP)
高级别胶质瘤 high-grade glioma(HGG)
功能缺失 loss-of-function(LOF)
功能性运动障碍 functional movement disorder(FMD)
谷氨酸脱羧酶65 glutamic acid decarboxylase 65(GAD65)
寡克隆区带 oligoclonal band(OB)
国际抗癫痫联盟 International League Against Epilepsy(ILAE)
海马硬化 hippocampal sclerosis(HS)
汉密尔顿焦虑量表 Hamilton Anxiety Rating Scale(HAMA)
汉密尔顿抑郁量表 Hamilton Depression Rating Scale(HAMD)
黑质网状部 substantia nigra reticulata(SNr)
红外微分干涉相衬 infrared differential interference contrast(IR-DIC)
红细胞沉降率 erythrocyte sedimentation rate(ESR)
红细胞生成素 erythropoietin(EPO)
琥珀酸脱氢酶 succinate dehydrogenase(SDH)
灰白质组织边界增强 gray-white matter tissue border enhancement(TBE)
活性氧 reactive oxygen species(ROS)
获得性癫痫性失语 acquired epileptic aphasia(AEA)
肌萎缩侧索硬化症 amyotrophic lateral sclerosis(ALS)
肌阵挛失神癫痫 epilepsy with myoclonic absence(EMA)
基于体素的形态学分析 voxel-based morphometry(VBM)
急性期脑出血试验 Acute Phase of Intracerebral Hameorrhage (PEACH) trial
疾病修饰治疗 disease modifying therapy(DMT)
加拿大蒙特利尔神经病学研究所 Montreal Neurological Institute(MNI)
家族性肌萎缩侧索硬化症 familial amyotrophic lateral sclerosis(fALS)
N-甲基-D-天冬氨酸 N-methyl-D-aspartate(NMDA)
N-甲基-D-天冬氨酸受体 N-methyl-D-aspartate receptor(NMDAR)
甲状腺过氧化物酶 thyroid peroxidase(TPO)
甲状腺球蛋白 thyroglobulin(TG)
甲状腺素 thyroxine(T_4)
钾-氯离子共转运体2 K^+-Cl^- co-transporter 2(KCC2)
间变性少突胶质细胞瘤 anaplastic oligodendroglioma(AOD)
间变性少突星形细胞瘤 anaplastic oligoastrocytoma(AOA)
间变性星形细胞瘤 anaplastic astrocytoma(AA)
间接免疫荧光法 indirect immunofluorescence assay(IIFA)
僵人综合征 stiff-person syndrome(SPS)
胶质母细胞瘤 glioblastoma(GBM)
接触蛋白相关蛋白-2 contactin-associated protein 2(CASPR2)
结构变异 structure variant (SV)
结构磁共振成像 structural magnetic resonance imaging(sMRI)
经颅磁刺激 transcranial magnetic stimulation(TMS)
静息态功能磁共振成像 resting-state functional magnetic resonance imaging (rs-fMRI)
局灶性进展为双侧强直-阵挛发作 focal to bilateral tonic-clonic seizure(FBTCS)
局灶性皮质发育不良 focal cortical dysplasia(FCD)
巨细胞病毒 cytomegalovirus(CMV)