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## 丘脑底核脑深部电刺激治疗帕金森病的临床分析\*

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**摘要 目的:**通过丘脑底核脑深部电刺激术治疗帕金森病,观察其肌肉僵直、静止性震颤、运动迟缓等症状的改善情况。**方法:**选取以丘脑底核为刺激靶点收治的帕金森病患者8例,对比手术前后患者肌强直、静止性震颤、运动迟缓等症状的改善情况,并进行UPDRS评分。**结果:**接受丘脑底核脑深部电刺激术治疗帕金森病6个月后,患者肌肉僵直、静止性震颤、运动迟缓等临床主症的改善上效果良好;与手术前相比,患者术后UPDRS评分均有所降低,差异具有统计学意义( $P < 0.05$ );患者术后美多巴服用量显著减少,差异具有统计学意义( $P < 0.05$ );患者术后没有产生永久性的并发症以及较明显的临床症状;但对大量油脂性渗出及典型面具性面容的治疗上未见明显疗效。**结论:**丘脑底核脑深部电刺激术治疗帕金森氏病,可以使帕金森病主要临床症状肌肉僵直、静止性震颤及运动迟缓得到明显改善,显著减少美多巴服药量,具有安全可靠的疗效,对临床具有指导意义,值得临床推广应用。

**关键词:**脑深部电刺激手术;丘脑底核;帕金森病;临床表现

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## Clinical Analysis of Targeting Subthalamic Nucleus for Deep Brain Stimulation for Parkinson's Disease\*

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**ABSTRACT Objective:** To observe the curative effects of targeting subthalamic nucleus for deep brain stimulation on the main clinical symptoms of muscles in patients with Parkinson's disease including muscle rigidity, resting tremor and bradykinesia. **Methods:** 8 cases of Parkinson's disease patients were selected and treated by stimulating subthalamic nucleus as the target. The improvement of symptoms, such as muscle rigidity, resting tremor, and bradykinesia were detected before and after surgery, and UPDRS scores were compared. **Results:** Six months after accepting the deep brain stimulation of subthalamic nucleus, the main clinical symptoms of muscles was obviously improved for the patients with Parkinson's disease including the muscle rigidity, resting tremor, bradykinesia, and so on. Compared with before surgery, postoperative UPDRS ratings reduced ( $P < 0.05$ ), and the postoperative madopar dose was also significantly decreased ( $P < 0.05$ ). No obvious permanent postoperative complications were detected; but the deep brain stimulation of subthalamic nucleus had no significant effect on the treatment of a large number of oil exudation and typical face of masks. **Conclusions:** The deep brain stimulation of subthalamic nucleus can significantly improve the main clinical symptoms of Parkinson's disease, including muscle rigidity, tremor and bradykinesia, and also can obviously reduce the dose of medication madopar, indicating safe and reliable curative effects.

**Key words:** Deep brain stimulation surgery; Subthalamic nucleus; Parkinson's disease; Clinical manifestations

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### 前言

帕金森病(PD)又称震颤麻痹,是一种最常见的运动障碍性疾病,其特征性表现为静止震颤、肌肉僵直和运动迟缓。其作用机制为纹状体和黑质中的多巴胺能神经元的变性所致<sup>[1]</sup>。约75%病人患病早期主要表现为静止不动时出现肢体震颤,运动后有所改善;患者四肢肌肉僵硬、屈伸不利、活动受限,不仅导致运动迟缓,还可导致患者面部表情僵硬、表情淡漠如戴面具,

语音低缓,甚至出现不自主的流涎现象;患者还存在躯体姿势异常的症状,其主要表现为患者只能短暂维持直立,而导致躯体始终俯曲;且患者皮肤常有大量油脂外溢<sup>[2-3]</sup>。相关病流行病学研究显示,帕金森病的发病年龄约为55岁,国内帕金森病患者人数已高达百万<sup>[4]</sup>。由于患病年龄较高,其早期症状易与自身机能的自然衰老相互混淆,导致错过早期治疗的时机,造成病情的加重。

脑深部电刺激术(Deep brain stimulation surgery, DBS),是

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通过电刺激脑组织深部的一项技术,通过立体定向技术的支持与引导,将一个可以产生特定的脉冲的电极,放置在到脑的深部神经核团(如丘脑底核),并进行长期慢性的电刺激<sup>[9]</sup>。通过立体定向针对神经结构进行探测,发现随着一定范围内的刺激率,电刺激可以影响和改变震颤,针对苍白球、丘脑乃至丘脑底核等危险部位达到治疗作用<sup>[9]</sup>。经过近一个世纪的研究与发展,目前脑深部电极刺激技术已经得到了医患的广泛认可,成为安全、可行的治疗方法之一。当今社会老龄化程度正快速推进,对帕金森病的脑深部电极刺激术的研究,意义深远。本研究观察丘脑底核脑深部电刺激术对帕金森病患者肌僵直、静止性震颤、运动迟缓等症状的改善情况,现报道如下。

## 1 资料与方法

### 1.1 一般资料

选取 2012 年 10 月至 2014 年 5 月,以帕金森病为诊断收入我院的患者共计 8 例,其中 5 例男性,3 例女性,年龄 54~62 岁,平均年龄 60.87 岁,患者病程 3~14 年,平均病程为 7.5 年。将患者随机编为 1~8 号,其中仅单侧震颤 3 例,双侧震颤发病 5 例。患者的一般资料相仿,差异无统计学意义( $P>0.05$ )。所有患者均符合帕金森病诊断标准,自愿参与本次研究,并签署知情同意书。

### 1.2 诊断标准

① 患者病早期表现为静止时肢体震颤,运动后有所改善;② 患者肌肉僵直、活动受限;③ 运动迟缓;④ 面部表情僵硬、表情淡漠,语音低缓,不自主的流涎;⑤ 躯体姿势异常;⑥ 油脂外溢皮肤。

### 1.3 纳入标准

符合上述诊断标准,确诊为帕金森病,患者临床表现为肌肉强直、运动迟缓、静止性震颤。患者(可独立行走)在服用美多巴后,症状有一定程度上的缓解;但服用药物后,不适症状仍持续不解;对于帕金森症状的控制,患者手术前后均口服相同规格的美多巴。

### 1.4 排除标准

① 多系统萎缩、血管性、药物性帕金森综合症患者;② MRI

禁忌症者;③ 严重精神或心理疾病者;④ 恶性肿瘤患者;⑤ 体质异常虚弱者;⑥ 颅内病变者(如占位及大面积脑梗等);⑦ 不配合本次研究者。

### 1.5 治疗方法

病人于术前 24 h 停止服药,遵从常规手术流程,术前 12 h 常规禁食、禁水。分别对单、双侧震颤的帕金森病患者,进行单、双侧丘脑底核脑深部电刺激术。于局麻状态下对患者安装立体定向基架,手术后进行 MRI 检测,按照靶点坐标植入刺激电极,进行试探性电刺激,观察每次刺激后患者临床症状的改变情况及患者的不适感觉,最终植入固定电极,于锁骨下埋置脉冲发生器。在手术后 2~4 周内将刺激器打开,观察并记录患者的症状及体征。

### 1.6 疗效判定标准

观察患者手术六个月后患者肌肉强直、静止性震颤运动、迟缓等临床症状,以及手术前后服用美多巴剂量的改变情况;在患者术前及术后半年关期状态下,使用 UPDRS II 与 UPDRS III 评分系统,分别评定患者的运动以及日常生活能力。

### 1.7 统计学分析

采用 SPSS19.0 统计分析包对所得数据进行分析,数据以平均数 $\pm$ 标准差( $\bar{x}\pm s$ )表示,计量资料采用 t 检验分析,计数资料采用卡方检验分析,以  $P<0.05$  认为差异显著,具有统计学意义。

## 2 结果

### 2.1 帕金森病主要症状的改善情况

经手术治疗后,8 例帕金森病患者肌肉强直、静止性震颤及运动迟缓的症状均得到了一定的改善,其中静止性震颤现象完全得到缓解 1 例。如表 1 结果显示,丘脑底核脑深部电刺激术在改善帕金森病临床症状上功效十分显著。

### 2.2 UPDRS 评分及美多巴调整情况

如表 2 所示,与手术前比较,术后患者 UPDRS II 日常活动评分及 UPDRS III 运动评分均明显减低( $P<0.05$ ),且其中 1 例患者术后 UPDRS II 评分为零;术后服用美多巴的剂量也有了显著的减少( $P<0.05$ )。经过丘脑底核治疗后,帕金森病患者的运动

表 1 术后 6 个月患者症状的改善情况

Table 1 The improvement of symptoms 6 months after operation

| Symptom         | Improvement the situation of disease | Case |
|-----------------|--------------------------------------|------|
| Muscle rigidity | The left side obviously alleviate    | 1    |
|                 | The right side obviously alleviate   | 2    |
|                 | Bilateral slightly alleviated        | 1    |
|                 | Bilateral obviously alleviated       | 4    |
| Resting tremor  | The left side obviously alleviate    | 1    |
|                 | The right side obviously alleviate   | 2    |
|                 | Bilateral slightly alleviated        | 2    |
| Slow movement   | Bilateral obviously alleviated       | 3    |
|                 | Improved obviously                   | 8    |
|                 | No improvement                       | 0    |

功能得到了一定的恢复,生活质量较术前有了显著的提高。

表 2 手术患者的 UPDRS 评分及美多巴调整情况( $\bar{x} \pm s$ )

Table 2 UPDRS score and Madopar adjustment( $\bar{x} \pm s$ )

| UPDRS II<br>(Activity of daily living) |                 | UPDRS III<br>(Kinetism) |                 | Madopar dosage<br>(mg/d) |                   |
|----------------------------------------|-----------------|-------------------------|-----------------|--------------------------|-------------------|
| Preoperative                           | Postoperative   | Preoperative            | Postoperative   | Preoperative             | Postoperative     |
| 31.4 $\pm$ 3.6                         | 20.8 $\pm$ 5.2* | 39.4 $\pm$ 4.8          | 23.6 $\pm$ 6.1* | 750.0 $\pm$ 150.0        | 250.0 $\pm$ 75.0* |

Note: \*P<0.05, compared with preoperative.

### 2.3 并发症情况

8 例患者在进行术后复查核磁共振时,发现 2 例患者的 MRI 提示脑室内存在少量的出血现象,其原因为术中电极针穿过脑室所致,但由于出血量较少,并没有引起患者不良反应的

发生。出现术后皮下感染的有 1 例,但经过抗炎消毒后,感染有所消退,没有进一步加重。术前有 1 例患者脸部皮肤存在大量油脂性渗出,并表现为典型面具性面容,经术后观察,以上症状未见明显好转。

表 3 患者治疗后并发症情况

Table 3 The complications after treatment

|                   | Small amount of bleeding | Subcutaneous infection | Grease exudation |
|-------------------|--------------------------|------------------------|------------------|
| Case(n)           | 2                        | 1                      | 1                |
| Incidence rate(%) | 25.0 %                   | 12.5 %                 | 12.5 %           |

## 3 讨论

帕金森的临床主要表现为肌肉僵直、震颤和运动迟缓,全球发病率约为 405/10 万,而我国约占发病总人数的 1/10<sup>[7,8]</sup>。帕金森的患病率随年龄的增长不断增加,高发年龄约在 55~65 岁之间<sup>[9,10]</sup>。我国目前正处于老龄化时期,对帕金森的研究不容忽视。帕金森主要是脑内丧失多巴胺能神经元,导致纹状体中多巴胺与乙酰胆碱之间的平衡失调所致<sup>[11,12]</sup>。虽然药物治疗能在一定范围内使症状得到好转,但服药 5 年以上会产生耐受性及大量不良反应,导致疗效减退<sup>[13,14]</sup>。

经过长达一个世纪的研究与发展,帕金森的外科治疗已日益成熟。其中立体定向苍白球毁损术,对改善帕金森病主要症状及药物所致的异动症的疗效明确<sup>[15]</sup>,但对于如翻身、起立等轴性症状的治疗并不理想,难以避免其永久性并发症(视野缺损、偏瘫、吞咽困难等)的发生。自脑深部电刺激术(DBS)问世以来,帕金森外科治疗得到发展。DBS 可根据患者不同的临床表现和病情变化作出调整,可用于同期双侧手术以及如丘脑底核(STN)等毁损术不适合的靶点,降低永久性并发症的发生率,可通过对电极触点的调节来缓解其副作用<sup>[16]</sup>。本研究显示经过丘脑底核脑深部电刺激术半年后,帕金森病患者肌肉僵直、静止性震颤、运动迟缓等主要症状得到了良好的改善;与手术前相比,手术后患者 UPDRS 评分均得到一定程度的降低,且美多巴的服用剂量明显减少;患者术后没有产生永久性的并发症以及较明显的临床症状。但对大量油脂性渗出及典型面具性面容的治疗上未见明显疗效。

近年来,在 STN DBS 成功应用于 PD 动物模型的基础上,关于临床治疗的研究日趋增多,这些结果显示<sup>[17,18]</sup>:① STN DBS 能明显改善 PD 运动症状,特别是僵直和动作不能,患者 UR-PDS 运动评分均显著改善,平均改善程度为 41%~71%,而认

知和行为评分未受影响;② STN DBS 对震颤也有明显的疗效。Karlsson F 等<sup>[19]</sup>对 27 例术前平均 UR-PDS 震颤评分达(11.3 $\pm$  5.6)患者行 STN DBS 手术,术后震颤评分降低 80%。提示 STN 电刺激术同样适用于伴有严重震颤的患者;③ 尽管 STN DBS 本身对左旋多巴所致异动症无作用,但可减少患者术后左旋多巴摄入量,从而减轻左旋多巴所致异动症;④ 与苍白球手术比较,Eisenstein SA 等<sup>[20]</sup>认为,STN DBS 对 PD 相关状态的症状改善优于苍白球毁损术和电刺激术,STN DBS 与苍白球 DBS 相比改善运动障碍更为有效,推测其原因可能是 STN 体积较小,低刺激参数即可达到效果,而苍白球体积较大,且各部分功能不同;理论上 STN 影响基底节主要传出核团苍白球和 SNr,而苍白球对 SNr 无作用。

综上所述,丘脑底核脑深部电刺激术在对帕金森病的治疗上,疗效显著且安全可行,对临床有较大的指导意义,值得推广应用。但由于本研究样本含量及观察时间的不充分,对某些指标的说明上存在争议,希望今后的研究能够加以改善,采用更加科学权威的研究方法,得出更加全面准确的研究结果。

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