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Multichannel Microelectrode Recording Influences Final Electrode Placement in Pallidal Deep Brain Stimulation for Parkinson's Disease: Report of Twenty Consecutive Cases

Parkinson Hastalığında Çok Kanallı Mikroelektrot Kaydının Derin Pallidal Uyarım İçin Yapılan Son Elektrot Yerleşimine Olan Etkisi

Mark K. LYONS[1], Kristine ZIEMBA[2], Virgilio EVIDENTE[2]

[1]Mayo Clinic Arizona, Department of Neurological Surgery, Phoenix/AZ, USA
[2]Mayo Clinic Arizona, Department of Neurology, Phoenix/AZ, USA

Correspondence address: Mark K. LYONS / E-mail: lyons.mark2@mayo.edu

ABSTRACT

AIM: Stereotactic placement of the permanent deep brain stimulating electrode can be based upon imaging guidance with or without microelectrode recordings (MER).

MATERIAL and METHODS: We conducted a retrospective study of 20 PD patients who underwent bilateral pallidal DBS placement with MER. There were 14 males and 6 females. The mean age at implantation was 67 years (range 42 - 80 years). Paired t-tests were used to compare initial imaging target coordinates versus final electrode coordinates based on intraoperative MER. United Parkinson's Disease Rating Scale (UPDRS) scores pre-operatively (medication off) and at 6 months post-operatively (medication off, stimulation on) and daily levodopa equivalents pre-operatively and 6 months post-operatively were analyzed.

RESULTS: The mean difference between calculated imaging target and final electrophysiological target was 3 mm (SD + 1.53 mm; $p < 0.0001$) in the dorsal-ventral plane and 1.2 mm the axial plane, resulting in a calculated final electrophysiology-based target adjustment of 3.4 mm (SD = 1.4 mm). Patients' average daily levodopa equivalent dose dropped by 52% at six months post-operatively (SD=40.9; $p = 0.002$). UPDRS scores dropped 26.9 points six months postoperatively (SD=20.4; $p = 0.0003$).

CONCLUSION: In our experience intraoperative microelectrode recordings can facilitate final electrode placement.

KEYWORDS: Microelectrode recording, Parkinson's disease, Globus pallidus internus, Targeting, Deep brain stimulation, Brain mapping

ÖZ

AMAÇ: Stereotaktik olarak yapılan derin beyin kalıcı uyarıcı elektrot yerleşimi görüntüleme kılavuzluğunun yanı sıra mikroelektrot kaydı ile veya mikroelektrot kaydı olmaksızın da yapılabilmektedir.

YÖNTEM ve GEREÇLER: Mikroelektrot kayıt yöntemi ile iki taraflı derin beyin uyarıcısı yerleştirilen 20 Parkinson hastası geriye dönük olarak incelenmiştir. Hastaların 14'ü erkek ve 6'sı kadındı. Hastaların ortalama yaş 67 yıl (yaş aralığı 42-80 yıl). Çiftlenmiş t-test kullanılarak , ilk görüntülere dayanarak elde edilen elektrot hedef noktaları ile operasyon sırasında gerçekleştirilen mikroelektrot kayıt yöntemi ile elde edilen elektrot hedef noktaları karşılaştırılmıştır. (UPRDS) Birleşik Parkinson hastalığı ölçütlemesine göre ameliyat öncesi dönemde (İlaç verilmeden), ameliyat sonrası 6. ayda (ilaçsız fakat, uyarı açık), ameliyat öncesi L-Dopa tedavisi altında ve ameliyat sonrası L-Dopa alan hastalarda inceleme yapıldı.

BULGULAR: İki farklı yöntemle yapılan ön-arka elektrot hedef belirleme sonuçlarının ortalama farkı 3 mm (SD +1,53 mm; $p<0.0001$), aksiyel planda 1,2 mm, elektrofizyolojik tabanlı hedef ayarlamasının hesap edilen nihai sonucu 3,4 mm'ydi (SD=1,4 mm). Hastaların günlük olarak kullandıkları ortalama L-Dopa dozları % 52 oranında azaldı, (SD=40,9; $p= 0.002$). (UPRDS) Birleşik Parkinson hastalığı ölçütlemesi skorları ameliyat sonrası 6. ayda 26,9 puan düşme gösterdi (SD=20,4; P=0.0003).

SONUÇ: Operasyon sırasında yapılan mikroelektrot kayıtları nihai elektrot yerleştirilmesinde kolaylaştırıcı bir yöntem olarak düşünülebilir.

ANAHTAR SÖZCÜKLER: Mikroelektrot kaydı, Parkinson hastalığı, Globus pallidus internus, Hedef belirleme, Derin beyin uyarımı, Beyin haritalaması

INTRODUCTION

Surgical implantation of deep brain stimulation (DBS) electrodes has become a useful adjuvant treatment for symptoms of Parkinson's disease in certain patient subgroups. Targets for DBS implantation include the ventral intermediate nucleus (Vim) of the thalamus, the internal globus pallidus (GPi) and the subthalamic nucleus (STN). Each of these targets has characteristic benefits and side effects, and must be matched to patient needs. Most centers prefer to target the STN, but GPi stimulation is also effective for parkinsonism and may be superior for treatment of dyskinesias. Ventral intermediate nucleus stimulation is useful for reducing tremor in the contralateral limb (9). In order to place the stimulating electrodes in the desired location, techniques and practices vary. Some neurosurgical centers use electrophysiological mapping to identify the target nucleus along with neuroimaging, and stereotactic guidance. Other centers target based upon neuroimaging alone (7). There remains debate, however, about the necessity of microelectrode recording (MER) during surgery to optimize final stimulator electrode placement. A 2004 review of DBS techniques for PD suggested that there was no difference in the outcome of surgery with or without microelectrode recording (3). However, the authors pointed out that their review only reflected "reported outcomes" of the included studies (3). A more recent case series report demonstrated that intraoperative MER techniques altered target locations "only slightly" (usually less than 1 mm), but did not address whether such alteration affected clinical outcomes following surgery (11). Currently, there is a lack of consensus regarding the use of intraoperative MER. Further analysis is needed to assess the benefit and effect of MER and microstimulation on DBS targeting and subsequent clinical outcomes.

MATERIAL and METHODS

We conducted a retrospective study of 20 PD patients who underwent bilateral pallidal DBS placement with MER at our institution from 2005 to 2008. All patients underwent bilateral electrode placement. There were 14 males and 6 females. The mean age at implantation was 67 years (range 42 - 80 years). All patients underwent awake bilateral stereotactic-guided globus pallidus internus deep brain stimulation surgery (Medtronic® DBS lead model 3387S) with an implantable programmable pulse generator (IPG). The GPi target was planned utilizing the coordinates: 2 mm anterior and 2 mm inferior to the mid-commissural point, and 20 mm lateral to the midpoint of the third ventricle. The Alpha-Omega Microguide system® was used for microelectrode nuclear mapping and microstimulation. Multiplanar post-operative cranial magnetic resonance imaging (MR) was performed to confirm accuracy of electrode placement in the GPi. Microelectrode recordings were done using five tungsten-tipped microelectrodes and simultaneously recording neuronal firing patterns. The microelectrodes were arranged in a pattern with a 2 mm space between adjacent electrode tips. The data collected included the following: calculated target based on neuroimaging; final electrode location based on intraoperative MER, UPDRS Part III scores pre-operatively (medications off) and at 6 months post-operatively (medications off, stimulation on) and daily levodopa equivalents pre-operatively and 6 months post-operatively. Paired t-tests were used to compare imaging target coordinates versus final electrode coordinates based on electrophysiology.

RESULTS

Twenty PD patients who underwent bilateral pallidal DBS surgery and were available for follow-up were reviewed. The average difference between the calculated imaging target and the final MER target in the dorsoventral plane was 3 mm (SD=1.53 mm; $p<0.0001$). The final target was also adjusted 2 mm in the axial plane in 23 of 40 lead placements (58%). These adjustments resulted in a mean total linear distance modification between the calculated imaging target and the final MER-based target of 3.4 mm (SD = 1.4 mm), with the distance ranging from 0.9 to 7.9 mm (Figure 1). Based on this MER-assisted final electrode targeting technique, patients' average daily levodopa equivalent dose dropped by 52% at six months post-operatively (SD=40.9; $p= 0.002$) (Figure 2). Their UPDRS Part III scores dropped 26.9 points six months postoperatively (SD=20.4; $p = 0.0003$) (Figure 2).

DISCUSSION

Deep brain stimulation is an appropriate therapeutic option for patients with advanced PD, especially for patients in whom high doses of levodopa are required, leading to more severe motor complications. Debate remains regarding the optimal target for PD, but both the STN and the GPi are utilized (1,4-6). All of the patients in our series underwent awake electrode placement in order to assess the response to intraoperative micro- and macro-stimulation. Others have reported equal success utilizing general anesthesia for electrode placement (7,10). The review by Khatib and co-workers found in their retrospective analysis that while age is an independent risk factor for complications in DBS surgery, monitored anesthesia is a safe technique (8). In addition to appropriate patient selection, the success of DBS surgery depends largely upon accurate placement of the stimulator. This study suggests that intraoperative microelectrode recordings, combined with high resolution magnetic resonance imaging data, can facilitate optimal placement. Although, previous authors have reported that the use of intraoperative microelectrode recordings and micro-stimulation have resulted in adjustment of final targeting of permanent electrode placement, they did not specify the degree to which it impacted the final placement (4,5).

The small incremental risk of hemorrhage during surgery with MER should not preclude its use, since improperly placed stimulators can lead to poor efficacy and/or increased stimulation-related side effects (5,6). While we had no intraoperative hemorrhages in our patient group, it is important to be aware of the potential risks associated with microelectrode placement. Maldonado et al. reported

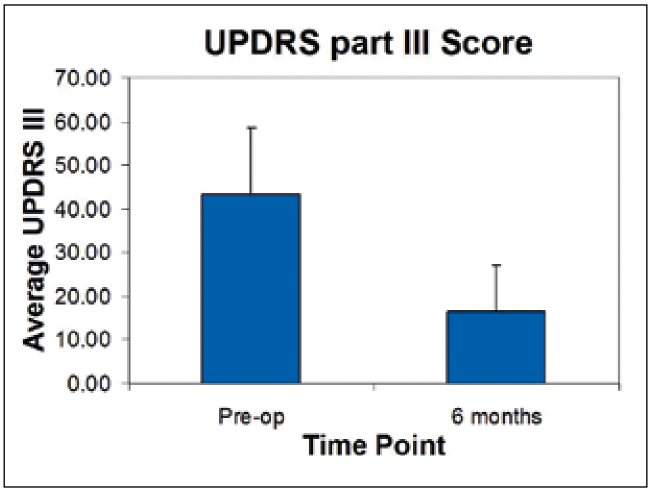

Figure 1: Average UPDRS motor score (Part III) prior to stimulator placement and 6 months after placement. Pre-operative scores were obtained in the "off-medication" state, and post-operative scores in the "off-medication, on-stimulation" state. Higher scores indicate greater disability. Scores decreased an average of 26.9 points, p = 0.0003. Bars indicate standard deviation.

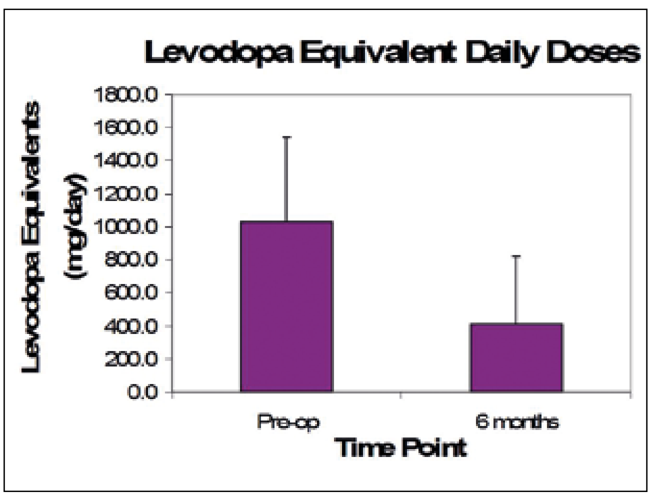

Figure 2: Levodopa equivalent daily doses* prior to stimulator placement and 6 months after placement. Required doses decreased 52% on average (p = 0.002). Bars indicate standard deviation.

**The following conversions were used to calculate levodopa equivalents:*

100 mg levodopa = 125 mg levodopa CR = 75 mg levodopa + 200 mg entacapone/tolcapone = 100 mg levodopa CR + 200 mg entacapone/tolcapone = 1 mg pergolide = 6 mg ropinirole = 200 mg amantadine = 10 mg bromocriptine = 2 mg apomorphine = 10 mg selegiline.

no perioperative intracerebral hemorrhages in their series of 194 patients undergoing 478 stereotactic placements of implanted electrodes with (10). All of their patients were done under general anesthesia without microelectrode recordings or intraoperative stimulation. In addition, their patient population was considerably younger than our patient population, with only 62 of the 194 patients over the age of 40. However, age has been associated with overall increased risk of DBS procedures and needs to be considered when determining patient selection and technique (2,8,10). In our center, the final location of DBS electrodes was significantly altered based upon intraoperative microelectrode recordings, when compared to original target coordinates based on imaging alone, with the distance ranging from 0.9 to 7.9 mm. The most important limitation of our report, similar to earlier ones, is that it was a retrospective study without a control cohort group undergoing electrode placement without MER and microstimulation. Although both approaches have been reported to be efficacious, no study has directly compared the short-term or long-term clinical benefits from DBS with or without electrophysiological targeting.

Our retrospective study shows that there can be a significant difference between imaging target and electrophysiological target in PD patients undergoing pallidal DBS. It is important to note that the sample size of this study is small and the results are preliminary. Although DBS can be successfully done with or without electrophysiology, there are no published studies comparing final clinical outcomes based on imaging alone versus imaging plus electrophysiology. The use of microelectrode recordings and intraoperative micro- and macro-stimulation is not required to achieve excellent clinical improvement in PD patients. In our series, however, we found that there was a significant impact of the intraoperative MER on final electrode placement. However, in order to critically determine whether the use of MER translates into drops in levodopa requirements and improvements in UPDRS scores, a randomized controlled study would be helpful to refine the best techniques for optimal electrode placement and assess the impact on the long-term clinical response.

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