Brain Stimulation 12 (2019) 893–900

Contents lists available at ScienceDirect

Brain Stimulation

journal homepage: http://www.journals.elsevier.com/brain-stimulation

Is awake physiological confirmation necessary for DBS treatment of Parkinson's disease today? A comparison of intraoperative imaging, physiology, and physiology imaging-guided DBS in the past decade

Zixiao Yin [a, c, 1], Yunyun Luo [a, c, 1], Yanwen Jin [a, d, 1], Yaqing Yu [b], Suyue Zheng [a], Jian Duan [a], Renxu Xu [b], Dongwei Zhou [a], Tao Hong [a], Guohui Lu [a, *]

[a] Department of Neurosurgery, The First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, PR China
[b] Department of Neurology, The First Affiliated Hospital of Nanchang University, Nanchang, Jiangxi, PR China
[c] The First Clinical Medical College of Nanchang University, Nanchang, Jiangxi, PR China
[d] The Second Clinical Medical College of Nanchang University, Nanchang, Jiangxi, PR China

ARTICLE INFO

Article history:
Received 3 November 2018
Received in revised form
4 March 2019
Accepted 5 March 2019
Available online 7 March 2019

Keywords:
Deep brain stimulation
Parkinson's disease
Intraoperative imaging
Microelectrode recording
Meta-Analysis

ABSTRACT

Background: Deep brain stimulation (DBS) is a well-established surgical therapy for Parkinson's disease (PD). Intraoperative imaging (IMG), intraoperative physiology (PHY) and their combination (COMB) are the three mainstream DBS guidance methods.
Objective: To comprehensively compare the use of IMG-DBS, PHY-DBS and COMB-DBS in treating PD.
Methods: PubMed, Embase, the Cochrane Library and OpenGrey were searched to identify PD-DBS studies reporting guidance techniques published between January 1, 2010, and May 1, 2018. We quantitatively compared the therapeutic effects, surgical time, target error and complication risk and qualitatively compared the patient experience, cost and technical prospects. A meta-regression analysis was also performed. This study is registered with PROSPERO, number CRD42018105995.
Results: Fifty-nine cohorts were included in the main analysis. The three groups were equivalent in therapeutic effects and infection risks. IMG-DBS ($p < 0.001$) and COMB-DBS ($p < 0.001$) had a smaller target error than PHY-DBS. IMG-DBS had a shorter surgical time ($p < 0.001$ and $p = 0.008$, respectively) and a lower intracerebral hemorrhage (ICH) risk ($p = 0.013$ and $p = 0.004$, respectively) than PHY- and COMB-DBS. The use of intraoperative imaging and microelectrode recording correlated with a higher surgical accuracy ($p = 0.018$) and a higher risk of ICH ($p = 0.049$).
Conclusions: The comparison of COMB-DBS and PHY-DBS showed intraoperative imaging's superiority (higher surgical accuracy), while the comparison of COMB-DBS and IMG-DBS showed physiological confirmation's inferiority (longer surgical time and higher ICH risk). Combined with previous evidence, the use of intraoperative neuroimaging techniques should become a future trend.

Introduction

Deep brain stimulation (DBS) is a well-established surgical therapy for Parkinson's disease (PD) [1,2]. Accurate electrode implantation is essential [3]. During the early stage, physiological (PHY) confirmation, namely, microelectrode recording (MER) and test stimulation, was routinely performed in almost all centers because it was considered very helpful in delineating the subthalamic nucleus (STN) boundaries and assessing the surgical effects [4,5]. Currently, most centers continue to employ this guidance technique in DBS surgery. However, awake PHY-guided surgery has some drawbacks, including patient discomfort and a possible higher

Abbreviations: DBS, Deep brain stimulation; PD, Parkinson's disease; MER, Microelectrode recording; STN, Subthalamic nucleus; PHY, Physiology; IMG, Imaging; COMB, Combination; ICH, Intracerebral hemorrhage; MRI, Magnetic resonance imaging; CT, Computed tomography; UPDRS, Unified Parkinson's Disease Rating Scale; LEDD, Levodopa equivalent dose; QOL, Quality of life; MOOSE, Meta-analysis of observational studies in epidemiology; ANOVA, Analysis of variance.

* Corresponding author. Department of Neurosurgery, The First Affiliated Hospital of Nanchang University, 17 Yong Wai Zheng Street, East Lake District, 330006, Nanchang, Jiangxi, PR China.
E-mail address: guohui-lu@163.com (G. Lu).
[1] Equally contributing author.

https://doi.org/10.1016/j.brs.2019.03.006
1935-861X/

intracerebral hemorrhage (ICH) risk [6,7]. In addition, as neuroimaging techniques have advanced remarkably over the past decade, the high-resolution visualization of neuroanatomy seems to provide an alternative to awake functional mapping [8]. Thus, several pioneering centers have started to use intraoperative magnetic resonance imaging (MRI)/computed tomography (CT) without physiological confirmation to guide lead implantation under general anesthesia [9,10]. Patients receiving intraoperative imaging (IMG)-guided DBS have also exhibited significant symptom improvement. In addition to PHY- and IMG-DBS, the surgical method of combining both guidance techniques is also very common in several centers [11,12]. Similar to pure PHY-DBS, psychology-imaging (COMB)-guided DBS is also conducted under local anesthesia. The difference is that further intraoperative imaging verification is performed after lead implantation before the pulse generator is implanted.

Some problems have hindered the comparison of the three DBS methods of PHY, IMG and COMB. First, to the best of our knowledge, most studies investigating IMG-DBS have used one-arm designs. Thus, to compare the effects of IMG- and PHY-DBS, the authors of these studies can compare their results only with data from the literature or the outcomes of their previous patients [13], which undoubtedly introduces bias. Second, two-arm studies, or control studies, are not only few in number but also retrospective in design. In addition, due to the small sample size in these studies, comparing the risk of important but rare complications, such as ICH and infection, is challenging. Third, comparative studies investigating COMB-DBS are scarce in the literature. Whether a combination of two guidance techniques could cause a change in DBS outcomes remains unknown.

Intraoperative imaging has been successfully employed in DBS surgery for the treatment of PD for approximately ten years. Given that IMG-DBS can be conducted in patients while asleep, some scholars [14,15] have started to doubt the necessity of awake physiological confirmation. Thus, to synthesize the direct and indirect evidence obtained over the past decade, we conducted this meta-analysis and systematic review to thoroughly compare the three DBS methods of IMG, PHY, and COMB.

Methods

Search strategy

A comprehensive literature search for relevant original English-language human research articles was conducted by two reviewers (YZX and LYY). The databases included PubMed, Embase, Cochrane Central Register of Controlled Trials, Cochrane Movement Disorders Group Trials Register, the System for Information on Grey Literature in Europe (OpenGrey) and ClinicalTrials.gov. To the best of our knowledge, the first study reporting the use of IMG-DBS for the treatment of PD was submitted in 2008 and published in 2010 [9]. Thus, we limited the search time window to between January 1, 2010, and May 1, 2018, to ensure that the studies included in the three groups were published during the same period. Standard searches were performed with the following key words: “Parkinson's disease”, “deep brain stimulation”, “bilateral/unilateral”, “MRI/CT”, and “MER”. The titles, abstracts and references of all identified reports were independently examined by two reviewers. If any disagreements occurred, in-depth discussions were required before reaching a consensus. Disagreements that could not be resolved were ultimately decided by the senior author (LGH).

Inclusion and exclusion criteria

All included studies had to clearly describe the surgical procedure and guidance method. For the different groups, (1) PHY-DBS was performed under local anesthesia. MER and stimulation tests were the only intraoperative guidance techniques used in this group. Studies using MER but not stimulation tests were thus excluded, and (2) COMB-DBS was also performed under local anesthesia. However, an additional intraoperative neuroimaging verification technique (MRI/CT/fluoroscopy) was performed after MER and the stimulation test before the pulse generator implantation, and (3) IMG-DBS was conducted under general anesthesia. Implantation was guided by intraoperative imaging techniques, including intraoperative CT, intraoperative MRI or interventional MRI. Preoperative imaging was not considered in the grouping.

Controlled studies that included cohorts using different guidance methods were regarded as studies containing separate cohorts. For example, if a study included two cohorts to compare PHY-DBS and IMG-DBS, each PHY and IMG group was added as one cohort to our study.

Studies were excluded if they (1) did not report the detailed surgical procedure; (2) used guidance techniques other than intraoperative imaging or MER and stimulation tests; (3) did not report the anesthesia method (general or local); (4) did not report the laterality (bilateral or unilateral) or the number of leads inserted; and (5) had a patient cohort size less than six. Given that most IMG studies reported only short-term outcomes, to ensure that the follow-up time was comparable, (6) studies with long-term follow-up (longer than 12 months) were excluded. In addition, (7) abstract-only articles, conference articles, editorials, expert opinions, republished articles, non-English-language articles and articles without complete data were also excluded from our analysis.

Definitions and data extraction

After the eligible articles were searched and reviewed, the data were extracted using a customized data extraction table. This process was also conducted independently by two reviewers. The cohort characteristic data included the patient number, lead number, patient age, disease duration, follow-up time, preoperative Unified Parkinson's Disease Rating Scale (UPDRS)-III scores (both on and off states), preoperative levodopa equivalent dose (LEDD), anesthesia method and guidance method. The outcome data included the percentage change in UPDRS-III, LEDD and quality of life (QOL), risk of ICH and infection, radial error and operative time. For the continuous outcomes, the mean values, standard deviations and number of observations were collected. For the dichotomous outcomes, the event numbers and number of observations were collected. Specifically, the QOL was evaluated through the UPDRS-II, Parkinson's Disease Questionnaire-39 and Schwab and England Activities of Daily Living, all of which are scales that are commonly used to measure quality of life [13,16,17]. ICH and infection were analyzed because they were the most frequently reported surgery-related complications and are of great concern to neurosurgeons [18,19]. Given that different centers may have different ways of measuring surgical accuracy, namely, radial error, scalar error, and vector error, we extracted the radial error whenever possible because this error was the most frequently reported error [20,21]. The radial error was defined as the 2D vector difference between the intended and actual lead placement measured in the axial plane used for the anatomical targeting [22]. The operative time was defined as the time from skin incision to skin closure [10].

Quality assessment

We performed a quality assessment of the included studies using the Meta-analysis Of Observational Studies in Epidemiology (MOOSE) tool for observation studies [23,24]. Each of the following criteria was given a score of one point, for a maximum score of six

points: (I) clear definition of the study population and a sufficient patient number ($n > 10$); (II) clear definition of outcomes and outcome assessment; (III) independent assessment of outcome parameters; (IV) clear description of follow-up; (V) no selective loss during follow-up (<10%); and (VI) identification of important confounders and prognostic factors. A study with a score ≥ 5 was considered methodologically sound. Only these studies were included in the main analysis. We included the methodologically unsatisfactory studies in the sensitivity analysis. This strategy can prevent the main analysis from being affected by small-sample and unclear studies while fully using all data in the sensitivity analysis.

Meta-regression and sensitivity analysis

We performed a regression analysis to identify the possible predictors of surgical accuracy and complication risk, including age, disease duration, preoperative UPDRS-III scores, surgery time, use of intraoperative imaging and use of intraoperative MER. We also investigated the correlation between the surgical accuracy and motor symptom improvement. A sensitivity analysis was performed by considering all studies, including studies with less clear methodologies (score ≤ 4 in the quality assessment).

Statistical analysis

Heterogeneity was assessed using the Standard Cochrane Q and I^2 statistics. If $p < 0.10$ or $I^2 \geq 50\%$, a random effect analysis model using generic-inverse variance was employed to pool the data. Otherwise, a fixed effects model was used. The pooled data are presented as the means ± standard error. To detect any differences in the baseline characteristics between the three groups, an analysis of variance (ANOVA) was conducted. A $p < 0.05$ indicated the need to perform pairwise comparisons of the pooled data. To analyze the main outcomes, including the therapeutic effects, surgical time, surgical accuracy and complication risks, pairwise comparisons of the three groups were performed directly. The p-values were determined based on Student's t-tests using a Bonferroni multiple comparisons correction [25]; $p < 0.0167$ (0.05/3) was considered statistically significant. A simple linear meta-regression was performed as the study variance was estimated by an unrestricted maximum likelihood model, and $p < 0.05$ indicated a significant correlation. All analyses were performed using Comprehensive Meta-Analysis 2.2 (Biostat, Englewood, NJ). The data management complied with the guidelines of the Cochrane Handbook for Systematic Reviews of Interventions and the Meta-analysis of Observational Studies in Epidemiology Group [24,26]. This study is registered with PROSPERO under number CRD42018105995.

Results

Search results

In total, we identified 3382 articles according to the keyword search. After removing duplicated articles and screening the titles and abstracts, 2814 articles were eliminated. The main reasons for elimination were that the studies were not related to PD, non-clinic-based studies, and articles reporting low-quality evidence (abstract-only articles, conference articles, editorials, and expert opinions). The remaining 568 articles were subjected to a secondary full-text screening based on the inclusion and exclusion criteria. We also screened the references of these articles. Finally, 70 studies from 51 centers met all the criteria and were included in the subsequent quality assessment. The specific filtering process is described in Fig. 1.

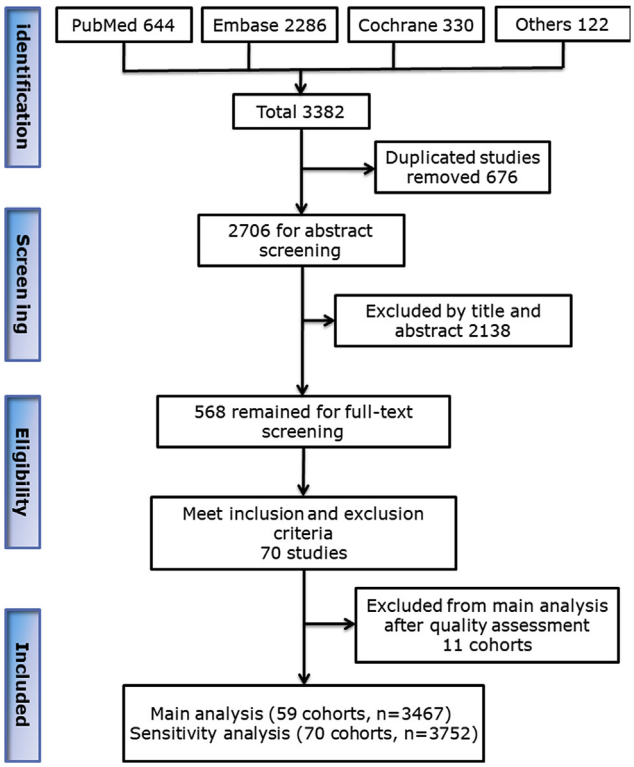

Fig. 1. PRISMA flow chart of the included studies.

Quality assessment of the studies eligible for the main analysis

According to the MOOSE quality assessment tool, 33.3% of the IMG studies lost points for failing to identify important confounders or prognostic factors, 23.1% of the PHY studies did not independently assess the outcome parameters and 25% of the COMB studies did not fully describe their follow-up (Supplementary Table 1). Thus, 11 of the 70 cohorts, including 285 patients and 535 leads, were considered methodologically less clear. Thus, these cohorts (2 in the IMG group, 6 in the PHY group and 3 in the COMB group) were excluded from the main analysis. The detailed information of all 70 cohorts is shown in Supplementary Table 2.

Of the remaining 59 cohorts ($n = 3467$, leads $= 6371$), 13 cohorts ($n = 424$, leads $= 819$) underwent IMG-guided DBS, 33 cohorts ($n = 2510$, leads $= 4543$) underwent PHY-guided DBS, and 13 cohorts ($n = 533$, leads $= 1009$) underwent COMB-guided DBS.

Baseline characteristics and treatment efficacy

The baseline characteristics did not significantly differ in terms of age, disease duration, length of follow-up, preoperative UPDRS "On" scores or LEDD between the three groups. However, the preoperative UPDRS "Off" scores in the COMB group were lower than those in the IMG group (Table 1).

DBS therapeutic effects and surgery-related outcomes

The three groups were equivalent in motor symptom improvement, LEDD decrease and QOL enhancement (Table 2). Notably, only the outcomes of STN-DBS were included in the LEDD synthesis because DBS targeting other nuclei, such as the globus pallidus interna, may not result in the same level of LEDD decrease as STN-DBS.

Table 1
Pooled value of patient characteristics[a].

	IMG-DBS	PHY-DBS	COMB-DBS	ANOVA (p value)
Age	62.4 ± 0.93 (412)	60.1 ± 0.60 (2282)	60.9 ± 1.18 (290)	0.267
Disease duration (years)	11.1 ± 0.38 (122)	12.1 ± 0.75 (1480)	11.5 ± 0.78 (268)	0.879
Length of follow-up (months)	8.35 ± 0.98 (404)	8.62 ± 0.59 (2042)	8.69 ± 0.91 (533)	0.976
Pre-operative UPDRS-III ON med	20.6 ± 1.29 (111)	19.3 ± 2.01 (546)	18.2 ± 1.62 (140)	0.895
Pre-operative UPDRS-III OFF med	45.4 ± 1.39 (249)	42.9 ± 1.78 (669)	37.8 ± 1.56 (341)	**0.039**[b]
LEDD	1173.5 ± 88.9 (142)	1177.1 ± 86.8 (869)	988.3 ± 116.0 (307)	0.462

ANOVA: analysis of variance; UPDRS: Unified Parkinson's Disease Rating Scale; LEDD: Levodopa equivalent doses.
[a] The data are represented by "mean ± standard error (observation numbers)" and the significant comparisons are highlighted.
[b] p-value of pairwise comparison of "Pre-operative UPDRS-III OFF med": IMG vs PHY = 0.268; **IMG vs COMB < 0.001**; PHY vs COMB = 0.031.

The IMG group had a significantly shorter operative time than the PHY and COMB groups, while no differences were observed between the PHY and COMB groups. The target error in the PHY group was significantly larger than that in the IMG and COMB groups, while there were no differences between the IMG and COMB groups. IMG-DBS had the lowest ICH risk among the three groups. The ICH risk with PHY-DBS was slightly lower than that with COMB-DBS, but the difference did not reach statistical significance. No differences were found in the infection risk.

Meta-regression analysis

The simple linear meta-regression analysis revealed that age (p = 0.376), disease duration (p = 0.741) and preoperative UPDRS-III (Off) scores (p = 0.362) were not significant predictors of surgical accuracy, while the use of intraoperative imaging was a significant predictor (Fig. 2A). The correlation between the percentage change in the UPDRS-III (Off) score and radial target error was not significant (Fig. 2B). Age (p = 0.526), disease duration (p = 0.723), and operative time (p = 0.930) were not significant predictors of the ICH risk. The use of MER was a significant predictor (Fig. 2C–1).

Sensitivity analysis

We added the 11 excluded cohorts and re-pooled the data from all 70 cohorts. Although the statistical values changed (Table 2), the significance of the data did not change in most outcomes with one exception. The correlation between the use of MER and the risk of ICH became non-significant in the sensitivity analysis (Fig. 2C–).

Discussion

By analyzing data from many samples from multiple centers, our study compared the three mainstream DBS methods of IMG, PHY, and COMB for the treatment of PD over the past 10 years. There were no differences in the therapeutic effects and risk of infection between the three groups. The target errors in the IMG and COMB groups were significantly smaller than those in the PHY group. The

Table 2
Pooled value of DBS therapeutic effects and surgery-related outcomes in the main and sensitivity analysis[a].

	IMG-DBS	PHY-DBS	COMB-DBS	IMG vs PHY	IMG vs COMB	PHY vs COMB
Main analysis						
Post UPDRS "On[b]"	17.5 ± 5.00 (41)	14.8 ± 1.59 (341)	12.9 ± 1.73 (103)	0.582	0.385	0.533
Post UPDRS "Off[c]"	23.4 ± 2.74 (208)	20.4 ± 1.30 (369)	18.9 ± 1.60 (301)	0.323	0.156	0.462
Post LEDD (mg/d)	526.7 ± 121.6 (82)	607.2 ± 97.6 (483)	498.7 ± 46.5 (233)	0.606	0.830	0.316
PI UPDRS "On"	16.8 ± 7.33 (62)	28.3 ± 10.5 (389)	25.6 ± 3.43 (103)	0.369	0.277	0.807
PI UPDRS "Off"	47.2 ± 4.54 (228)	49.2 ± 8.49 (1122)	52.4 ± 2.43 (323)	0.835	0.313	0.717
PI LEDD	47.3 ± 4.39 (139)	48.9 ± 1.63 (720)	54.9 ± 2.90 (233)	0.733	0.149	0.070
PI QOL	32.6 ± 6.54 (187)	43.1 ± 5.38 (226)	40.7 ± 7.53 (83)	0.211	0.417	0.810
Surgical time (mins)	232.1 ± 17.9 (258)	361.4 ± 31.7 (278)	347.1 ± 42.9 (57)	**<0.001**	**0.008**	0.789
Target error (mm)	0.902 ± 0.094 (350)	1.297 ± 0.043 (663)	0.674 ± 0.081 (106)	**<0.001**	0.066	**<0.001**
ICH (%)	1.3 ± 0.4 (524)	2.7 ± 0.4 (2905)	3.9 ± 0.8 (406)	**0.013**	**0.004**	0.179
Infection (%)	2.6 ± 0.5 (796)	1.9 ± 0.4 (2503)	2.2 ± 0.6 (236)	0.274	0.608	0.677
Sensitivity analysis						
Post UPDRS "On"	17.5 ± 5.00 (41)	14.8 ± 1.59 (341)	14.3 ± 1.46 (128)	0.582	0.539	0.817
Post UPDRS "Off"	23.4 ± 2.74 (208)	22.9 ± 1.51 (341)	19.7 ± 1.71 (344)	0.873	0.252	0.161
Post LEDD (mg/d)	526.7 ± 121.6 (82)	607.2 ± 97.6 (483)	552.1 ± 57.8 (258)	0.606	0.850	0.627
PI UPDRS "On"	16.8 ± 7.33 (62)	28.3 ± 10.5 (389)	24.5 ± 2.23 (128)	0.369	0.315	0.723
PI UPDRS "Off"	47.2 ± 4.54 (228)	47.4 ± 7.48 (1189)	51.9 ± 2.27 (366)	0.982	0.355	0.565
PI LEDD	47.3 ± 4.39 (139)	49.0 ± 1.58 (732)	54.9 ± 2.90 (233)	0.716	0.149	0.285
PI QOL	32.6 ± 6.54 (187)	41.9 ± 4.70 (256)	40.7 ± 7.53 (83)	0.249	0.417	0.897
Surgical time (mins)	232.1 ± 17.9 (258)	361.2 ± 27.8 (310)	347.1 ± 42.9 (57)	**<0.001**	**0.008**	0.783
Target error (mm)	0.860 ± 0.091 (380)	1.297 ± 0.043 (663)	0.711 ± 0.077 (168)	**<0.001**	0.211	**<0.001**
ICH (%)	1.7 ± 0.4 (580)	3.4 ± 0.2 (3104)	3.9 ± 0.8 (406)	**<0.001**	**0.014**	0.544
Infection (%)	2.5 ± 0.5 (852)	3.0 ± 0.3 (2702)	2.2 ± 0.6 (236)	0.391	0.701	0.233

DBS: deep brain stimulation; Post: postoperative scores; PI: percentage improvement postoperatively; UPDRS: Unified Parkinson's Disease Rating Scale; LEDD: Levodopa equivalent doses; QOL: quality of life; ICH: intracerebral hemorrhage.
[a] The data are represented by "mean ± standard error (observation numbers)". The outcomes of pairwise comparison are demonstrated by p value and the significant comparisons are highlighted.
[b] "On" indicates DBS on and medication on.
[c] "Off" indicates DBS on and medication off.

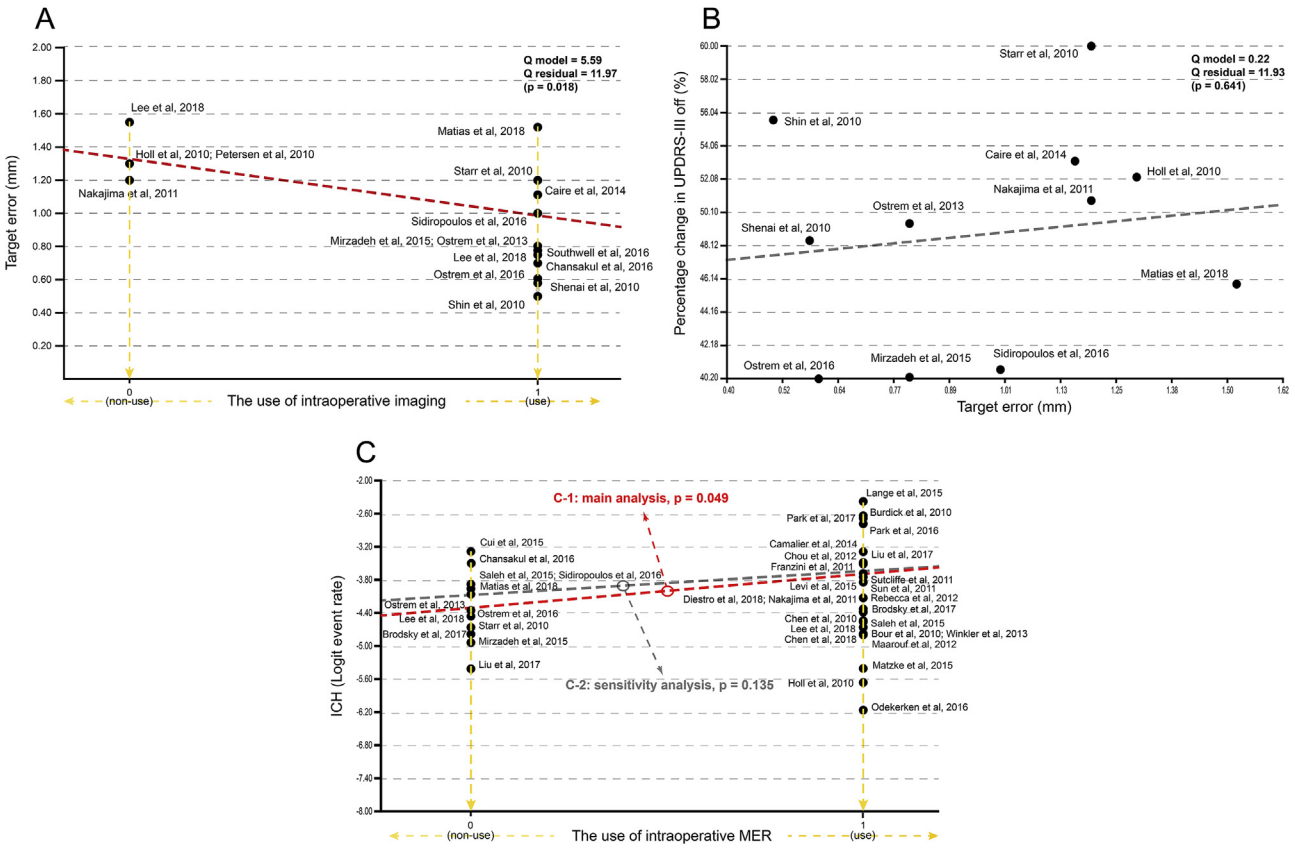

Fig. 2. Simple linear meta-regression of the target error and motor symptom improvement. **A:** Correlation between the use of intraoperative imaging and the target error. **B:** Correlation between the target error and percentage change in UPDRS-III (off). **C-1:** Correlation between MER and ICH risk in the main analysis. **C-2:** Correlation between MER and ICH risk in the sensitivity analysis.

IMG group had a shorter operative time and a lower risk of ICH than the PHY and COMB groups.

Target error, therapeutic effects and stimulation-related side effects

Our results of the DBS efficacy as assessed by UPDRS-III improvement, LEDD decrease and QOL enhancement were consistent with most previous studies and suggested that PHY-DBS and IMG-DBS were equally effective in alleviating patients' motor symptoms [27,28]. In addition, the combination of the two guidance techniques did not result in a gain of additional efficacy. Notably, of all 13 COMB-DBS studies included, 12 were conducted in Asian and European countries. Based on the finding that the preoperative UPDRS-III Off score was significantly lower in the COMB group, we assumed that neurologists in Asia and Europe may be more cautious and more willing to suggest that PD patients should receive DBS surgery at an early stage.

Previous studies have provided different opinions regarding the use of MER [29,30]. As reported by the most recent study, compared with preoperative imaging alone, MER can reduce the dislocation rate by 20% [31]. However, some studies have also found that the number of MER penetrations is positively correlated with intracranial air, brain shift and ICH [32–34], all of which are factors that can negatively influence target accuracy in DBS surgery [35,36]. Our study observed a higher target error in the PHY group. Although MER was also employed in the COMB group, the further neuroimaging verification enhanced the surgical accuracy to the same level as that observed in the IMG group. In summary, we hypothesize that MER can undoubtedly improve target accuracy; however, compared with intraoperative imaging, MER may be inferior.

Accuracy, as a consensus, is essential for DBS surgery. However, the significantly higher target error did not translate into a lower treatment efficacy in our study. Lee et al. [37] also observed this phenomenon and explained that a small error is unlikely to manifest in global outcome indices. We hypothesize that postoperative programming may play an important role. The adjustment of the stimulation parameters can be a buffer zone for DBS efficacy. By increasing or decreasing the stimulation voltage, DBS efficacy can maintain stability [31]. Thus, how large must a target error be to influence the treatment effects? Richardson et al. [38] analyzed 8 patients who underwent lead revision and found that at least a 2-mm change in the lead position was needed to produce significant changes in the therapeutic effects. These authors also found a significantly negative correlation between the target error and UPDRS-III improvement within the error limits of 2–5 mm. Our study filled vacancies for a target error of 0–2 mm, which is indeed a more common error range [39]. The results of our meta-regression analysis showed that based on existing evidence, a target error of less than 1.55 mm may not influence motor symptom improvement. Thus, a lead position revision of < 1.55 mm may not result in improved motor function compared with that before the revision. In addition to postoperative programming, the fact that the lead could slide back to its original trajectory may also be an explanation.

Although a target error of 0–1.55 mm may not influence motor symptom improvement, it could possibly induce significant non-motor symptoms or stimulation-related complications. Lee et al. [37] found that PHY-DBS resulted in a lower side effect programming threshold than IMG-DBS, suggesting that stimulation-related complications could start to appear at a much lower voltage in

patients who underwent PHY-DBS. In addition, Brodsky et al. [40] reported that PHY-DBS patients had much worse speech function than IMG-DBS patients postoperatively, which may be due to the subclinical direct pyramidal tract activation owing to spread current [41]. Shamir et al. [42] also found that stimulation of a different subregion of the STN could induce significantly different nonmotor outcomes. These studies show that, considering nonmotor symptoms or stimulation-related side effects, small target errors should not be ignored.

Hardware-related side effects

The pooled risk of ICH in our study was 3.3 ± 0.3%, which is close to the results reported in the previous meta-analysis (3.2–5%) [43–45]. A significant correlation was observed between MER and the ICH risk in the main analysis, but this correlation disappeared in the sensitivity analysis, indicating that this correlation is not very stable. However, most authors agree that the use of MER could be potentially risky. In their study, Kimmelman et al. [32] found that the per-trajectory of MER could increase the ICH risk by 1.57% because each penetration of MER carries a certain degree of risk of breaking an artery. In addition, the sharp tip used in MER is more likely to penetrate small arteries than a blunt-tipped permanent electrode [46]. As hypertension is also considered a high risk factor for ICH [47], the general anesthesia employed in the IMG group could better control intraoperative blood pressure. This finding may also contribute to the lower ICH risk in the IMG group in our study.

Although some authors have reported that the operative time may influence the postoperative infection rate [48], no correlation was observed between the operative time and infection risk in our study. Kim et al. [48] hypothesized that prophylactic and perioperative use of antibiotics may play an important role in reducing the infection risk. The duration of the prophylactic use of intravenous antibiotics in patients with infection was 3.7 days, while in those without infection, the duration was 6.4 days. Properly prolonging the time of antibiotic use after DBS surgery may reduce the infection risk.

Operative time and patient experience

As previously reported by Saley et al. [28] in 2015, the operative time in the IMG group was longer than that in the PHY group. However, in 2018, Jakobs et al. [34] reported that 8 years of experience with IMG-DBS surgery could significantly shorten the operative time by over 2 h. In our study, the IMG group had a shorter surgical time than the PHY and COMB groups, indicating that the abandonment of MER and stimulation tests may save time [49,50]. As previously reported [51], it takes approximately only 20 min to achieve an intraoperative imaging confirmation with an O-arm. Asleep surgery with a shorter operative time can undoubtedly decrease patient discomfort during DBS surgery. LaHue et al. [52] analyzed the intraoperative experiences of 88 patients who underwent IMG- or PHY-DBS through customized questionnaires. These authors found that patients were more willing to choose asleep surgery and were less likely to feel regret after choosing IMG-DBS. IMG-DBS was also recommended for patients with a history of claustrophobia, chronic pain and significant off-medication symptoms [52].

Historically, the influence of general anesthesia on MER electrophysiological signals and stimulation tests hindered attempts of performing asleep DBS surgery [53]. However, in recent years, many studies have proven that general anesthesia, with great control of the depth of anesthesia, does not hamper the adequate performance of MER [54,55]. Thus, why do most centers still perform awake DBS surgery? We assume that the key factor is the stimulation test, the function of which is to facilitate determination of the optimal stimulation site and determination of a high threshold for side effects. However, in 2017, Blume et al. [56] found that the real effects of permanent stimulation are not predictable by the intraoperative test stimulation. These studies question the necessity of awake DBS surgery. In 2017, Ho et al. [57] also argued that asleep DBS surgery may lead to fewer treatment-induced side effects than awake surgery and can produce equal therapeutic effects.

Technical prospects

The high purchase cost of intraoperative imaging equipment was usually considered the major factor restricting the popularization of this technique [7]. However, the shorter operative time and larger patient population suitable for IMG-DBS may be translated into higher hospital efficiency. Furthermore, the cost for patients who underwent IMG-DBS did not seem to increase much. As reported by Brodsky et al. [40] in 2018, the patient cost for IMG-DBS was even lower than that for PHY-DBS in their center. Concerning the technological prospects of the two guidance techniques, in 2018, Shamir et al. [58] developed a neuroimaging method combining 7-T MRI with machine learning, which can accurately visualize the STN using standard clinical MRI. Regarding MER, a software package for automatically estimating the border of the STN was also developed in 2018 [59]. Undoubtedly, both techniques are progressing. However, we believe that IMG-DBS is an emerging technique that may have more room for progress. In addition, as more tools and algorithms are established to optimize DBS imaging [60,61], the specific functions of the subregions of the nucleus are becoming clearer [62,63]. With a better understanding of these subregions, a personalized targeting plan may well address individual patients' main symptoms in the near future. Intraoperative neuroimaging, which has a higher surgical accuracy, may perform better in helping reach the planned target.

Limitations

There were several limitations in our study.

First, given that no studies performed direct comparisons of these three guidance techniques, most data were collected from nonrandom and noncontrolled studies. This design had advantages and disadvantages. The disadvantage was that the heterogeneity resulting from differences in surgical instruments, imaging modalities and operation habits was difficult to control, introducing biases and reducing the level of evidence. The benefits were that we included a large sample size of patients and collected data from multiple centers. The large sample size increased the statistical power and the applicability of our results. Actually, one-arm studies can also provide valuable clinical information in a meta-analysis if the results are interpreted cautiously [64,65].

Second, the number of included outcome indices was not sufficient. Data for only two types of complications were extracted, and nonmotor symptoms were not included in the quantitative analysis. In fact, inaccurate electrode implantation was more likely to cause adverse nonmotor effects due to the spread of electrical currents [66]. Therefore, including nonmotor symptoms as evaluation indicators in future clinical trials is important.

Finally, the follow-up duration (average of 8.5 months) of the included studies was short. Consequently, the long-term effects and mortality data could not be considered or compared.

Conclusions

Considering COMB-DBS as a bridge in the comparison of the three groups, the comparison of COMB-DBS and PHY-DBS showed the superiority of intraoperative imaging (higher surgical accuracy), while the comparison of COMB-DBS and IMG-DBS showed the inferiority of physiological confirmation (longer surgical time and higher ICH risk). Combined with previous evidence, this study revealed that PHY-DBS was no better or worse than IMG-DBS in surgical accuracy, UPDRS-III improvement, LEDD decrease, QOL enhancement, stimulation-related complications (e.g., speech disorders), hardware-related complications (e.g., ICH and infection), operative time, patient experience and individual technique prospects. Thus, we believe that awake physiological confirmation may no longer be a necessity in current DBS treatment for PD and that the use of intraoperative imaging for DBS guidance should be a future trend.

Declarations of interest

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Funding

This work was supported by the National Natural Science Foundation of China (CN) (81560220), Youth Science Fund of Jiangxi Province (20151BAB215014) and the Key project of Jiangxi Youth Science Foundation (20171ACB21054).

Acknowledgements

None.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2019.03.006.

References

[1] Liu Y, Li W, Tan C, Liu X, Wang X, Gui Y, et al. Meta-analysis comparing deep brain stimulation of the globus pallidus and subthalamic nucleus to treat advanced Parkinson disease. J Neurosurg 2014;121:709–18. https://doi.org/10.3171/2014.4.jns131711.

[2] Deuschl G, Schade-Brittinger C, Krack P, Volkmann J, Schafer H, Botzel K, et al. A randomized trial of deep-brain stimulation for Parkinson's disease. N Engl J Med 2006;355:896–908. https://doi.org/10.1056/NEJMoa060281.

[3] Chandran AS, Bynevelt M, Lind CR. Magnetic resonance imaging of the subthalamic nucleus for deep brain stimulation. J Neurosurg 2016;124:96–105. https://doi.org/10.3171/2015.1.jns142066.

[4] Zaidel A, Spivak A, Shpigelman L, Bergman H, Israel Z. Delimiting subterritories of the human subthalamic nucleus by means of microelectrode recordings and a Hidden Markov Model. Mov Disord 2009;24:1785–93. https://doi.org/10.1002/mds.22674.

[5] Deffains M, Holland P, Moshel S, Ramirez de Noriega F, Bergman H, Israel Z. Higher neuronal discharge rate in the motor area of the subthalamic nucleus of Parkinsonian patients. J Neurophysiol 2014;112:1409–20. https://doi.org/10.1152/jn.00170.2014.

[6] Chang WS, Kim HY, Kim JP, Park YS, Chung SS, Chang JW. Bilateral subthalamic deep brain stimulation using single track microelectrode recording. Acta Neurochir Wien 2011;153:1087–95. https://doi.org/10.1007/s00701-011-0953-1.

[7] Azmi H, Gupta F, Vukic M, Kreitner J, Kera E, Nicola G, et al. Interventional magnetic resonance imaging-guided subthalamic nucleus deep brain stimulation for Parkinson's disease: patient selection. Surg Neurol Int 2016;7:S557–63. https://doi.org/10.4103/2152-7806.187537.

[8] Boone CE, Wojtasiewicz T, Moukheiber E, Butala A, Jordao L, Mills KA, et al. MR-guided functional neurosurgery: laser ablation and deep brain stimulation. Top Magn Reson Imag 2018;27:171–7. https://doi.org/10.1097/rmr.0000000000000152.

[9] Starr PA, Martin AJ, Ostrem JL, Talke P, Levesque N, Larson PS. Subthalamic nucleus deep brain stimulator placement using high-field interventional magnetic resonance imaging and a skull-mounted aiming device: technique and application accuracy. J Neurosurg 2010;112:479–90. https://doi.org/10.3171/2009.6.jns081161.

[10] Martin AJ, Larson PS, Ziman N, Levesque N, Volz M, Ostrem JL, et al. Deep brain stimulator implantation in a diagnostic MRI suite: infection history over a 10-year period. J Neurosurg 2017;126:108–13. https://doi.org/10.3171/2015.7.jns15750.

[11] Maier F, Lewis CJ, Horstkoetter N, Eggers C, Kalbe E, Maarouf M, et al. Patients' expectations of deep brain stimulation, and subjective perceived outcome related to clinical measures in Parkinson's disease: a mixed-method approach. J Neurol Neurosurg Psychiatry 2013;84:1273–81. https://doi.org/10.1136/jnnp-2012-303670.

[12] Fonoff ET, Azevedo A, Angelos JS, Martinez RC, Navarro J, Reis PR, et al. Simultaneous bilateral stereotactic procedure for deep brain stimulation implants: a significant step for reducing operation time. J Neurosurg 2016;125:85–9. https://doi.org/10.3171/2015.7.jns151026.

[13] Ostrem JL, Ziman N, Galifianakis NB, Starr PA, Luciano MS, Katz M, et al. Clinical outcomes using ClearPoint interventional MRI for deep brain stimulation lead placement in Parkinson's disease. J Neurosurg 2016;124:908–16. https://doi.org/10.3171/2015.4.jns15173.

[14] Burchiel KJ, McCartney S, Lee A, Raslan AM. Accuracy of deep brain stimulation electrode placement using intraoperative computed tomography without microelectrode recording. J Neurosurg 2013;119:301–6. https://doi.org/10.3171/2013.4.jns122324.

[15] Aviles-Olmos I, Kefalopoulou Z, Tripoliti E, Candelario J, Akram H, Martinez-Torres I, et al. Long-term outcome of subthalamic nucleus deep brain stimulation for Parkinson's disease using an MRI-guided and MRI-verified approach. J Neurol Neurosurg Psychiatry 2014;85:1419–25. https://doi.org/10.1136/jnnp-2013-306907.

[16] Chen T, Mirzadeh Z, Chapple KM, Lambert M, Shill HA, Moguel-Cobos G, et al. Clinical outcomes following awake and asleep deep brain stimulation for Parkinson disease. J Neurosurg 2018:1–12. https://doi.org/10.3171/2017.8.jns17883.

[17] Hu X, Jiang X, Zhou X, Liang J, Wang L, Cao Y, et al. Avoidance and management of surgical and hardware-related complications of deep brain stimulation. Stereotact Funct Neurosurg 2010;88:296–303. https://doi.org/10.1159/000316762.

[18] Franzini A, Cordella R, Messina G, Marras CE, Romito LM, Carella F, et al. Deep brain stimulation for movement disorders. Considerations on 276 consecutive patients. J Neural Transm Vienna 2011;118:1497–510. https://doi.org/10.1007/s00702-011-0656-z.

[19] Park CK, Jung NY, Kim M, Chang JW. Analysis of delayed intracerebral hemorrhage associated with deep brain stimulation surgery. World Neurosurg 2017;104:537–44. https://doi.org/10.1016/j.wneu.2017.05.075.

[20] Chansakul T, Chen Jr PN, Lee TC, Tierney T. Interventional MR imaging for deep-brain stimulation electrode placement. Radiology 2016;281:940–6. https://doi.org/10.1148/radiol.2015151136.

[21] Kochanski RB, Kerolus MG, Pal G, Metman LV, Sani S. Use of intraoperative CT to predict the accuracy of microelectrode recording during deep brain stimulation surgery. A proof of concept study. Clin Neurol Neurosurg 2016;150:164–8. https://doi.org/10.1016/j.clineuro.2016.09.014.

[22] Starr PA, Markun LC, Larson PS, Volz MM, Martin AJ, Ostrem JL. Interventional MRI-guided deep brain stimulation in pediatric dystonia: first experience with the ClearPoint system. J Neurosurg Pediatr 2014;14:400–8. https://doi.org/10.3171/2014.6.peds13605.

[23] Phan K, Tian DH, Cao C, Black D, Yan TD. Systematic review and meta-analysis: techniques and a guide for the academic surgeon. Ann Cardiothorac Surg 2015;4:112–22. https://doi.org/10.3978/j.issn.2225-319X.2015.02.04.

[24] Stroup DF, Berlin JA, Morton SC, Olkin I, Williamson GD, Rennie D, et al. Meta-analysis of observational studies in epidemiology: a proposal for reporting. Meta-analysis of Observational Studies in Epidemiology (MOOSE) group. Jama 2000;283:2008–12.

[25] Christensen R, Hsu JC. Multiple comparisons: theory and methods. Technometrics 1997;39:232. https://doi.org/10.2307/1270920.

[26] Higgins JPT, Green S. Cochrane Handbook for systematic reviews of Interventions. 2011. p. 2011.

[27] Liu X, Zhang J, Fu K, Gong R, Chen J, Zhang J. Microelectrode recording-guided versus intraoperative magnetic resonance imaging-guided subthalamic nucleus deep brain stimulation surgery for Parkinson disease: a 1-year follow-up study. World Neurosurg 2017;107:900. https://doi.org/10.1016/j.wneu.2017.08.077. 5.

[28] Saleh S, Swanson KI, Lake WB, Sillay KA. Awake neurophysiologically guided versus asleep MRI-guided STN DBS for Parkinson disease: a comparison of outcomes using levodopa equivalents. Stereotact Funct Neurosurg 2015;93:419–26. https://doi.org/10.1159/000442425.

[29] Schlaier JR, Habermeyer C, Janzen A, Fellner C, Hochreiter A, Proescholdt M, et al. The influence of intraoperative microelectrode recordings and clinical testing on the location of final stimulation sites in deep brain stimulation for Parkinson's disease. Acta Neurochir Wien 2013;155:357–66. https://doi.org/10.1007/s00701-012-1592-x.

[30] Kocabicak E, Alptekin O, Ackermans L, Kubben P, Kuijf M, Kurt E, et al. Is there still need for microelectrode recording now the subthalamic nucleus can be

well visualized with high field and ultrahigh MR imaging? Front Integr Neurosci 2015;9:46. https://doi.org/10.3389/fnint.2015.00046.
[31] Lozano CS, Ranjan M, Boutet A, Xu DS, Kucharczyk W, Fasano A, et al. Imaging alone versus microelectrode recording-guided targeting of the STN in patients with Parkinson's disease. J Neurosurg 2018:1–6. https://doi.org/10.3171/2018.2.jns172186.
[32] Kimmelman J, Duckworth K, Ramsay T, Voss T, Ravina B, Emborg ME. Risk of surgical delivery to deep nuclei: a meta-analysis. Mov Disord 2011;26:1415–21. https://doi.org/10.1002/mds.23770.
[33] Ivan ME, Yarlagadda J, Saxena AP, Martin AJ, Starr PA, Sootsman WK, et al. Brain shift during bur hole-based procedures using interventional MRI. J Neurosurg 2014;121:149–60. https://doi.org/10.3171/2014.3.jns121312.
[34] Jakobs M, Krasniqi E, Kloss M, Neumann JO, Campos B, Unterberg AW, et al. Intraoperative stereotactic MRI for deep brain stimulation electrode planning in patients with movement disorders. World Neurosurg 2018. https://doi.org/10.1016/j.wneu.2018.07.270.
[35] Elias WJ. Editorial: deep brain stimulation and intraoperative MRI. J Neurosurg 2016;2016:59–61. https://doi.org/10.3171/2015.2.JNS1556.test.
[36] Cui Z, Pan L, Song H, Xu X, Xu B, Yu X, et al. Intraoperative MRI for optimizing electrode placement for deep brain stimulation of the subthalamic nucleus in Parkinson disease. J Neurosurg 2016;124:62–9. https://doi.org/10.3171/2015.1.jns141534.
[37] Lee PS, Weiner GM, Corson D, Kappel J, Chang YF, Suski VR, et al. Outcomes of interventional-MRI versus microelectrode recording-guided subthalamic deep brain stimulation. Front Neurol 2018;9:241. https://doi.org/10.3389/fneur.2018.00241.
[38] Richardson RM, Ostrem JL, Starr PA. Surgical repositioning of misplaced subthalamic electrodes in Parkinson's disease: location of effective and ineffective leads. Stereotact Funct Neurosurg 2009;87:297–303. https://doi.org/10.1159/000230692.
[39] Falowski SM, Bakay RA. Revision surgery of deep brain stimulation leads. Neuromodulation 2016;19:443–50. https://doi.org/10.1111/ner.12404.
[40] Brodsky MA, Anderson S, Murchison C, Seier M, Wilhelm J, Vederman A, et al. Clinical outcomes of asleep vs awake deep brain stimulation for Parkinson disease. Neurology 2017;89:1944–50. https://doi.org/10.1212/wnl.0000000000004630.
[41] Mahlknecht P, Akram H, Georgiev D. Pyramidal tract activation due to subthalamic deep brain stimulation in. Parkinson's Dis 2017;32:1174–82. https://doi.org/10.1016/j.parkreldis.2017.04.01010.1002/mds.27042.
[42] Dafsari HS, Silverdale M, Strack M, Rizos A, Ashkan K, Mahlstedt P, et al. Nonmotor symptoms evolution during 24 months of bilateral subthalamic stimulation in. Parkinson's Dis 2018;33:421–30. https://doi.org/10.1002/mds.27283.
[43] Zrinzo L, Foltynie T, Limousin P, Hariz MI. Reducing hemorrhagic complications in functional neurosurgery: a large case series and systematic literature review. J Neurosurg 2012;116:84–94. https://doi.org/10.3171/2011.8.jns101407.
[44] Kleiner-Fisman G, Herzog J, Fisman DN, Tamma F, Lyons KE, Pahwa R, et al. Subthalamic nucleus deep brain stimulation: summary and meta-analysis of outcomes. Mov Disord 2006;21(Suppl 1):S290–304. https://doi.org/10.1002/mds.20962.
[45] Videnovic A, Metman LV. Deep brain stimulation for Parkinson's disease: prevalence of adverse events and need for standardized reporting. Mov Disord 2008;23:343–9. https://doi.org/10.1002/mds.21753.
[46] Xiaowu H, Xiufeng J, Xiaoping Z, Bin H, Laixing W, Yiqun C, et al. Risks of intracranial hemorrhage in patients with Parkinson's disease receiving deep brain stimulation and ablation. Park Relat Disord 2010;16:96–100. https://doi.org/10.1016/j.parkreldis.2009.07.013.
[47] Sansur CA, Frysinger RC, Pouratian N, Fu KM, Bittl M, Oskouian RJ, et al. Incidence of symptomatic hemorrhage after stereotactic electrode placement. J Neurosurg 2007;107:998–1003. https://doi.org/10.3171/jns-07/11/0998.
[48] Kim MS, Jeong JS, Ryu HS, Choi SH, Chung SJ. Infection related to deep brain stimulation in patients with Parkinson disease: clinical characteristics and risk factors. J Neurol Sci 2017;383:135–41. https://doi.org/10.1016/j.jns.2017.10.031.
[49] Foltynie T, Zrinzo L, Martinez-Torres I, Tripoliti E, Petersen E, Holl E, et al. MRI-guided STN DBS in Parkinson's disease without microelectrode recording: efficacy and safety. J Neurol Neurosurg Psychiatry 2011;82:358–63. https://doi.org/10.1136/jnnp.2010.205542.
[50] Mirzadeh Z, Chen T, Chapple KM, Lambert M, Karis JP, Dhall R, et al. Procedural variables influencing stereotactic accuracy and efficiency in deep brain stimulation surgery. Oper Neurosurg 2018. https://doi.org/10.1093/ons/opy291.
[51] Lee DJ, Zwienenberg-Lee M, Seyal M, Shahlaie K. Intraoperative computed tomography for intracranial electrode implantation surgery in medically refractory epilepsy. J Neurosurg 2015;122:526–31. https://doi.org/10.3171/2014.9.jns13919.
[52] LaHue SC, Ostrem JL, Galifianakis NB, San Luciano M, Ziman N, Wang S, et al. Parkinson's disease patient preference and experience with various methods of DBS lead placement. Park Relat Disord 2017;41:25–30. https://doi.org/10.1016/j.parkreldis.2017.04.010.
[53] Hertel F, Zuchner M, Weimar I, Gemmar P, Noll B, Bettag M, et al. Implantation of electrodes for deep brain stimulation of the subthalamic nucleus in advanced Parkinson's disease with the aid of intraoperative microrecording under general anesthesia. Neurosurgery 2006;59:E1138. https://doi.org/10.1227/01.neu.0000245603.77075.55. discussion E1138.
[54] Lettieri C, Rinaldo S, Devigili G, Pauletto G, Verriello L, Budai R, et al. Deep brain stimulation: subthalamic nucleus electrophysiological activity in awake and anesthetized patients. Clin Neurophysiol 2012;123:2406–13. https://doi.org/10.1016/j.clinph.2012.04.027.
[55] Lin SH, Chen TY, Lin SZ, Shyr MH, Chou YC, Hsieh WA, et al. Subthalamic deep brain stimulation after anesthetic inhalation in Parkinson disease: a preliminary study. J Neurosurg 2008;109:238–44. https://doi.org/10.3171/jns/2008/109/8/0238.
[56] Blume J, Schlaier J, Rothenfusser E, Anthofer J, Zeman F, Brawanski A, et al. Intraoperative clinical testing overestimates the therapeutic window of the permanent DBS electrode in the subthalamic nucleus. Acta Neurochir Wien 2017;159:1721–6. https://doi.org/10.1007/s00701-017-3255-4.
[57] Ho AL, Ali R, Connolly ID, Henderson JM, Dhall R. Awake versus asleep deep brain stimulation for Parkinson's disease: a critical comparison and meta-analysis, vol. 89; 2017. p. 687–91. https://doi.org/10.1136/jnnp-2016-314500.
[58] Shamir RR, Duchin Y, Kim J, Patriat R, Marmor O, Bergman H, et al. Microelectrode recordings validate the clinical visualization of subthalamic-nucleus based on 7T magnetic resonance imaging and machine learning for deep brain stimulation surgery. Neurosurgery 2018. https://doi.org/10.1093/neuros/nyy212.
[59] Thompson JA, Oukal S, Bergman H, Ojemann S, Hebb AO, Hanrahan S, et al. Semi-automated application for estimating subthalamic nucleus boundaries and optimal target selection for deep brain stimulation implantation surgery. J Neurosurg 2018:1–10. https://doi.org/10.3171/2017.12.jns171964.
[60] Horn A, Li N, Dembek TA, Kappel A, Boulay C, Ewert S, et al. Lead-DBS v2: towards a comprehensive pipeline for deep brain stimulation imaging. Neuroimage 2019;184:293–316. https://doi.org/10.1016/j.neuroimage.2018.08.068.
[61] Ewert S, Horn A, Finkel F, Li N, Kühn AA, Herrington TM. Optimization and comparative evaluation of nonlinear deformation algorithms for atlas-based segmentation of DBS target nuclei. Neuroimage 2019;184:586–98. https://doi.org/10.1016/j.neuroimage.2018.09.061.
[62] Conrad EC, Mossner JM, Chou KL, Patil PG. Atlas-independent, electrophysiological mapping of the optimal locus of subthalamic deep brain stimulation for the motor symptoms of Parkinson disease. Stereotact Funct Neurosurg 2018;96:91–9. https://doi.org/10.3233/jpd-17127210.1159/000486643.
[63] Koivu M, Huotarinen A, Scheperjans F, Laakso A, Kivisaari R, Pekkonen E. Motor outcome and electrode location in deep brain stimulation in Parkinson's disease. Brain Behav 2018:e01003. https://doi.org/10.1002/brb3.1003.
[64] Ho AL, Ali R, Connolly ID, Henderson JM, Dhall R. Awake versus asleep deep brain stimulation for Parkinson's disease: a critical comparison and meta-analysis, vol. 89; 2017. p. 687–91. https://doi.org/10.1136/jnnp-2016-314500.
[65] Weaver F, Follett K, Hur K, Ippolito D, Stern M. Deep brain stimulation in Parkinson disease: a metaanalysis of patient outcomes. J Neurosurg 2005;103:956–67. https://doi.org/10.3171/jns.2005.103.6.0956.
[66] Kim HJ, Jeon BS, Yun JY, Kim YE, Yang HJ, Paek SH. Initial cognitive dip after subthalamic deep brain stimulation in Parkinson disease. J Neurol 2013;260:2130–3. https://doi.org/10.1007/s00415-013-6959-2.