Electrode Penetration of the Caudate Nucleus in Deep Brain Stimulation Surgery for Parkinson's Disease

Bot, M.; van den Munckhof, P.; Schmand, B.A.; de Bie, R.M.A.; Schuurman, P.R.

Published in:
Stereotactic and Functional Neurosurgery

DOI:
10.1159/000489944

Clinical Study

Stereotactic and Functional Neurosurgery

Stereotact Funct Neurosurg 2018;96:223–230
DOI: 10.1159/000489944

Received: June 5, 2017
Accepted after revision: May 10, 2018
Published online: September 3, 2018

Electrode Penetration of the Caudate Nucleus in Deep Brain Stimulation Surgery for Parkinson's Disease

Maarten Bot[a] Pepijn van den Munckhof[a] Ben A. Schmand[b] Rob M.A. de Bie[c] P. Richard Schuurman[a]

[a]Department of Neurosurgery, Academic Medical Center, Amsterdam, The Netherlands; [b]Department of Psychology, Academic Medical Center, Amsterdam, The Netherlands; [c]Department of Neurology, Academic Medical Center, Amsterdam, The Netherlands

Keywords

Caudate nucleus · Deep brain stimulation · Parkinson's disease · Cognition

Abstract

Objective: To evaluate the possible influence of electrode trajectories penetrating the caudate nucleus (CN) on cognitive outcomes in deep brain stimulation (DBS) surgery for Parkinson's disease (PD). ***Background:*** It is currently unclear how mandatory CN avoidance during trajectory planning is. ***Design/Methods:*** Electrode trajectories were determined to be inside, outside, or in border region of the CN. Pre- and postoperative neuropsychological tests of each trajectory group were compared in order to evaluate possible differences in cognitive outcomes 12 months after bilateral STN DBS. ***Results:*** One hundred six electrode tracks in 53 patients were evaluated. Bilateral penetration of the CN occurred in 15 (28%) patients, while unilateral penetration occurred in 28 (53%). In 19 (36%) patients tracks were located in the border region of the CN. There was no electrode penetration of the CN in 10 (19%) patients. No difference in cognitive outcomes was found between the different groups. ***Conclusion:*** Cognitive outcome was not influenced by DBS electrode tracks penetrating the CN. It is both feasible and sensible to avoid electrode tracks through the CN when possible, considering its function and anatomical position. However, penetration of the CN can be considered without major concerns regarding cognitive decline when this facilitates optimal trajectory planning due to specific individual anatomical variations.

Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is currently an effective neurosurgical treatment for reducing motor symptoms in Parkinson's disease (PD) [1]. Cognitive decline following surgery is an almost invariably identified adverse event, but it is reported to varying degrees and identification of the causal factors contributing to this decline remains challenging [2–4].

Both patient and surgical characteristics are considered as possible factors. An older age, impaired attention, and a low levodopa response at baseline are patient-related factors which correlate negatively with outcome on

KARGER

E-Mail karger@karger.com
www.karger.com/sfn

Maarten Bot, MD
Department of Neurosurgery, Academic Medical Center
Meibergdreef 9
NL–1105 AZ Amsterdam (The Netherlands)
E-Mail m.bot@amc.nl

postoperative neuropsychological tests [5, 6]. Surgical aspects evaluated are predominantly stimulation related; the location of the electrode contact used for chronic stimulation together with stimulation settings are generally considered to influence cognition due to effect on different functional regions within the STN [7]. However, patients who underwent DBS surgery showed comparable decline in cognitive functioning when the DBS system was left off in comparison with patients whose system was turned on [8].

Passing through the caudate nucleus (CN) with the electrode trajectory is a surgical element considered to be a risk factor for cognitive deterioration [6]. A prefrontal entrance is typically chosen during trajectory planning, with avoidance of sulci, blood vessels, and ventricles. By complying with these conditions, the periventricular CN could occasionally be traversed by the course of the optimal trajectory. Recently, the relation between penetration of the CN and postoperative cognitive decline was studied, with contradictory conclusions [9–11].

The CN is part of the striatum and plays a key role in reward-based behavior, working memory, and strategic planning processes [12]. In neurodegenerative diseases such as Alzheimer's, atrophy of the CN is seen and ischemic lesions of the CN are associated with an increase in perseverative behavior [13, 14]. Diffusion tensor imaging (DTI) indicates that the CN is part of a loop connecting cortical regions with each other through the globus pallidus and the thalamus. Different subdivisions within the nucleus are assumed. The anterior (associative) part of the CN connects with prefrontal areas, whereas the posterior (sensorimotor) tail mainly shows connections with the motor and premotor cortices. Longitudinal fibers seen within the CN on DTI possibly connect the different subdivisions [15]. Altogether, the CN seems to play an essential role in facilitating higher cognitive functions and contains a complex architecture. It could well be that passing an electrode through this structure during DBS surgery carries the risk of influencing cognition.

As it is currently unclear how mandatory avoidance of the CN during trajectory planning is, we retrospectively evaluated the relationship of CN penetration during DBS surgery with postoperative cognitive changes.

Methods

Patients

Patients were retrospectively included from a multicenter prospective controlled study on neuropsychological effects of STN stimulation which recruited between April 2000 and June 2005, during which time no particular emphasis was placed yet on avoiding the CN during trajectory planning [5]. Patients were considered for the current analysis if they underwent DBS surgery in our institution and had a postoperative CT scan for electrode localization, so it was possible to reevaluate the electrode implantation trajectories.

Surgical Procedure

On the day of surgery, the Leksell frame was placed and patients underwent preoperative 1.5-T stereotactic MRI with axial and coronal T2-weighted and post-gadolinium (Gd) 3-D volumetric T1-weighted sequences. STN target planning was started using standard stereotactic coordinates calculated from the midcommissural point as follows: 12 mm lateral, 2 mm posterior, and 4 mm ventral. Target planning was subsequently optimized based on red nucleus and STN representation on T2 sequences. Trajectory planning was done using a post-Gd volumetric T1-weighted sequence. Entry points were chosen as follows: precoronal and 3–4 cm lateral from the midline on a suitable gyrus. During the period of inclusion of this cohort, planned trajectories were inspected and adjusted to avoid penetration of ventricles and blood vessels only. Planning was done using SurgiPlan software (Elekta Instrument AB, Stockholm, Sweden). All patients were operated on under local anesthesia with the head frame secured to the operating table. Patients were placed in the supine position with the head elevated 20–30° to minimize the outflow of cerebrospinal fluid through burr hole trepanation. Surgery started contralateral to the most affected side. When performing microelectrode recordings, 1–5 parallel steel cannulas and microelectrodes were used. In procedures without microelectrode recordings a macroelectrode (Elekta) was used for test stimulation. After the optimal track and depth had been determined, the DBS electrode (model 3389; Medtronic, Minneapolis, MN, USA) was implanted under fluoroscopic guidance and fixed at the border of the burr hole with a custom-made titanium microplate and plastic covering to prevent electrode damaging. Implantation of 1 or 2 pulse generator(s) was done in a subcutaneous pocket in the infraclavicular region under general anesthesia. Postoperative CT imaging (2-mm slice thickness) used in this study for electrode trajectory evaluation was performed between 1 day and 8 years postoperatively (average of 2.5 years).

During the start of data collection (April 2000) we began implementing postoperative CT. In the following years CT was increasingly performed more consistently on the first postoperative day, resulting in our current practice of always performing CT on the first postoperative day. This resulted in patients not having a first-postoperative-day CT – it was performed later during follow-up after an average of 2.5 years, with an outlier at 7 years. A wide span of time is noted, however, as the electrode is not expected to change its location with respect to the CN; this is expected not to influence findings of the current study.

Evaluation of Trajectories

Postoperative CT was coregistered to preoperative stereotactic axial T1-weighted MRI used for target and trajectory planning and the final electrode positions were examined to evaluate whether penetration of the CN occurred. When penetrating the CN, the electrodes were evaluated for being located in the head or body division of the nucleus. The head subdivision was determined to be the part of the CN rostral to the interventricular foramen of Monro adjacent to the anterior horn of the lateral ventricle. Electrode localization was categorized into the following 3 groups: (1) CN penetration, (2) no CN penetration, and (3) highly lateral CN penetration, i.e. border region (Fig. 1). Occurrence of penetration was categorized into the following 3 groups for comparison: (1) bilateral CN penetration, (2) no CN penetration, and (3) unilateral CN penetration. The outcome was determined for 3 groups in 2 different analyses as follows: (1) considering electrodes in the border region as penetrating the CN and (2) considering electrodes in the border region as not penetrating the CN.

Neuropsychological Tests

Neuropsychological assessments at baseline were performed in the on-medication phase. Follow-up assessment was done in the on-medication and on-neurostimulation phase 12 months after surgery in all of the patients. Neuropsychological examination included the Mattis Dementia Rating Scale, category fluency (animals and occupations for 1 min each), alternating fluency (body parts/cities or pieces of clothing/countries), letter fluency, the Stroop Color and Word Test, and the Trail Making Test Parts A and B. These specific neuropsychological assessments were chosen for evaluation due to their ability to detect decline in cognitive functions such as memory and verbal fluency and are widely used for evaluation of cognition [5, 9]. We analyzed possible predictors of cognitive outcomes including age, disease duration, attention, levodopa response, and performance of microelectrode recordings.

Statistical Analysis

Calculated mean differences in the scores of every test for each of the 3 groups were compared using analysis of variance (ANOVA). The distributions of change scores were first examined for deviation from normality (a normal distribution was found). Group differences in possible predictors of outcomes were compared and when significance was found, used as a covariate (ANCOVA).

Results

A total of 106 electrode trajectories were evaluated in 53 PD patients who underwent bilateral STN DBS. In 37 cases microelectrode recordings were performed. The baseline characteristics of the patient sample are listed in Table 1. The average sagittal and coronal angles for the trajectories were 78° and 14°, respectively. CN group characteristics are shown in Figure 2 and Table 1.

In the right hemisphere 18 (34%) electrodes penetrated the CN, 24 (45%) did not penetrate the CN, and 11 (21%) were in the border region of the CN. In the left

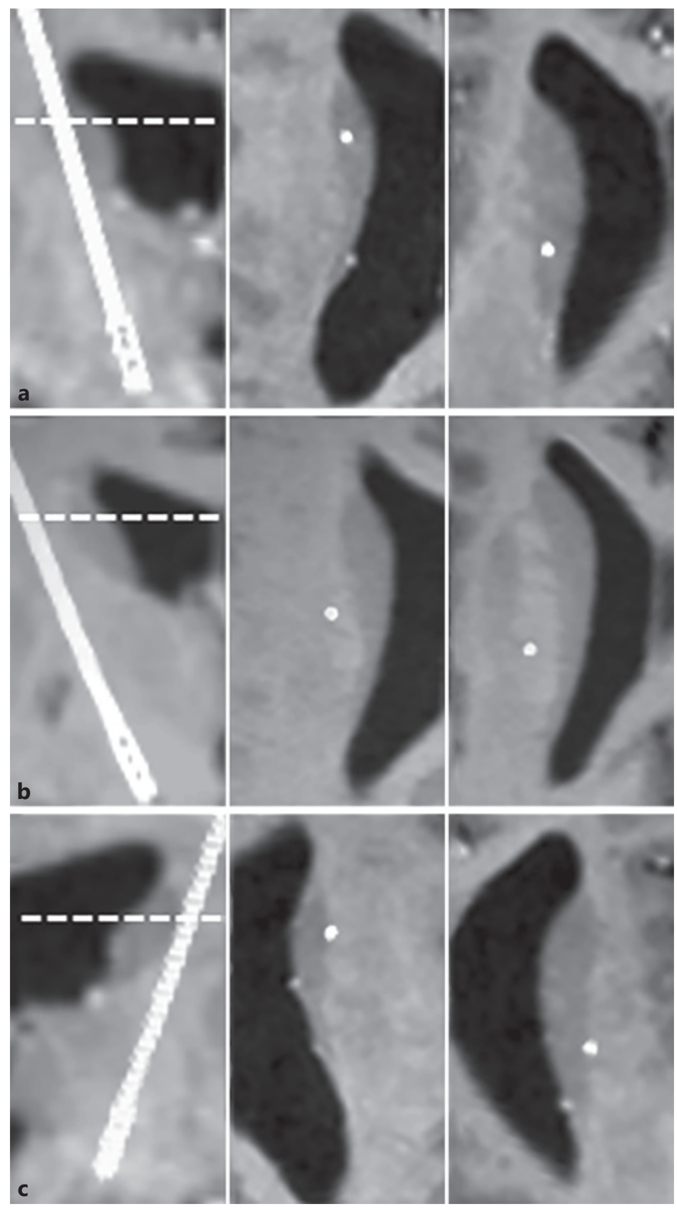

Fig. 1. Electrode penetration of the CN. **a** Left to right: coronal trajectory view and corresponding axial and axial trajectory views of stereotactic 1.5-T T1 MRI of the unilateral (right) CN region with coregistered postoperative CT. The dotted line in the coronally orientated image indicates the depth of the corresponding axial planes. The trajectory view (either coronal or axial) is a plane in line with the course of the electrode path as determined on CT. The electrode is penetrating the CN (hypointense area adjacent to the lateral ventricle) as the electrode artefact (displayed as a white/hyperdense round dot on axially orientated images) is completely surrounded by CN representation. **b** Comparable design of another (right) CN region on 1.5-T T1 MRI with coregistered postoperative CT. The electrode artefact is fully surrounded by white matter (corona radiata) and does not penetrate the CN. **c** Comparable design of another (left) CN region on 1.5-T T1 MRI with coregistered postoperative CT. The electrode is located in the border region of the CN. The electrode artefact is bordered by CN representation on the medial side; however, the artefact is bordered by white matter on the lateral side.

Table 1. Baseline characteristics of the 3 groups

	Bilateral CN penetration	No CN penetration	Unilateral CN penetration	Total	*p* value
Patients, *n*	15	10	28	53	
Male/female ratio	12/3	6/4	16/12	34/19	0.3
Attention span, min	34.3±2.1	35.2±2.0	35.3±1.7		0.6
Age, years	54.3±7.7	56.6±9.7	55.7±8.4		0.8
Improvement on the levodopa challenge test, %	47.9±19.8	51.7±21.8	48.5±16.9		0.9
Disease duration, years	9.8±3.3*	14.3±5.4	13.8±4.8*		0.02
Microelectrode recording (yes/no)	9/6	8/2	20/8	37/16	0.5

Border region electrodes are considered as penetrating the CN. No differences in characteristics were found when considering border region electrodes as not penetrating the CN (numbers not shown). Values are means ± SD unless otherwise stated. *p* values were calculated by χ^2 (gender, microelectrode recording) or ANOVA (remaining values) tests. * Significantly different at $p < 0.05$. Attention is expressed as the means *z* score on the Trail Making Test Part B and the Stroop Color and Word Test.

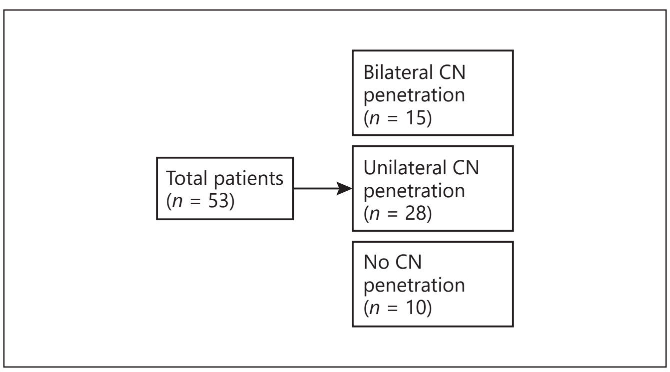

Fig. 2. Patient flow diagram.

hemisphere 20 (38%) electrodes penetrated the CN, 23 (43%) did not penetrate the CN, and 10 (19%) were in the border region of the CN. Of all of the electrodes penetrating the CN, 12 (31%) were in the head subdivision and 26 (69%) were in the body subdivision. In 11 cases, one of the electrodes was located outside and the other one was located in the border region of the CN. In 6 cases, one of the electrodes was located inside and the other one was located in border region of the CN. In 2 cases both electrodes were located in the border region of the CN.

When considering border region electrodes as penetrating the CN, in 15 (28%) cases bilateral penetration occurred, in 10 (19%) cases no penetration occurred, and in 28 (53%) cases unilateral penetration occurred. When considering border region electrodes as not penetrating the CN, in 8 (15%) cases bilateral penetration occurred, in 23 (43%) no penetration occurred, and in 22 (42%) cases unilateral penetration occurred.

There was no significant difference in cognitive outcomes between the group with bilateral CN penetration, the group with unilateral CN penetration, and the group without CN penetration. Outcome was not influenced when border region electrodes were considered as either penetrating or not penetrating the CN (Table 2). The sole baseline characteristic, considered as a possible predictor of outcome, that significantly differed between groups was disease duration. This characteristic did not significantly influence cognitive outcomes.

Discussion

CN Penetration and Cognitive Outcome

In the years 2000–2005, electrode implantation for DBS frequently led to penetration of the CN due to the fact that no particular care was taken yet to avoid this nucleus during trajectory planning. The main factors determining the path were entry on top of a gyrus and avoidance of ventricles and vessels. However, we found no influence of CN penetration by DBS electrodes on cognitive outcomes 12 months after bilateral STN DBS for PD. Our comparison is the largest study to date evaluating this issue.

Table 2. Overview of outcomes for neuropsychological tests between the different CN groups

	Decline in performance, %	Border region (in)[a]	*p* value	*n*	Border region (out)[b]	*p* value	*n*
MDRS (total score)	52	B: –2.5 (–6.4 to 1.5) N: –1.7 (–6.9 to 3.4) U: –1.9 (–3.5 to –0.2)	0.94	B: 13 N: 9 U: 28	B: –3.5 (–13.5 to 6.5) N: –1.4 (–3.6 to 0.8) U: –2.1 (–4.0 to –0.3)	0.68	B: 6 N: 22 U: 22
Category fluency (*n* of words)	80	B: –5.7 (–9.3 to –2.3) N: –3.2 (–8.0 to 1.5) U: –6.1 (–8.5 to –3.6)	0.47	B: 13 N: 9 U: 28	B: –4.0 (–11.6 to 3.6) N: –4.5 (–7.2 to –1.8) U: –6.9 (–9.5 to –4.2)	0.36	B: 6 N: 22 U: 22
Alternating fluency (*n* of words)	69	B: –6.3 (13.1 to 0.6) N: –3.8 (–10.1 to 2.5) U: –6.3 (–11.1 to –1.6)	0.81	B: 11 N: 9 U: 25	B: –4.3 (–16.0 to 9) N: –6.2 (–11.5 to –1.0) U: –5.8 (-10.5 to –1.1)	0.89	B: 4 N: 20 U: 21
Letter fluency (*n* of letters)	58	B: –5.8 (–12.1 to 1.6) N: –1.6 (–9.9 to 6.8) U: –3.6 (–7.0 to –0.2)	0.60	B: 13 N: 9 U: 28	B: –1.5 (–12.1 to 9.1) N: –3.4 (–8.1 to 1.4) U: –4.9 (–9.0 to –0.8)	0.73	B: 6 N: 22 U: 22
Stroop Color and Word Test (s)	63	B: –22.6 (–49.3 to 4.1) N: 22.2 (–65.2 to 109.7) U: –20.6 (–36.9 to –4.3)	0.17	B: 13 N: 9 U: 27	B: –30.7 (–92.3 to 30.1) N: –9.0 (–48.3 to 30.3) U: –12.5 (–24.9 to –0.2)	0.76	B: 6 N: 21 U: 22
Trail Making Test Part A (s)	48	B: –1.9 (–13.4 to 9.6) N: 5.2 (–5.4 to 15.8) U: –4.7 (–11.3 to 1.9)	0.32	B: 13 N: 9 U: 28	B: 2.7 (–4.2 to 9.5) N: –3.1 (–10.1 to 4.9) U: –2.7 (–10.1 to 5.6)	0.76	B: 6 N: 22 U: 22
Trail Making Test Part B (s)	44	B: –38.6 (–81.1 to 3.9) N: 8.6 (–34.7 to 51.8) U: –20.9 (–40.8 to –1.1)	0.17	B: 13 N: 9 U: 28	B: –35.5 (–94.3 to 22.3) N: –25.3 (–54.9 to 4.3) U: –11.0 (–33.5 to 11.5)	0.57	B: 6 N: 22 U: 22

Comparison of cognitive outcomes between the 3 CN groups after 12 months of follow-up. No significant differences were found ($p < 0.05$). MDRS, Mattis Dementia Rating Scale; B, bilateral CN penetration; N, no CN penetration; U, unilateral CN penetration. [a] Mean change scores (95% CI) for the 3 groups with border region electrodes considered as penetrating the CN. [b] Mean change scores (95% CI) after 12 months compared to baseline for the 3 groups with border region electrodes considered as not penetrating the CN.

Four other groups evaluated the influence of CN penetration by DBS electrodes on cognitive outcomes after STN DBS. York et al. [16] reported the occurrence of caudate penetration in 17 PD patients, but their focus was on trajectory angle and contact localization on verbal fluency. For the other 3 reports, neuropsychological examinations were comparable to those of our study, which enabled direct comparisons. Morishita et al. [10] evaluated a total of 29 cases of mostly unilateral STN DBS for PD with usage of postoperative CT after a mean follow-up of 15 months and noted 12 patients with CN penetration. They concluded that there was no influence on cognitive outcomes due to CN penetration. Isler et al. [11] evaluated 30 cases (all bilateral) of STN DBS for PD with usage of postoperative MRI and CT and noted 10 patients with CN penetration. They found a significant difference in the Trail Making Test Part B after 3 months of follow-up; however, they found no influence on cognitive outcomes due to CN penetration after 12 months of follow-up. They concluded that electrode trajectories are allowed to be planned through the CN if otherwise a highly lateral entry point is indicated since penetration influences cognitive outcomes only in the short term. Witt et al. [9] analyzed 31 cases of mostly bilateral STN DBS for PD with usage of normalized stereotactic coordinate space to determine CN penetration using postoperative MRI. They found a subtle but significant decline in cognitive functioning related to CN penetration, as indicated by decreases in the Mattis Dementia Rating Scale and backward digit span after 6 months of follow-up, and concluded that electrode trajectories should be planned outside of the CN. However, the exact test (numeric) decline could not be deduced from their data. They reported on 12 cases of bilateral and 14 cases of unilateral CN penetration, which left a small no-penetration group and resulted in hampered comparisons between groups. Decline in the entire DBS group (containing both CN and no CN penetration) was given (compared to the best medical treatment) without subdividing for CN penetration. Normalization of the data was applied, which facilitated comparisons between subjects; however, the individual interrelationship between DBS trajectory and CN was lost [9, 17]. Taking the findings of Isler et al. [11] into account, these differences are possibly due to short-term follow-up.

For all 3 groups an uneven occurrence of CN penetration was noted. Morishita et al. [10] analyzed predominantly unilateral DBS procedures and Isler et al. [11] noted unilateral caudate penetration in the majority of cases. Witt et al. [9] noted CN penetration in the majority of their patients, leaving almost none with no penetration. In the current study, the possible influence of both bilateral and unilateral penetration of the CN on cognitive outcome was evaluated. The occurrence of unilateral CN penetration in our study was equally divided between the left and right hemispheres, which prevented the outcome from being based on mainly one hemisphere. However, left or right CN penetration was not separately evaluated.

Although T1-weighted imaging did not provide a detailed delineation of subdivisions within the CN as, for example, DTI could [15], visual inspection indicated that electrode tracks in the current study mainly penetrated the body region of the CN. When examining the localization of CN penetration in the study by Witt et al. [9] it appeared that this occurred mainly in the head of the nucleus. Since the head is more voluminous, this would most likely result in a larger total penetrated (or lesion) CN volume. A larger total penetrated CN volume may have resulted in the observed cognitive decline. However, in the results of Morishita et al. [10], no difference was found in cognitive outcomes between medially and laterally located electrode tracks in the CN. Lateral tracks most likely result in smaller penetration volumes, although this was not explicitly evaluated by Morishita et al. [10]. Finally, penetration of the head itself (apart from lesion volume) may have contributed to the cognitive decline found by the Witt et al. [9]. Isler et al. [11] did not report on the location of caudate penetration. Differences in the location of CN penetration could be due to differences in the trajectory angles chosen; however, these were not reported by any of the 3 groups.

Should the CN Be Avoided during Trajectory Planning?

Representation of the CN is well delineated on both T1 and T2 MRI sequences, which are considered standard imaging elements enabling optimal trajectory and target planning during DBS procedures [3]. Clear visualization of the lateral CN borders on MRI allows evaluation of this nucleus during the planning phase. Throughout the years 2000–2005, our group did not specifically evaluate the interrelationship between planned electrode trajectories and the CN. Currently, we do explicitly evaluate this during trajectory planning for DBS procedures, and this change in surgical approach was induced by recent literature evaluating CN penetration. When evaluating a recent cohort (during the years 2012–2014) of our institution (published elsewhere) [18], the average sagittal and coronal angles of contemporary implantations were 78° and 19°, respectively, compared to 78° and 14° in our historical cohort used for the current study. Strict avoidance of the CN during trajectory planning thus results in a more lateral chosen entry point, which can be expected due to the periventricular localization of the CN. In our recent experience, avoiding the CN during trajectory planning can be well implemented together with choosing an entry point on top of a gyrus and avoiding blood vessels and ventricles.

The CN is an extensively inter- and intraconnected structure which is essential for cognitive functioning. In our opinion it would be sensible to avoid penetration of this structure in order to minimize the risk of dysfunction caused by penetration lesions. Although penetration of a DBS electrode does not evidently interfere with the correct functioning of the CN when measuring cognition, a larger lesion (hemorrhage/infarction) induced by penetration would be more likely to do so [13]. Most CT imaging in this study was performed several years after surgery, which hampers evaluation for the occurrence of CN hemorrhage. The rate of hemorrhage induced by DBS surgery has been reported to be around 1% [1], but hematomas in CN are usually not separately reported. However, it is evident that the risk of occurrences decreases when penetration of this nucleus is avoided during the planning phase.

Trajectories within the CN are close to the ventricular wall due to the close interrelationship this nucleus has with the wall of the lateral ventricle. In our cases, penetration of the CN occurred mainly in the body of the nucleus. This slim part in comparison to its more voluminous round head leaves little space toward the ventricular wall. Transgression of the ventricular wall during DBS surgery is associated with an increased risk of hemorrhage and decline of postoperative cognition [19]. Despite pursuing optimal burr hole placement, we have to adjust our ring and arc occasionally by several degrees for exact alignment of the cannulas and burr hole. Medial adjustment of the arc results in a more medially orientated trajectory, which leads to a closer relationship with medially situated structures such as the CN and lateral ventricle. A trajectory planned laterally alongside the CN could possibly penetrate the CN after medial correction, but it is usually unlikely that this correction will be substantial enough to reach the ventricular wall.

Limitations of This Study

We retrospectively analyzed a cohort of patients who underwent STN DBS for PD. At the time these patients underwent DBS surgery, our group did not evaluate localization of the CN during trajectory planning as compared to that of blood vessels and ventricles. This unawareness of the CN does not ensure random occurrence of trajectory penetration as trajectory planning is also influenced by brain atrophy and correspondingly the lateral ventricles. Brain atrophy was not measured in the current study.

It is unclear whether the DBS electrodes located in the border region (which resulted in minimal contact between the electrode and the nucleus) of the CN should be classified as either penetrating the CN or not. In advance, we did not anticipate the existence of the border region group but found it most correct to take this group into account during our analysis. We decided to determine outcomes considering the electrodes located in the border region as penetrating the CN and, in a separate analysis, considering them as not penetrating the CN. It could be suggested that the border region group should preferably be considered as a separate group. In our current cohort, however, this would have resulted in multiple small groups from which no meaningful statistical result could be derived.

Electrode penetration was determined on axial and coronal T1 MRI sequences and it was determined to be in the CN, outside of the CN, or in border region of the CN. Since the CN is assumed to be composed of multiple subdivisions, it could be of importance which of these subdivisions is penetrated by a DBS electrode. Applied imaging did not allow clear visualization of these subdivisions or their different interconnections with surrounding regions and could therefore not be fully analyzed.

Electrode penetration was evaluated at an average of 2.5 years after implantation. During electrode insertion a lesional effect can occur, which is assumed to result from both edema formation and physical penetration during electrode insertion. The edema resolves in days; however, the penetration effect does not as the electrode remains in position. The current study only offers insight into the effect of penetration of the CN, not the possible edema which can arise immediately after electrode insertion.

We did not analyze the possible influence of the location of the electrode contact used for chronic stimulation or individual stimulation settings in relation to different functional regions within the STN as a possible predictor of the cognitive outcome, which was beyond the scope of the current study.

Conclusion

The current study contributes to a more substantiated framework for optimal trajectory planning. The cognitive outcome after 12 months of follow-up was not influenced by DBS electrode tracks penetrating the CN. It is both feasible and sensible to avoid electrode tracks through the CN when possible, considering its function and anatomical position. However, penetration of the CN can be considered without major concerns regarding cognitive decline when this facilitates optimal trajectory planning due to specific individual anatomical variations.

Disclosure Statement

The DBS team of the Academic Medical Center received unrestricted research grants from Medtronic and financial compensation for teaching courses for the European Continued Medical Training Program. M. Bot received travel grants from Medtronic. P.R. Schuurman acts as independent advisor for Medtronic and Elekta. P. van den Munckhof, R.M.A de Bie, and B.A. Schmand have no disclosures to report.

References

1 Odekerken VJ, van Laar T, Staal MJ, Mosch A, Hoffmann CF, Nijssen PC et al. Subthalamic nucleus versus globus pallidus bilateral deep brain stimulation for advanced Parkinson's disease (NSTAPS study): a randomised controlled trial. Lancet Neurol. 2013 Jan;12(1):37–44.
2 Moro E, Lozano AM, Pollak P, Agid Y, Rehncrona S, Volkmann J et al. Long-term results of a multicenter study on subthalamic and pallidal stimulation in Parkinson's disease. Mov Disord. 2010 Apr;25(5):578–86.
3 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 Dec;85(12):1419–25.

4 Merola A, Rizzi L, Zibetti M, Artusi CA, Montanaro E, Angrisano S et al. Medical therapy and subthalamic deep brain stimulation in advanced Parkinson's disease: a different long-term outcome? J Neurol Neurosurg Psychiatry. 2014 May;85(5):552–9.
5 Smeding HM, Speelman JD, Huizenga HM, Schuurman PR, Schmand B. Predictors of cognitive and psychosocial outcome after STN DBS in Parkinson's Disease. J Neurol Neurosurg Psychiatry. 2011 Jul;82(7):754–60.
6 Witt K, Daniels C, Volkmann J. Factors associated with neuropsychiatric side effects after STN-DBS in Parkinson's disease. Parkinsonism Relat Disord. 2012 Jan;18 Suppl 1:S168–70.
7 Eisenstein SA, Koller JM, Black KD, Campbell MC, Lugar HM, Ushe M et al. Functional anatomy of subthalamic nucleus stimulation in Parkinson disease. Ann Neurol. 2014 Aug;76(2):279–95.
8 Okun MS, Gallo BV, Mandybur G, Jagid J, Foote KD, Revilla FJ et al.; SJM DBS Study Group. Subthalamic deep brain stimulation with a constant-current device in Parkinson's disease: an open-label randomised controlled trial. Lancet Neurol. 2012 Feb;11(2):140–9.
9 Witt K, Granert O, Daniels C, Volkmann J, Falk D, van Eimeren T et al. Relation of lead trajectory and electrode position to neuropsychological outcomes of subthalamic neurostimulation in Parkinson's disease: results from a randomized trial. Brain. 2013 Jul;136(Pt 7):2109–19.
10 Morishita T, Okun MS, Jones JD, Foote KD, Bowers D. Cognitive declines after deep brain stimulation are likely to be attributable to more than caudate penetration and lead location. Brain. 2014 May;137(Pt 5):e274.
11 Isler C, Albi A, Schaper FL, Temel Y, Duits A. Neuropsychological outcome in subthalamic nucleus stimulation surgeries with electrodes passing through the caudate nucleus. Stereotact Funct Neurosurg. 2016;94(6):413–20.
12 Grahn JA, Parkinson JA, Owen AM. The cognitive functions of the caudate nucleus. Prog Neurobiol. 2008 Nov;86(3):141–55.
13 Nys GM, van Zandvoort MJ, van der Worp HB, Kappelle LJ, de Haan EH. Neuropsychological and neuroanatomical correlates of perseverative responses in subacute stroke. Brain. 2006 Aug;129(Pt 8):2148–57.
14 Ryan NS, Keihaninejad S, Shakespeare TJ, Lehmann M, Crutch SJ, Malone IB et al. Magnetic resonance imaging evidence for presymptomatic change in thalamus and caudate in familial Alzheimer's disease. Brain. 2013 May;136(Pt 5):1399–414.
15 Kotz SA, Anwander A, Axer H, Knösche TR. Beyond cytoarchitectonics: the internal and external connectivity structure of the caudate nucleus. PLoS One. 2013 Jul;8(7):e70141.
16 York MK, Wilde EA, Simpson R, Jankovic J. Relationship between neuropsychological outcome and DBS surgical trajectory and electrode location. J Neurol Sci. 2009 Dec;287(1-2):159–71.
17 Chakravarty MM, Sadikot AF, Germann J, Hellier P, Bertrand G, Collins DL. Comparison of piece-wise linear, linear, and nonlinear atlas-to-patient warping techniques: analysis of the labeling of subcortical nuclei for functional neurosurgical applications. Hum Brain Mapp. 2009 Nov;30(11):3574–95.
18 Bot M, Bour L, de Bie R, Contarino MF, Schuurman R, van den Munckhof P. Can we rely on susceptibility-weighted imaging (SWI) for subthalamic nucleus identification in deep brain stimulation surgery? Neurosurgery. 2015 Mar;78(3):353–60.
19 Gologorsky Y, Ben-Haim S, Moshier EL, Godbold J, Tagliati M, Weisz D et al. Transgressing the ventricular wall during subthalamic deep brain stimulation surgery for Parkinson disease increases the risk of adverse neurological sequelae. Neurosurgery. 2011 Aug;69(2):294–9.