Acta Neurochirurgica (2019) 161:1579–1588
https://doi.org/10.1007/s00701-019-03975-5

ORIGINAL ARTICLE - FUNCTIONAL NEUROSURGERY - PAIN

Dorsal anterior cingulate cortex (ACC) deep brain stimulation (DBS): a promising surgical option for the treatment of refractory thalamic pain syndrome (TPS)

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Received: 19 April 2019 / Accepted: 5 June 2019 / Published online: 17 June 2019

Abstract

Background Neuroimaging evidences and previous successful case series of cingulotomy for cancer pain have disclosed the key-role of the dorsal anterior cingulate cortex (ACC) in the generation of the empathic and affective dimension of pain. The aim of this study is to assess the effectiveness and safety of ACC neuromodulation for the treatment of the thalamic pain syndrome (TPS), a chronic neuropathic disease often complicated by severe affective and emotional distress in the long term.

Method From January 2015 to April 2017, 5 patients with pure drug-refractory TPS underwent ACC deep brain stimulation (DBS) at our institution. Quantitative assessment of pain and health-related quality of life were performed 1 day before surgery and postoperatively at 6 and 18 months by using the numeric rating scale (NRS), the 36-item short-form health survey (SF-36), and the McGill pain and the EuroQol5-domain questionnaires.

Results Mean age at surgery was 56.2 years (range, 47–66). NRS score improved by 37.9% at 6 months (range, − 22.2 to − 80%) and by 35% at 18 months (range, − 11.1 to − 80%). At the last follow-up, one patient reported a relevant pain reduction (NRS 2), only complaining of mild pain poorly interfering with activities of daily living. Concomitant improvements in the McGill and EuroQol5-domain pain questionnaires, SF-36 total and sub-item scores were also noticed at each follow-up. No surgical or stimulation-related complications occurred during the study period.

Conclusions ACC DBS may be a safe and promising surgical option to alleviate discomfort and improve the overall quality of life in a patient affected by drug-resistant TPS. Further prospective, larger, and randomized studies are needed to validate these findings.

Keywords Thalamic pain syndrome · Dejerine-Roussy syndrome · Neuropathic pain · Deep brain stimulation

Introduction

Thalamic pain syndrome (TPS), previously known as Dejerine-Roussy syndrome, is a rare chronic neuropathic disease caused by lesions of somatosensory thalamic nuclei or spino/trigemino-thalamic pathways [8, 14]. TPS is characterized by bothersome thermal dysesthesias, allodynia, and unrelenting pain often associated with the onset of severe emotional and affective distress in long term [24]. About 8–12% of thalamic strokes and traumatic and iatrogenic injuries will result in TPS-related pain within the first year [32]. The results of current conservative treatments for TPS remain questionable. The syndrome is highly refractory to the commonly available analgesics, while other potential pharmacological alternatives are still poorly studied [4, 9, 14, 22, 32].

Although the exact physiopathology background of TPS is still largely unknown, it is thought that lesions interfering with spinothalamic, trigemino-thalamic, and thalamo-cortical network (lateral pain system) may result in an abnormal sensitive signal processing and filtering [9, 12, 19, 32]. Besides lateral pain system dysfunction, TPS may also be accompanied by metabolic changes in areas involved in the affective and

This article is part of the Topical Collection on *Functional Neurosurgery - Pain*

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emotional components of pain. As far as pain's empathic and affective dimension is concerned, imaging and neurophysiological evidences have pointed out the key-role of the dorsal anterior cingulate cortex (ACC; Broadmann area 24) [26]. Positron emission tomography (PET) and functional MRI studies have consistently demonstrated the activation of the human ACC in relation to empathic and experienced pain, while PAG and VPL/VPM DBS have been shown to partially exert their analgesic effect by modulating ACC activity [13, 17, 21, 23, 25, 31]. In addition, ACC hypoactivity has been also shown in those patients affected by central pain due to Wallenberg syndrome experiencing post-stroke allodynia [18]. All these findings, along with the historical good results reported for cingulotomy in the treatment of refractory cancer pain, opened up the way to the possibility of ACC electrical modulation for the relief of intractable neuropathic disorders [28]. In 2007, Spooner and colleagues were the first to pioneer high-frequency electrical stimulation of ACC with good results in a patient who had developed a severe drug-resistant pain syndrome after a complete spinal cord injury at the C-4 level [29].

More recently, Boccard et al. showed ACC DBS effectiveness in terms of emotional distress reduction and quality of life improvement in a series of 22 patients affected by heterogenous neuropathic pain syndromes involving both the central and peripheral nervous system [3]. Given the previous neurophysiological considerations and the promising data reported by the abovementioned studies, we thought to apply ACC DBS in a cohort of 5 patients suffering only from well-defined TPS. All these patients suffered from ischemic or iatrogenic thalamic injuries, with consequent development of a drug-refractory painful syndrome involving the contralateral side of the body. Patient-reported outcome measures of pain and quality of life were analysed, and results of ACC DBS for pain and TPS are then discussed.

Materials and methods

Patients selection

From January 2015 to April 2017, 5 patients with TPS were referred to our institution. The following inclusion criteria were considered to identify patients suffering from pure drug-resistant TPS: (1) development of severe contra-lateral pain and/or allodynia with onset at or after thalamic stroke, traumatic injury, or iatrogenic insult; (2) MRI-confirmed lesion affecting the thalamus with or without brain stem involvement; (3) chronic neuropathic pain refractory to at least 3 classes of analgesic medications for at least 2 years; and (4) no other organic substrate for pain [7]. Exclusion criteria included psychiatric disorders and medical contraindications to surgery such as coagulopathy or ventriculomegaly. Informed consent was obtained from all the patients, after a thorough counselling aimed at explaining the off-label nature of the study and the possibility that DBS might have provided no benefit. Our ethical committee approved this study.

Surgical procedure

The method applied for imaging, planning, and implantation was previously extensively reported in the literature [6]. The brain target chosen was the one previously described by the group from Oxford for chronic neuropathic pain (20 mm posterior to the anterior tip of the frontal horns of the lateral ventricles). Similarly, the trajectory was planned in order to place the contacts mostly in the cingulum bundle, with the deepest contact in the corpus callosum [2].

Surgery was always performed bilaterally under stereotactic conditions and general anaesthesia using the Maranello frame (Maranello, Maranello, Italy) and without intraoperative testing, micro-recordings, or trial period. A non-rechargeable internal pulse generator (Activa PC, Medtronic USA) was initially placed in all cases. A post-operative CT merged with the pre-operative MRI was used immediately after surgery to confirm the electrode correct positioning. Eventually, the position in the Montreal Neurological Institute (MNI) space of all DBS leads was checked and three-dimensionally reconstructed by the Lead-DBS Matlab toolbox [11]. The initial parameters of stimulations at 2 V, 130 Hz, and 450 μs across all 4 lead contacts with the case as anode were set in all cases.

Outcome assessment

Quantitative assessment of pain and health-related quality of life were performed 1 day before surgery and postoperatively at 6 and 18 months by an independent, blinded trained psychologist (R.C) unaware of the details regarding the electrical parameters given. The numeric rating scale (NRS) was used to rate pain intensity [10]. NRS consists of an 11-point scale ranging from 0 (no pain) to 10 (the worst pain one can imagine). Pain severity was then categorized as the following: mild pain interfering little with activities of daily living (NRS scores 1–3); moderate pain interfering significantly with activities of daily living (NRS scores 4–6); and severe pain completely impairing activities of daily living (NRS scores 7–10).

Patients were submitted both pre-operatively and at each follow-up visit to the Italian version of the 36-item short-form health survey (SF-36) on quality of life, the McGill pain questionnaire, and the EuroQol5-domain questionnaire [1]. The SF-36 responses were regrouped into 8 domains: physical functioning, physical role, body pain, general health, vitality, social functioning, emotional role, and mental health. The SF-36 total score was then calculated for each patient.

Results

Patient baseline characteristics

Patient baseline demographics, pain characteristics, and pre-operative pharmacological burden are shown in Table 1. All patients suffered from pain severely impairing activities of daily living, with an overall mean pre-operative NRS score of 8.6 (range, 7–10), a mean SF-36 total score of 301.2 (range, 229–343), a mean McGill pain questionnaire score of 48.8 (range, 32–56), and a mean EQ-5D pain questionnaire score of 7.8 (range, 7–8).

Causes of pain were in all cases thalamic ischemic lesions arisen as a consequence of the following: surgical removal of thalamic cavernoma (2 cases), thalamic abscess (1 case), giant cerebellopontine angle epidermoid (1 case), and endovascular embolization of an intracranial dural arteriovenous fistula (1 case). Mean pain duration was 5 years (range, 3–7). In 3 patients, pain was localized in the whole contra-lateral hemi-body. In the 2 remaining subjects, pain was almost referred to the contra-lateral hemi-facial region, with mild and erratic irradiation to the upper and lower limbs. These two patients had previously undergone unsuccessful percutaneous radiofrequency rhizotomy and motor cortex stimulation (MCS), respectively.

Clinical outcome

Post-operative outcomes are presented in Table 2. NRS score improved by 37.9% at 6 months (range, − 22.2 to − 80%) and by 35% at 18 months (range, − 11.1 to − 80%). At the last follow-up, one patient reported a significant pain reduction (NRS 2), only complaining of mild pain poorly interfering with activities of daily living. Concomitant improvements in the McGill and EuroQol5-domain pain questionnaires, SF-36 total scores, and sub-items were also noticed in all patients at each follow-up (Table 3). Mean stimulation parameters at the last follow-up were 4.5 V (range, 4–5.5 V), 130 Hz, and with a pulse width of 450 μs on all 4 lead contacts with the case as an anode. No surgical or stimulation-related complications were observed during the immediate post-operative period and the follow-up. Three-dimensional lead reconstruction showed correct placement in the MNI space for all the 10 electrodes (Figs. 1 and 2). At the IPG end-of-service, all the five patients asked to have their IPG replaced, three of them opting for an

Table 1 Patients' demographic and pre-operative characteristics

Patient	Sex	Age at surgery (years)	Previous surgical treatments	Pharmacological therapy	Pain		Symptoms duration (years)
					Location	Cause	
1	M	47	None	Gabapentin Tramadol Levetiracetam Tapentadol Amitriptyline	Left hemi-body	Right haemorrhagic thalamic angioma	7
2	M	66	ITM	Pregabalin Fentanyl Lidocaine patch Amitriptyline	Right hemi-body	Left thalamic cerebral abscess	3
2	F	58	None	Paroxetine Amitriptyline Gabapentin	Left hemi-body	Right thalamic infarction during the removal of a right temporal-insular cavernous hemangioma	6
4	M	46	MCS	Pregabalin Duloxetine Carbamazepine Gabapentin Buprenorphine Clonazepam Midazolam	Right hemiface with occasional hemi-body involvement	Left thalamic-pontocerebellar epidermoid cyst	5
5	M	62	Trigeminal PRZ	Duloxetine Tramadol Carbamazepine Clonazepam Oxycodone/naloxone Valproate	Right hemiface with occasional hemi-body involvement	Left capsule-thalamic ischemia following endovascular embolization of a ruptured tentorial dural fistula	4

NRS, numerical rating scale; *ITM*, intrathecal morphine; *MCS*, motor cortex stimulation; *PRZ*, percutaneous radiofrequency rhizotomy

Table 2 Baseline and post-operative values of NRS, SF-36 sub-items, SF-36 total scores, McGill pain questionnaire, and EQ-5D questionnaire

Patient	Follow-up (months)	NRS	McGill pain questionnaire	Physical functioning	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health	Short-form 36 total	EuroQol 5-domain questionnaire	Pharmacological therapy
1	Pre-operative	7	32	35	15	22	45	20	25	34	64	321	8	See Table 1
	6	5	34	44	17	22	60	35	62	34	72	422	8	Duloxetine, clonazepam
	18	5	34	62	17	41	30	40	25	24	48	312	8	Duloxetine, clonazepam
2	Pre-operative	9	56	30	28	22	30	25	12	24	36	343	7	See Table 1
	6	7	40	30	28	30	45	35	37	24	44	334	5	Unchanged
	18	7	50	70	28	22	45	70	62	24	44	325	5	Unchanged
3	Pre-operative	10	50	20	28	22	20	35	25	55	44	302	8	See Table 1
	6	7	42	40	35	22	30	60	25	45	48	366	6	Unchanged
	18	7	52	35	28	22	30	35	50	34	32	266	8	Unchanged
4	Pre-operative	7	56	24	24	22	55	25	12	24	60	311	8	See Table 1
	6	5	51	22	22	41	60	35	37	24	60	372	5	Unchanged
	18	6	42	22	22	22	45	20	25	24	32	212	5	Unchanged
5	Pre-operative	10	50	35	17	22	30	20	0	24	32	229	8	See Table 1
	6	2	33	35	45	42	35	30	37	55	40	379	6	Unchanged
	18	2	20	80	49	61	30	55	50	55	60	440	4	Carbamazepine Clonazepam Duloxetine

Table 3 Improvement rates of SF-36 sub-items, SF-36 total scores, McGill pain questionnaire, and EQ-5D questionnaire at 6 and 18 months for the entire cohort

Follow-up (months)	NRS	McGill pain questionnaire	Physical functioning	Role physical	Bodily pain	General health	Vitality	Social functioning	Role emotional	Mental health	Short-form 36 total	EuroQol5-domain questionnaire
6	− 37.9%	− 16.2%	+ 23.5%	+ 38.9%	+ 42.7%	+ 31.8%	+ 55.3%	+ 92.3%	+ 22.2%	+ 13.8%	+ 23.7%	− 23.2%
18	− 35%	− 17.1%	+ 81.1%	+ 38.6%	+ 52.7%	+ 9.7%	+ 87%	+ 92.3%	+ 12.3%	+ 2.1%	+ 4.1%	− 23.2%

upgrade with a rechargeable device (ACTIVA RC - Medtronic Inc. Minneapolis, MN, USA).

Summary of the cases

Case 1 A 47-year-old man underwent surgical removal of a right thalamic-insular cavernous angioma at our institute 7 years before, with immediate post-operative onset of a left hemiparesis associated with thermic dysesthesia, hyperalgesia, and constant burning sensation. After a short period of physical therapy, the motor deficit markedly improved, while pain remained unchanged, heavily interfering with the patient's daily activities. Extensive medical treatment (gabapentin, pregabalin, oxycodone, duloxetine, topiramate, amitriptyline, tapentadol, tramadol) was ineffective. At the last follow-up after ACC DBS, the patient reported minimal benefit from the stimulation on pain intensity (− 28%) and a slight improvement of overall physical and mental wellness. Yet, when the patient was asked whether he wanted to have the IPG replaced or not, he decided to proceed with the replacement.

Case 2 A 66-year-old man, presenting with progressive alteration of consciousness, right hemiparesis, and hyperpyrexia, urgently underwent surgical evacuation of a cerebral abscess in the region of the left internal capsule and thalamus. After 3 months of intensive physical therapy, he complained of an intermittent freezing painful sensation involving his entire right hemi-body which was usually followed by anaesthesia dolorosa, only relieved by sleep (4–5 episodes per day). After a few months, the pain was chronically present in daytime. The patient was then referred to a pain clinic and lidocaine patches, pregabalin, fentanyl, and tapentadol were uselessly administered. Then, the patient underwent ACC DBS. After 18 months of stimulation, despite the small decrease in pain intensity (NRS 9 to 7), the patient stated that he was no longer worried about his condition, due to the fact that he was finally able to bear the uncomfortable cold sensation.

Case 3 A 58-year-old woman had a 6-year history of mild paresis and constant pain in the left hemi-body. Symptoms developed immediately after a contra-lateral thalamic-capsular infarction, occurring during the removal of a right temporal-insular cavernous haemangioma. The pain was described as continuous, intense (NRS 10), with some occasional cold dysesthesias, and responsible for a severe emotional distress and fatigue. No triggering or relieving factors were reported. Several therapeutic cycles of different analgesics had no effect on pain. At the last follow-up after ACC DBS, the patient still suffered from severe and relentless pain (NRS 7), but a great improvement in her vitality SF-36 sub-score was noticed (+ 71%). She reported to endure the fatigue better, which led her to partially return to her daily life activities.

Case 4 A 46-years-old man had a long history (5 years) of neuropathic pain, which was initially reported after the removal of a recurrent giant left thalamic-pontocerebellar epidermoid cyst. Symptoms, involving the entire right hemiface with sporadic irradiation to the remaining hemisoma, were characterized by persistent high-intensity burning pain, worsened by any abrupt change in temperature. After several cycles of unsuccessful pain management drug therapies, the patient first underwent motor cortex stimulation in 2014 without benefit and eventually bilateral ACC DBS. At the 18-month follow-up, the pain symptoms were almost unchanged, with only a small decrease in pain intensity (− 14.3%). A better social functioning was reported though, as confirmed by the improvement in the relative SF-36 sub-score.

Case 5 A 62-year-old man underwent urgent endovascular embolization of a ruptured tentorial dural fistula in 2012. The post-operative course was complicated by a vast left capsule-thalamic ischemia with consequent severe right hemiparesis requiring an intensive rehabilitation program. During the physical therapy, he gradually developed ceaseless burning painful paraesthesias, allodynia, and reduced cold sensation in the right hemiface, with occasional episodes of brachio-crural involvement (2–3 times per day). These symptoms prevented the patient from continuing his physical therapy. No pain relief was achieved with either medical treatment (gabapentin, carbamazepine, oxycodone, valproate, duloxetine, clonazepam) or percutaneous trigeminal radiofrequency thermal lesioning. The patient was then submitted to ACC DBS. After 18 months, a relevant decrease in pain intensity (− 80%) and marked improvement of social

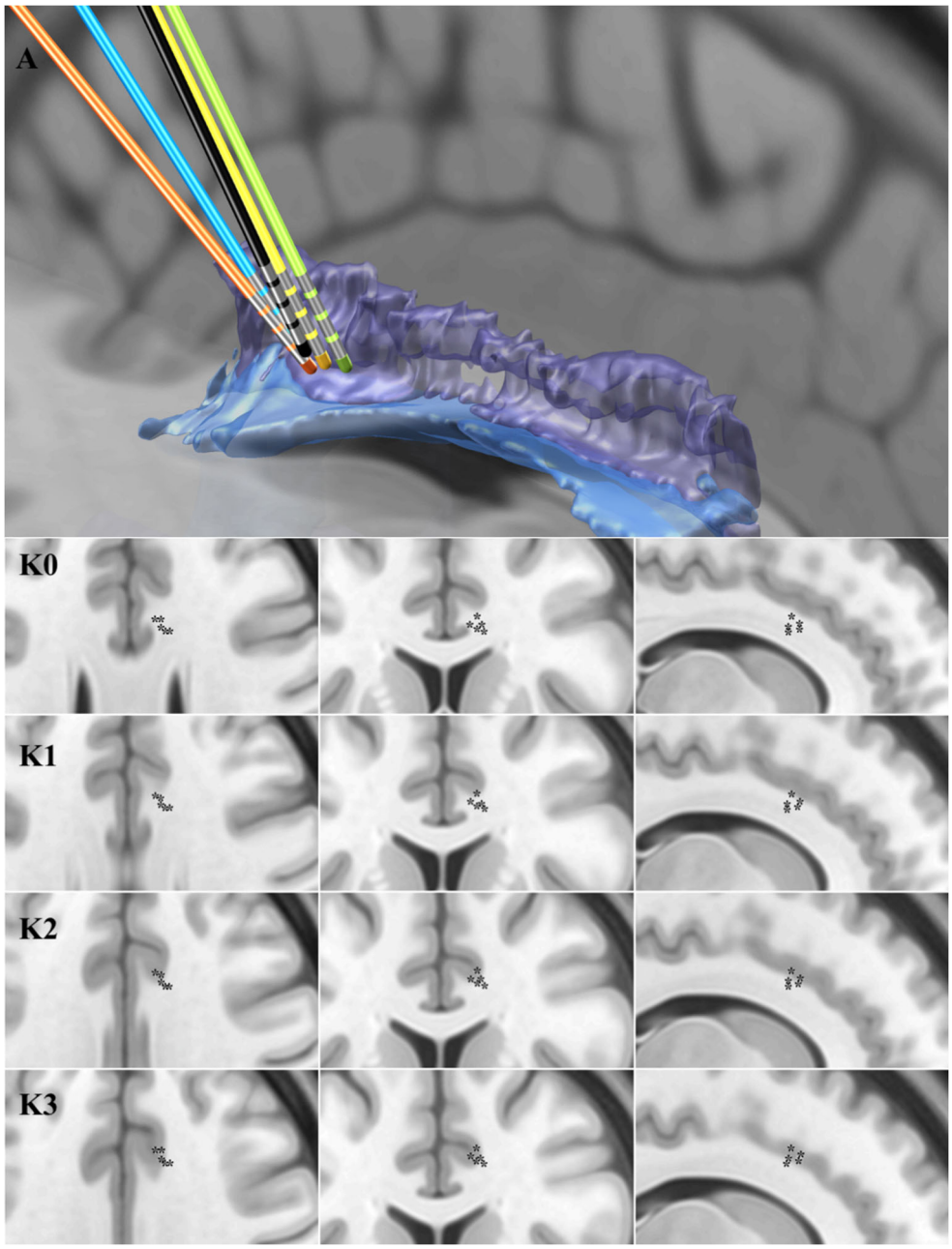

Fig. 1 **Panel A** Three-dimensional reconstruction of the five left leads, showing their correct placement in the cingulum bundle (blue, corpus callosum; purple, cingulate cortex). **Panel K0** Axial, coronal, and sagittal T1 MRI showing position of contact 0 for all patients (black asterisks). **Panel K1** Axial, coronal, and sagittal T1 MRI showing position of contact 1 for all patients (black asterisks). **Panel K2** Axial, coronal, and sagittal T1 MRI showing position of contact 2 for all patients (black asterisks). **Panel K3** Axial, coronal, and sagittal T1 MRI showing position of contact 3 for all patients (black asterisks)

functioning and body pain SF-36 sub-scores were observed. The patient was then keen on resuming his physical therapy program.

Discussion

In our case series, we observed a slight pain intensity reduction after ACC DBS at 6 months (− 37.9%) and 18 months (− 35%). Although with this poor decrease in pain intensity, several aspects should be considered to possibly encourage the use of DBS in such patients. First of all, the entire cohort asked to maintain the stimulation ON and to have the IPG replaced. Moreover, 3 of them opted for an upgrade to a rechargeable device. Secondly, two patients were able to reduce their pain medications over time (Table 2). As already suggested by Boccard and colleagues, we believe these improvements might be explained by the changes in the way patients "experienced" and "got used" to their pain [3]. After 18 months of ACC DBS, in fact, they still referred to their symptoms as quite intense during the day, but now the pain was perceived with less emotional distress. It was then neither a cause of suffering nor it interfered with patient activities of daily living because they were eventually able to neglect pain. Curiously,

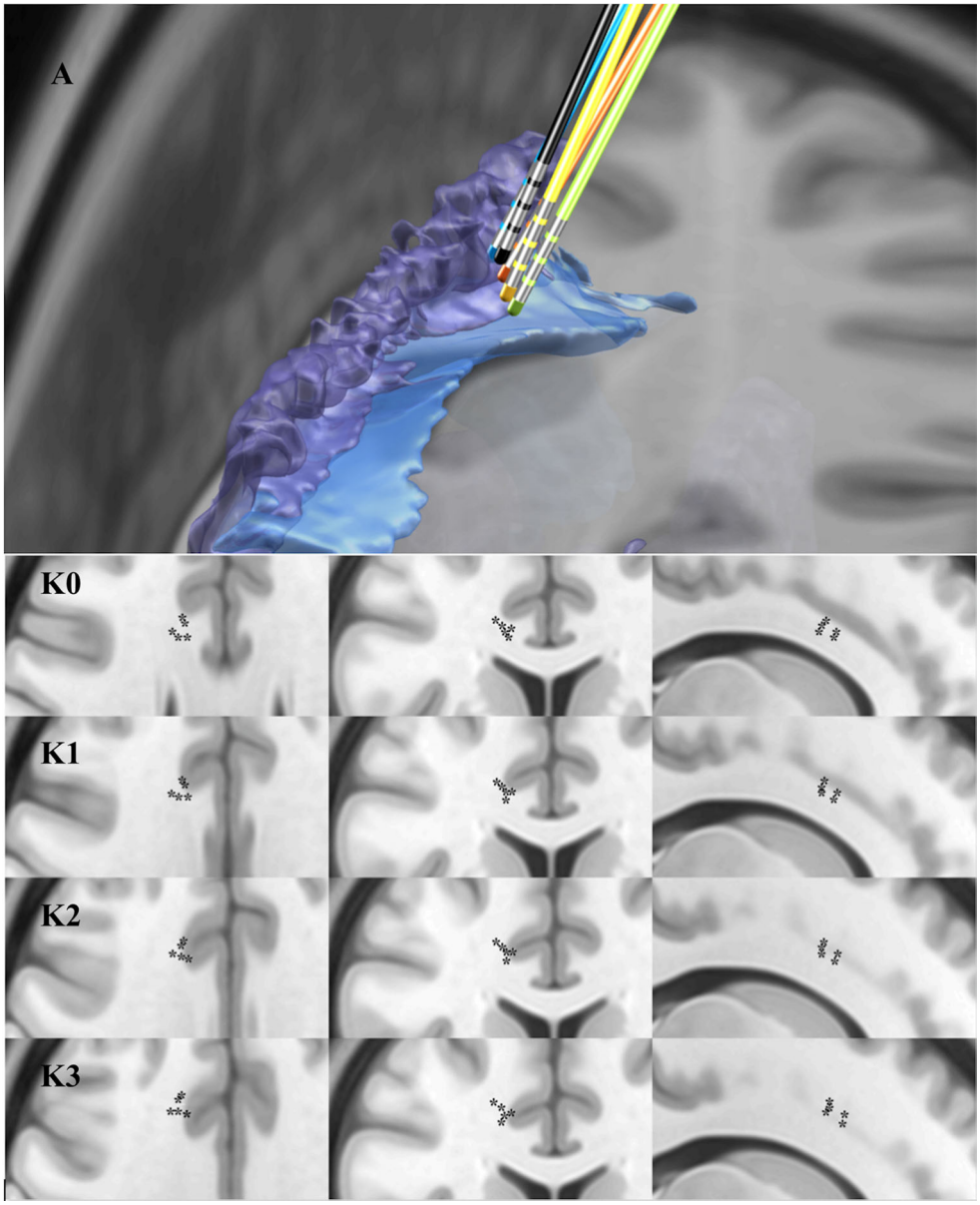

Fig. 2 **Panel A** Three-dimensional reconstruction of the five right leads, showing their correct placement in the cingulum bundle (blue, corpus callosum; purple, cingulate cortex). **Panel K0** Axial, coronal, and sagittal T1 MRI showing position of contact 0 for all patients (black asterisks). **Panel K1** Axial, coronal, and sagittal T1 MRI showing position of contact 1 for all patients (black asterisks). **Panel K2** Axial, coronal, and sagittal T1 MRI showing position of contact 2 for all patients (black asterisks). **Panel K3** Axial, coronal, and sagittal T1 MRI showing position of contact 3 for all patients (black asterisks)

these statements are quite similar to those used by Foltz and White to describe the effect of cingulotomy [5]. This change in pain affective perception was also confirmed by relevant concomitant improvements at 18 months in the physical functioning (+ 81.1%), vitality (+ 87%), and social functioning (+ 92.3%) sub-items of the SF-36.

To the best of our knowledge, only 9 patients with TPS have been treated with electrodes in the ACC so far (Table 4). All these patients were included in the prospective long-term study recently published by Boccard et al. [3]. Five of them (55.5%) experienced a significant reduction in the McGill pain questionnaire scores (from 39.4 to 34.0, $p = 0.028$) at the 6-month follow-up, with a generalized loss of efficacy in the long term (mean follow-up, 39.6 months).

Interestingly, in the series from Oxford, four patients experienced seizures/epilepsy onset after long-term stimulation, two of whom suffered from breakthrough seizures despite being off-stimulated and taking anti-epileptics [3]. Although the target location and patterns of stimulation were similar between the two studies, in our series, ACC neuromodulation has been proven safe, and we did not observe any stimulation-related adverse events or induced epilepsy. This difference might be explained taking into account several factors, such as the lower number of subjects included in our study, patients' different typology of pain and follow-up. Nevertheless, the relation between ACC stimulation and epilepsy deserves further considerations in our opinion. De novo seizure onset has been already described for cingulotomy indeed, but never after

Table 4 Characteristics and follow-up of the nine patients with TPS treated so far by ACC DBS

Patient	Sex	Age at surgery (years)	Previous DBS	Pain cause	Pain location	Lead location	Follow-up available	NRS	McGill pain questionnaire	Short-form 36 total	EuroQol5-domain questionnaire	Complications	Outcome
1	M	50	Bilateral PVG	Post-stroke	Right hemi-body	Left ACC	Baseline	6	N/A	N/A	N/A	Infection	DBS removed after 4 months—no pain relief
2	M	72	No	Post-stroke	Right hemi-body	Left ACC	Baseline	8	N/A	N/A	N/A	None	IPG not implanted because unsuccessful trial
3	F	42	Bilateral PVG/VPL	Post-stroke	Right leg	Bilateral ACC	Baseline	8	N/A	N/A	N/A	None	DBS removed after 3 months because of patient's poor compliance
4	M	53	No	Post-stroke	Right hand	Bilateral ACC	Baseline	8	31	223	6	Infection	DBS removed after 2 years
							5 months	10	28	186	6		
							18 months	N/A	31	182.7	6		
5	M	63	No	Post-stroke	Right hemi-body	Bilateral ACC	Baseline	9	40	185	6	None	Initial improvement for 6 months, with recrudescence at the last follow-up
							6	5	17	214	6		
							12	8	42	214	6		
							36	9	43	173	7		
							42	8	44	206	7		
6	M	58	No	Post-stroke	Left arm and chest	Bilateral ACC	Baseline	6	23	195	7	Seizures	Pain free for 1 year before pain returned
							6	1	0	238	2		
							12	3	14	285	6		
							36	3	3	220	4		
							42	3	7	259	5		
7	M	48	Right PVG	Post-stroke	Right hemi-body	Bilateral ACC	Baseline	5	57	284	5	None	Good pain relief for 1 year before pain recrudescence
							6	1	30	234	4		
							12	3	49	282	4		
							36	6	27	251	4		
							42	7	9	N/A	N/A		
8	M	71	No	Post-stroke	Left arm	Bilateral ACC	Baseline	6	N/A	N/A	N/A	Absence seizures	DBS OFF after 12 months
9	M	56	No	Post-stroke	Face	Bilateral ACC	Baseline	10	46	215	9	None	Good pain relief, but DBS OFF after 20 months because patient unable to manage device
							6	0	N/A	N/A	N/A		
							24	8	N/A	202	8		
							36	8	54	219	5		

DBS stimulation of any other brain target, thus confirming the potential epileptogenic role of the cingulum itself [28]. One potential explanation could be found considering that the cingulum is part of the Papez or limbic circuit. It receives projection from the anterior thalamic nuclei, interconnecting the cingulate cortex with the ventral hippocampus (entorhinal cortex) [27]. Both these structures, the anterior thalamic nuclei and the entorhinal cortex, are often involved in epileptogenic mechanisms [15, 20]. Thus, lesion or stimulation of the cingulum may induce organic or functional modifications in an epilepsy-prone electrical network. Supporting this hypothesis, a DTI study showed that patients with intractable temporal lobe epilepsy are associated with a bilateral reduction of cingulum association fibres projecting from the cingulate cortex to the entorhinal cortex [30]. If these speculations were confirmed by further research or clinical studies, an ethical dilemma regarding the risk-benefit ratio of ACC stimulation should be taken into consideration [16].

This study has several strengths. First of all, this is the first case series evaluating ACC DBS in a cohort of patients suffering only from well-defined TPS, with a homogeneous preprocedural evaluation and follow-up. Moreover, the prospective nature of the study and the use of objective pain measurement scales allowed a careful evaluation of all pain's different aspects. On the other hand, there are some limitations that need to be considered, such as the lack of an appropriate control group. Without any case-control and randomization, it is not possible to rule out a placebo effect of the procedure indeed. In addition, the number of consistency of the sample analysed was not sufficient to allow any statistical comparison and consequently to draw any definitive conclusions. Given these drawbacks, which are partially due to the rarity of the disorder treated, our results need to be interpreted with caution.

Conclusions

This prospective case series shows that ACC DBS may be a safe and promising surgical option to alleviate discomfort in patients affected by drug-resistant TPS by improving their overall quality of life. Further prospective, larger, and randomized studies are needed to validate these findings.

Statement of authorship VL and RC contributed to the conception and design of the article, to the data acquisition, analysis, and interpretation. All the other authors were involved in critically drafting/revising the article for important intellectual content. Finally, they all gave final approval of the version to be published.

Compliance with ethical standards

Conflict of interest Vincenzo Levi is a medical advisor at NEWRONIKA SRL (deep brain stimulation internal pulse generator manufacturer). All the authors declare that they have no financial or other conflicts of interest in relation to this research and its publication. The authors also declare that they received no specific funding for this work.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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