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CASE REPORT

# Treatment of Hemichoreoathetosis with Arrhythmic Proximal Tremor after Stroke: The Role of Zona Incerta as a Target for Deep Brain Stimulation

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## ABSTRACT

Deep brain stimulation (DBS) of the zona incerta has shown promising results in the reduction of medically refractory movement disorders. However, evidence supporting its efficacy in movement disorders secondary to hemorrhagic stroke or hemichoreoathetosis is limited. We describe a 48-year-old man who developed progressive hemichoreoathetosis with an arrhythmic, proximal tremor in his right arm following a thalamic hemorrhagic stroke. Pharmacological treatment was carried out with no change in the Abnormal Involuntary Movement Scale (AIMS) score after 4 weeks (14). After six sessions of botulinum toxin treatment, a subtle improvement in the AIMS score (13) was registered, but no clinical improvement was noted. The arrhythmic proximal movements were significantly improved after DBS of the zona incerta with a major decrease in the patient's AIMS score (8). The response to DBS occurring after the failure of pharmacological and botulinum toxin treatments suggests that zona incerta DBS may be an alternative for postthalamic hemorrhage movement disorders.

**Key Words** Deep brain stimulation; zona incerta; hemorrhagic stroke; arrhythmic proximal tremor; hemichoreoathetosis; chorea.

Intracerebral hemorrhage is the second leading cause of stroke with thalamic involvement varying from 6% to 25% of all cases. Movement disorders are uncommon complications of intracerebral hemorrhage, but their frequency tends to be higher when thalamic and subthalamic areas are affected.[1]

The pathophysiology of hyperkinetic movement disorders after infarction or hemorrhagic cerebral lesions remains uncertain. A few authors have hypothesized an association between monoamine over-activity and cholinergic deficiency, but no consensus has yet been reached.[2]

Although the most frequent motor disorder following thalamic lesions is focal hand dystonia, other involuntary movements such as ballism, chorea, and athetosis have been described.[3] These conditions usually manifest in days to months after the thalamic lesion, and the pharmacological management of these conditions tends to be insufficient, leaving a residual disorder that persists despite the improvement of other deficits.[2]

Deep brain stimulation (DBS) has shown promising results

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in the reduction of medically refractory movement disorders in both primary (e.g., Parkinson's disease, essential tremor, Tourette syndrome) and acquired conditions (e.g., ischemic stroke).[4] However, evidence supporting the efficacy of DBS in movement disorders secondary to hemorrhagic stroke is still limited.

This report describes a patient with hemichoreoathetosis and arrhythmic proximal tremor secondary to a thalamic hemorrhagic stroke; the patient did not respond to clinical treatment or therapy with botulinum toxin but exhibited a substantial improvement in hyperkinetic symptoms after undergoing DBS of zona incerta.

## CASE REPORT

A 48-year-old man with long-term hypertension and dyslipidemia presented with right hemiparesis and sensory loss. Clinical examination revealed moderate right hemiparesis with hemihypesthesia and mild dysarthria. A CT scan at the time showed a left thalamic hematoma involving the posterior thalamic region with compression and dislocation of the third ventricle to the opposite side (Figure 1).

Cardiovascular evaluation revealed moderate left atrium enlargement and moderate diastolic dysfunction. Laboratory tests performed at the time were within normal limits.

Forty-five days after hospital admission, the patient's motor and sensory deficits improved significantly. He continued to display subtle dysarthria but began to present progressive involuntary choreoathetoid movement in his right arm. The movement was arrhythmic and hyperkinetic, with a low frequency (2–3 Hz) and large amplitude. This continuous movement occurred in distal and proximal regions; the movement improved but did not disappear with the rest. In addition, it worsened with actions of the arm, and it presented associated dystonic and myoclonic components as well as moments that resembled ballism. The patient's right hand showed more choreic finger movements; however, this could have been pseudoathetosis because the patient still had sensory deficits. The patient had no control of these abnormal movements but noticed exacerbation by anxiety. The patient's Abnormal Involuntary Movement Scale (AIMS) at that time was 14.

After a week, a new re-evaluation showed persistent movement disorder. Risperidone and haloperidol were administered,

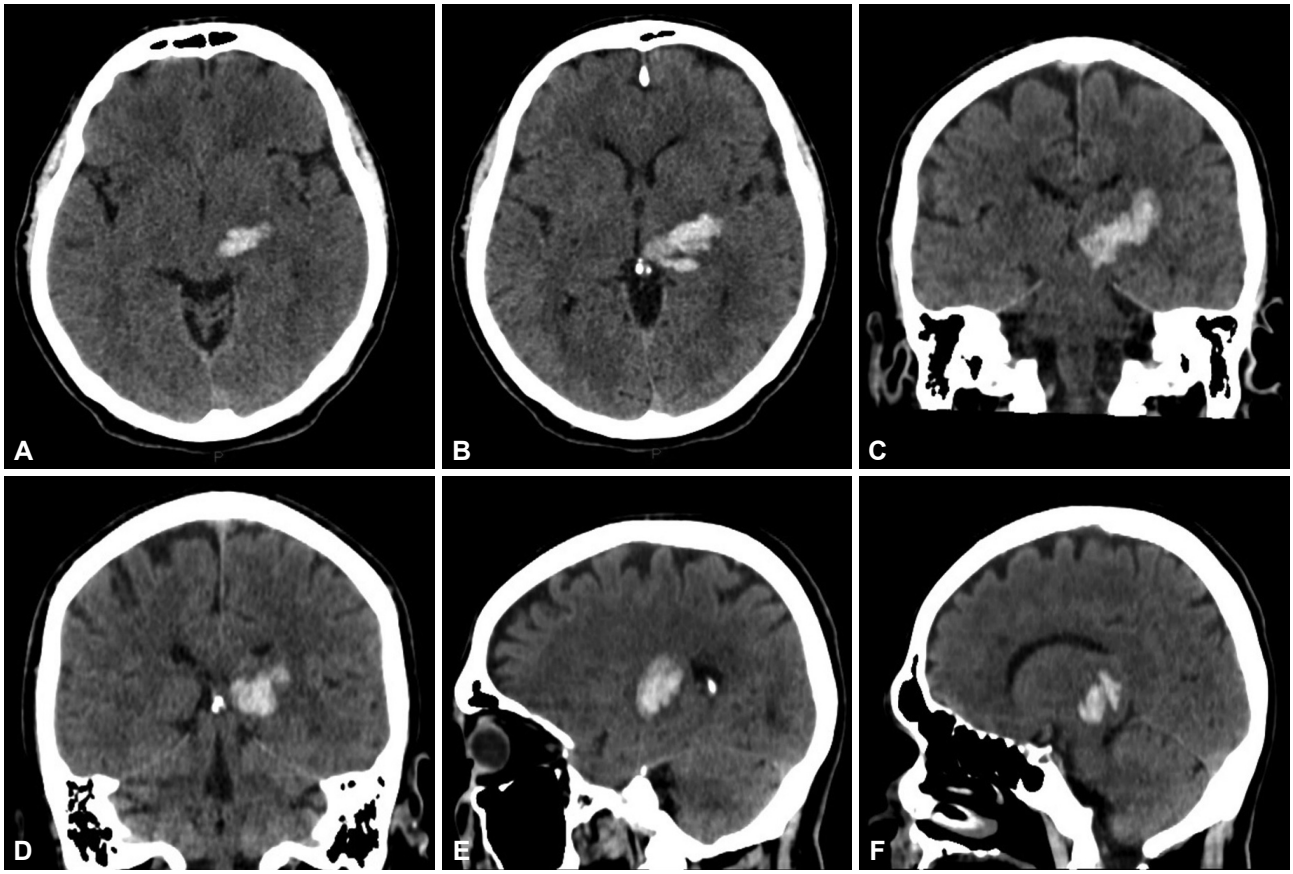


**Figure 1.** CT scans show a hematoma in the left lobe involving the posterior thalamic region as well as mild compression and dislocation of the third ventricle. A and B: axial view, C and D: coronal view, E and F: sagittal view.

but there was no improvement in the AIMS score (14). Due to inadequate clinical response and severe functional impairment, treatment with botulinum toxin was offered. The patient underwent 6 sessions of botulinum toxin therapy and was evaluated after each session to determine the level of improvement in the movement disorder. At the end of the treatment, there was only a subtle improvement in AIMS score (14 to 13). Therefore, no significant clinical improvement was noticed, and the patient's quality of life did not improve. No adverse effects were noted by the patient in any session. MRI performed 2 years after the stroke showed gliosis and attenuation of white matter extending from the left thalamus to a region between the subthalamic and the red nuclei (Figure 2A-D).

DBS of the zona incerta was then offered as an alternative for management of the movement disorder. Microelectrode recording was performed intraoperatively to redefine the structures surrounding the subthalamus. Typical activity of the left thalamus, zona incerta, subthalamic nucleus and substantia nigra was recorded. A St Jude DBS lead (Abbott St. Jude Medical DBS System, Austin, TX, USA) was implanted with the first electrode in the transition between the subthalamic nucleus and the zona incerta, and electrodes 2 and 3 were located in the zona incerta itself. This procedure was carried out unilaterally. A nonrechargeable pulse generator was implanted.

The patient then underwent a stereotactic CT on the day after frame removal for evaluation of electrode positioning (Figure 2E-J).

The device was turned on fifteen days after the surgery and tests were performed. At the first moment, a high frequency (190 Hz) and double monopolar stimulation appeared to offer

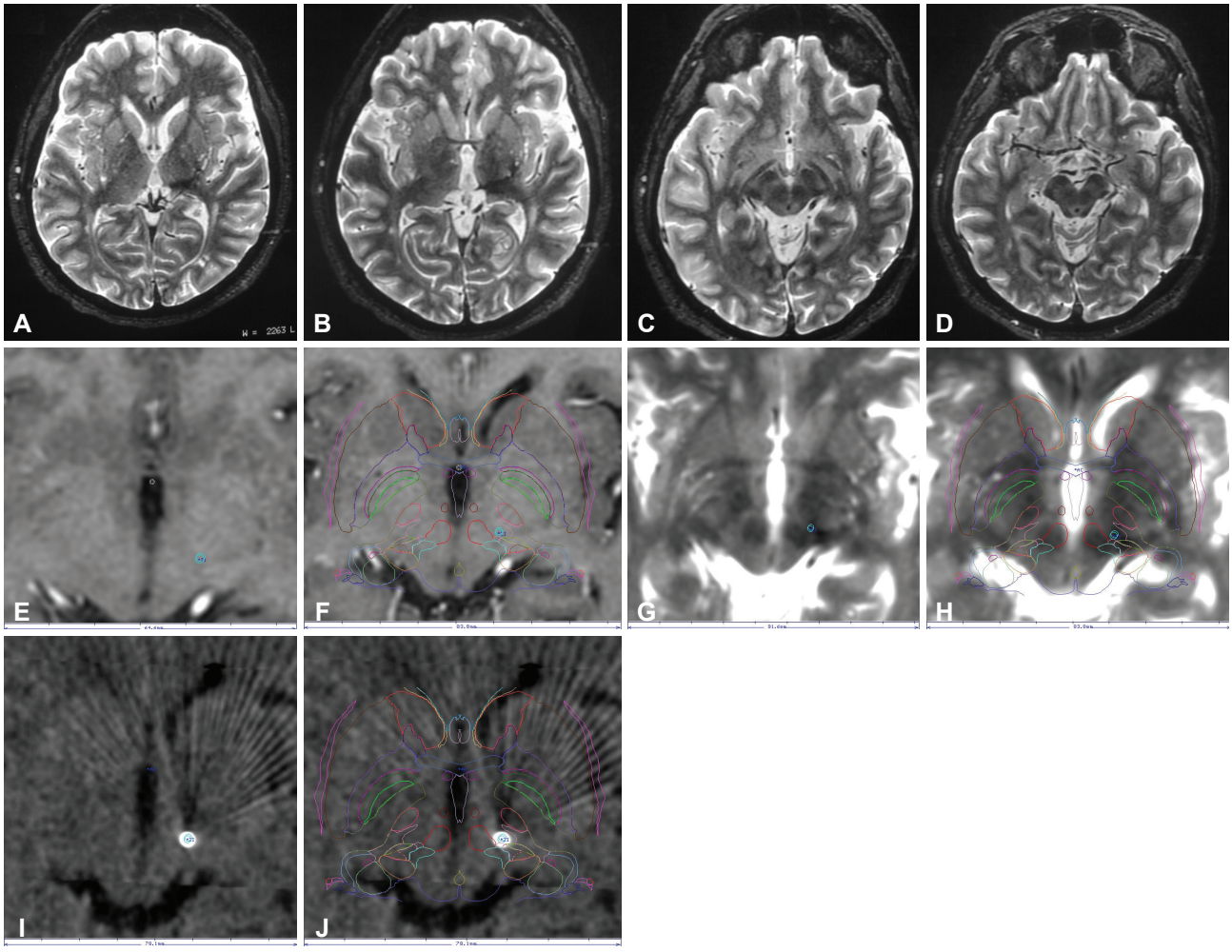


**Figure 2.** Brain imaging (MRI) 2 years after thalamic lesion. A-D: Axial T2-weighted sections of cranial MRI (1.5T; Siemens Symphony, Siemens Healthineers, Erlagen, Germany) show a posthemorrhagic lesion in the left thalamus with gliosis and attenuation of the white matter. E-J: Preoperative planning images and postoperative images showing lead location. E: Preoperative axial T1-weighted sections of cranial MRI showing the zona incerta as a target. F: Preoperative axial T1-weighted sections of cranial MRI fused with atlas showing the zona incerta as a target. G: Preoperative axial T2-weighted sections of cranial MRI showing the zona incerta as a target. H: Preoperative axial T2-weighted sections of cranial MRI fused with atlas showing the zona incerta as a target. I: Postoperative axial CT scan showing the lead location. J: Postoperative axial CT scan fused with atlas showing the lead location.

some response, while a lower frequency and single monopolar stimulation showed no improvement. A slight improvement was further noticed in the weeks following the start of the stimulation. In the follow up, the frequency was reduced to maintain a working battery. Nonetheless, the symptoms continued to improve despite the frequency reduction.

After the optimal stimulation parameters were reached, no side effects were observed. There was gradual suppression of movement. Remarkable improvement of the movement disorder was noticed from the sixty-sixth month onwards. Further improvement occurred in the following months. The patient did not present any side effects such as gait, speech disorder or weakness.

One year after the procedure, the symptoms abruptly recurred. The device evaluation indicated that the pulse generator battery was depleted. The patient was submitted to a new procedure to implant a rechargeable St Jude generator (Abbott St. Jude Medical DBS System). The generator was programmed the same way as before. The hemichoreoathetosis with arrhythmic proximal tremor slowly decreased in the following months, and optimal results were achieved six months after the generator replacement.

Evaluation performed at 1, 6, 12 and 24 months after the first surgery revealed a major improvement in the AIMS score (13 to 8) with a significant reduction in the patient's symptoms as noted at physical examination (Supplementary Video 1 in the online-only Data Supplement). The postoperative video was taken at 24 months after the surgery. The patient also reported an important change in his quality of life due to an improvement in his basic personal care (e.g., bathing, dressing and feeding). Three years after the first surgery there was no recurrence of symptoms.

This study obtained full informed consent from the patient for publication.

## DISCUSSION

Thalamic lesions, as in this case, have been previously associated with involuntary movement disorders, such as choreoathetosis and hemidystonia, which have been described in other studies.[2,4] According to Lee et al.,[5] the occurrence of both motor incoordination and tremor relies on the disturbance of data (peripheral sensory pathways, basal ganglia and cerebellum) transmitted from the thalamus to the cerebral cortex.

To our knowledge, this is the first study to describe DBS of the zona incerta in the treatment of hemichoreoathetosis with arrhythmic proximal tremor. The distinctive element of our case is the control of dyskinetic movements despite the failure of pharmacological and botulinum toxin treatments.

The target of choice for DBS in this case was particularly challenging due to the complexity of the patient's movement disorder and the lack of evidence on DBS treatment for hyperkinetic movement following intracerebral hemorrhage. However, recent studies have presented conflicting evidence regarding its use for movement disorders secondary to stroke. In two similar series[6,7] in which pallidal stimulation was performed after cerebral infarction, vastly conflicting outcomes were noted. Witt et al.[6] reported a limited benefit in all cases (nonsignificant increase or unsustainable improvement in Burke-Fahn-Marsden Dystonia Rating Scale motor score); Fuller et al.[7] noticed a major improvement in the patient's quality of life despite the large striatal infarction, with clear improvements in pain, amelioration of dystonic tremor, absence of trunk spasm, writing rehabilitation and normal speech.

The left thalamus itself would not have been a suitable target due to the formation of a glial scar in the area previously affected by the hematoma. It has been postulated that an area of glial scar tends to be electrically inactive; therefore, it is not a viable option for DBS.[8] Additionally, according to Fytagoridis et al.,[9] the disposition of white matter tracts in the posterior subthalamic area would make the zona incerta a more potent area for stimulation.

The choice of targeting the zona incerta was based on physiological knowledge, as the caudal portion of zona incerta is responsible for the generation of axial and proximal limb movements.[10] According to Fytagoridis et al.,[9] the caudal portion of the zona incerta transmits GABAergic input from the basal ganglia to the cerebello-thalamo-cortical circuits. Therefore, a targeted DBS in this area could downregulate or inhibit abnormal thalamic oscillations.

The data collected in this report suggests that chronic stimulation of zona incerta can provide long-term improvements to choreoathetoid movement following thalamic hemorrhage with no significant side effects. There is a latency period of some months until the zona incerta stimulation becomes effective in controlling hemichoreoathetosis with arrhythmic proximal tremor.

Further case studies and prospective multicenter studies in controlled scenarios are necessary to extend and validate the role of zona incerta as the target of DBS in similar scenarios.

### Supplementary Video Legends

Video 1. Preoperative and Postoperative footage of patient with hemichoreoatetosis after thalamic hemorrhagic stroke submited to Zona Incerta Deep Brain Stimulation.

### Supplementary Materials

The online-only Data Supplement is available with this article at https://doi.org/10.14802/jmd.18032.

## Conflicts of Interest

The authors have no financial conflicts of interest.

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