Neurosurgical treatment of spasticity: a potential return to the cerebellum

Daniel D. Cummins, MD, Hyun Joo Park, MD, and Fedor Panov, MD

Department of Neurosurgery, Mount Sinai Health System, New York, New York

Objective Neurosurgical targeting of the cerebellar dentate nucleus via ablative dentatotomy and stimulation of the dentate nucleus was historically used for effective treatment of spasticity. Yet for decades, neurosurgical treatment of spasticity targeting the cerebellum was bypassed in favor of alternative treatments such as intrathecal baclofen pumps and selective dorsal rhizotomies. Cerebellar neuromodulation has recently reemerged as a promising and effective therapy for spasticity and related movement disorders.

Methods In this narrative review, the authors contextualize the historical literature of cerebellar neuromodulation, comparing it with modern approaches and exploring future directions with regard to cerebellar neuromodulation for spasticity.

Results Neurosurgical intervention on the cerebellum dates to the use of dentatotomy in the 1960s, which had progressed to electrical stimulation of the cerebellar cortex and dentate nucleus by the 1980s. By 2024, modern neurosurgical approaches such as tractography-based targeting of the dentate nucleus and transcranial magnetic stimulation of cerebellar cortex have demonstrated promise for treating spasticity.

Conclusions Cerebellar neuromodulation of the dentate nucleus and cerebellar cortex are promising therapies for severe cases of spasticity. Open areas for exploration in the field include the following: tractography-based targeting, adaptive cerebellar stimulation, and investigations into the network dynamics between the cerebellar cortex, deep cerebellar nuclei, and the subcortical and cortical structures of the cerebrum.

https://thejns.org/doi/abs/10.3171/2024.3.FOCUS2446

Keywords spasticity; cerebellum; dentate nucleus; DBS; deep brain stimulation; neuromodulation; transcranial magnetic stimulation

Neurosurgical targeting of the cerebellar dentate nucleus for spasticity dates to the 1960s. Early reports of dentatotomy for spasticity yielded numerous important findings. Across several conditions treated by Siegfried et al., the best results were noted for cerebral palsy. The precise anatomical target within the dentate nucleus also proved to be critical, with optimal safety and efficacy noted with ventrolateral targets within the dentate nucleus. This original target was described as follows: “10mm behind the line tangent to the floor of the fourth ventricle, 5mm below the line perpendicular to the floor of the fourth ventricle passing through the apex of this structure, and 14mm lateral to the midline.” Overall, approximately 30% of patients who received a dentatotomy appeared to have a marked improvement, with 50% experiencing facilitation of rehabilitation with treatment. This principle of combined efforts between neurosurgical intervention and rehabilitation for synergistic clinical efficacy, founded in the 1960s with dentate nucleus lesioning, is one we see persisting to this day.

By the 1980s, electrical cerebellar dentate nucleus stimulation (DNS) was pursued more often than dentatotomy, offering the obvious advantages of adjustability and reversibility. Schvarcz described the efficacy of DNS in 22 patients after 2–6 years of follow-up, primarily for patients with cerebral palsy, but also for those with spasticity after traumatic brain injury and cardiac arrest. Although objective measures of spasticity and quality of life were not reported, after DNS, most patients were reported to have improvements in complex voluntary movements, posture, gait, speech, and respiration. Stimulation of the dentate nucleus also revealed objective changes in peripheral and central electrophysiology. These included improvements in the peripheral H reflex recovery curve and cortical silent...
period duration. While primarily occurring ipsilateral to stimulation, some bilateral effect was reported.\(^3\) DNS may therefore induce cortical plasticity that allows increased cortical descending inhibition of tonic muscle activation.

Surface cerebellar stimulation was also the subject of trials, with fair success in this period. In a report by Davis et al. on 262 patients with cerebral palsy, spasticity was found to improve in 90% of patients who received surface cerebellar cortex stimulation, resulting in notable improvements in feeding, dressing, and ambulation.\(^9\) Cooper et al. similarly implemented cerebellar cortex stimulation for effective spasticity reduction at approximately the same time period.\(^5\) Cerebellar cortex stimulation may activate Purkinje cells and subsequently inhibit target dentate nuclei (thus indirectly accomplishing the same outcome as direct DNS).\(^3\) However, the precise interactions between cerebellar cortex and DNS, and their clinical efficacy, remain to be explored.

By the 1990s and early 2000s, neurosurgical targeting (ablation or stimulation) of the cerebellum had fallen out of favor. This was due in part to alternative medical and neurosurgical interventions for spasticity, such as systemic and intrathecal baclofen,\(^6\) and the wide adoption of selective dorsal rhizotomies for spasticity.\(^7\) However, even with modern surgical approaches, dorsal rhizotomy carries a complication profile including scoliosis in more than 20% of pediatric patients, constipation in more than 10%, and a small risk of sensory changes or urinary incontinence.\(^8\) Similarly to the procedure itself, these complications are often irreversible. Although they are reversible, intrathecal baclofen pumps similarly carry high complication rates; 41% across the literature, including infection and device malfunction.\(^9\) To date, there thus remains a need for alternative neurosurgical approaches to spasticity.

**Modern DNS for Spasticity**

Recently, there has been a resurgent interest in cerebellar neuromodulation for movement disorders. In 2023, Baker et al. demonstrated a modern return to dentate nucleus neurosurgical targeting, but in this case for stroke, with changes in spasticity included as a secondary outcome.\(^10\) Spasticity was measured by the modified Ashworth scale (MAS), with scores ranging from 0 for no spasticity to 5 for complete joint rigidity. A median decrease in MAS score of 1.0 points (interquartile range [IQR] decrease of 2.0 points to no change) was noted with dentate nucleus deep brain stimulation (DBS) paired with rehabilitation, compared to a median increase of 0.5 points in MAS scores with rehabilitation alone (IQR decrease of 2.5 to increase of 1.5).\(^10\) In part due to a sample size of 10 and 8 patients (with and without DNS, respectively), no statistically significant treatment effects were detected. Notably, patients with severe spasticity (MAS score of 4 or higher) were excluded from this study. This limited the translatability of findings to patients with severe spasticity who would normally be considered for surgical intervention for the spasticity itself, and possibly hampered the statistical power to detect a treatment effect.\(^10\) Yet, a trend toward reduction in MAS score was seen with DNS plus rehabilitation compared to rehabilitation alone, based on the data presented by Baker et al.\(^10\) To demonstrate a statistically significant positive effect of DNS for spasticity, a larger sample of patients with severe spasticity may be necessary. Another study specifically evaluated patients with spasticity from cerebral palsy who were treated with deep anterior cerebellar stimulation. This work by Sokal et al. documented significant reductions in spasticity as measured by MAS scores from before to after cerebellar stimulation, in both the upper extremities (median 3–1.5, \(p = 0.01\)) and lower extremities (median 3–1.75, \(p = 0.02\)).\(^11\)

**Cerebellar Stimulation Parameters for Spasticity**

Stimulation parameters are a critical factor that may alter efficacy of DNS for spasticity. In their recent work targeting patients with stroke, Baker et al. used 30-Hz constant beta stimulation,\(^10\) motivated by animal models of stroke recovery.\(^12\) This differs from the high-frequency (100 Hz or higher) stimulation paradigms used historically for DNS,\(^13\) and in modern work successful use of deep cerebellar stimulation, with significant improvements in spasticity.\(^11\) It therefore appears that higher-frequency stimulation may be necessary for improvements in spasticity. Similar studies on cerebellar cortex stimulation for spasticity have also used high-frequency stimulation (100–200 Hz) for effective spasticity reduction.\(^4,5\) Presumably, both high-frequency cerebellar cortical stimulation and cerebellar DNS lead to dentate nucleus inhibition, which is relayed through the thalamus and then the cerebral cortex via the dentatorubrothalamic tract (DRTT). Modulation of this pathway may encourage increased cortical plasticity and inhibition of peripheral muscle activation, resulting in reduced spasticity.

Given that improvement in spasticity from cerebellar stimulation may be driven by adaptive changes in cortical plasticity, it stands to reason that adaptive stimulation could offer improved clinical efficacy, compared to static stimulation parameters. The availability of sensing-enabled pulse generators allows chronic local field potential recordings from stimulated structures, including the dentate nucleus. Cajigas et al. reported the first chronic dentate nucleus electrophysiology recordings over 57 days of stimulation, demonstrating reduced local field potential signal variability over time in recordings with stimulation.\(^14\) Access to such electrophysiology data and correlation of these data with clinical responses may help direct adaptive stimulation of the dentate nucleus for spasticity and other movement disorders. Adaptively modulating cerebellar stimulation parameters to optimize spasticity is an avenue of research that has not yet been explored. However, lessons from other movement disorders such as Parkinson disease suggest that adaptive stimulation could provide increased therapeutic efficacy over continuous, static stimulation parameters.\(^15\)

**Tractography-Based Dentate Nucleus Targeting**

Along with stimulation settings, the precise anatomic target may drastically affect clinical outcomes of DNS
for spasticity. Whereas early results with dentatotomy indicated better outcomes with ventrolateral targets, modern imaging tools allow much greater precision. Diniz et al. recently demonstrated the feasibility of tractography-based targeting of the dentate nucleus for treatment for ataxia, dystonia, and tremor. In this study, 3 patients were treated with a dentate nucleus target, aiming the tip of the stimulating lead near the DRTT. While not specifically used for spasticity, this study demonstrates the feasibility of tractography-based targeting. Cajigas et al. similarly demonstrated the clinical efficacy of DNS targeting near the DRTT for dystonic symptoms. Results from DBS for both movement disorders and psychiatric conditions have demonstrated that activation of specific white matter tracts with stimulation may be crucial to improving specific clinical symptoms. Prospective studies on clinical efficacy with tractography data incorporated may help further refine the optimal surgical target of cerebellar stimulation for spasticity.

Cerebellar Transcranial Magnetic Stimulation Improves Spasticity

As shown in earlier work by Cooper et al. and Davis et al., indirect modulation of the dentate nucleus and the DRTT through cerebellar cortex neuromodulation could permit similar clinical results to direct DNS, perhaps by less invasive methods. A recent randomized study by Chen et al. implemented intermittent theta-burst cerebellar transcranial magnetic stimulation (TMS) for spasticity. This study demonstrated significant improvements in MAS scores with cerebellar theta-burst TMS compared to sham stimulation. It remains an open area for investigation how this form of cerebellar neuromodulation affects deep cerebellar nuclei and downstream subcortical and cortical structures. However, these positive results further motivate a focus on cerebellar neuromodulation for spasticity and related movement disorders.

Conclusions

The cerebellum has long been a target of neurosurgical intervention for spasticity. Recent work has again demonstrated the promise of cerebellar neuromodulation for spasticity, both using direct invasive DNS and using methods such as noninvasive cerebellar TMS. Visual depictions of these approaches to cerebellar neuromodulation for spasticity and related neurological conditions are demonstrated in Fig. 1. Several areas of inquiry may yield improvement in cerebellar-based neuromodulation for spasticity, including tractography-based targeting, adaptive cerebellar stimulation, and investigations into the network dynamics between the cerebellar cortex, deep cerebellar nuclei, and subcortical and cortical structures of the cerebrum.

References


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

Author Contributions
Conception and design: Cummins, Panov. Acquisition of data: Cummins. Analysis and interpretation of data: Cummins. Drafting the article: Cummins, Panov. Critically revising the article: Park, Panov. Reviewed submitted version of manuscript: Park. Approved the final version of the manuscript on behalf of all authors: Cummins. Administrative/technical/material support: Panov. Study supervision: Panov.

Correspondence
Daniel D. Cummins: Mount Sinai Health System, New York, NY. daniel.cummins@mountsinai.org.