Clinical Case Reports

ISSN: 2675-3626

Combined Anteromedial and Posteroventral Radiofrequency Pallidotomy in the Management of Severe Generalized Dystonia and Aggressivity in Lesch-Nyhan Syndrome

Luciano Furlanetti, Bernardo Assumpção de Monaco, Fabio Okuda Furokawa, Guilherme Corsaletti Gregório, Jessie Navarro, Ana Tereza di Lorenzo Alho, Bianca Dalmaso, Eduardo Joaquim Lopes Alho

Clínica de Dor e Funcional, São Paulo, Brazil

Luciano Furlanetti, MD

e-mail: neuro.furlanetti@gmail.com

Available at:
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Background: Lesch-Nyhan syndrome (LNS) is a rare genetic disorder caused by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT). It typically presents in infancy with compulsive self-injurious behavior accompanied by severe generalized dystonia and dyskinesia. The clinical management of affected individuals is particularly complex and poses significant challenges for both healthcare providers and caregivers.
Objectives: Pallidal deep brain stimulation (DBS) has been described as an adjuvant surgical treatment in LNS. We report the use of combined anteromedial and posterolateral radiofrequency pallidotomy in a pediatric patient with LNS, targeting both the limbic and sensorimotor networks.
Methods: Preoperative and postoperative functional assessment data prospectively collected by a multidisciplinary motor disorders team, including neuropsychology and neurophysiology evaluations were analyzed with regards to motor and behavioral control. Additionally, advanced image processing was conducted to analyze network connectivity patterns.
Results: An adolescent male with LNS was submitted to a right-sided combined anteromedial and posteroventral RF pallidotomy and followed-up (FU) for 48 months. Functional improvement was observed right after the surgery and remained stable throughout the FU time. Structural connectivity profile revealed completely distinct networks targeted within the GPi in the management of his motor and behavioral manifestations.
Conclusion: Combined anteromedial and posteroventral RF pallidotomy may be considered as an option for managing refractory dystonia and self-harm behavior in LNS patients, especially in cases where invasive neuromodulation with deep brain stimulation is not available or desirable. A multi-disciplinary team-based approach is essential to achieve functional improvement and alleviate the overall disease burden for patients and caregivers.

Keywords: Lesch-Nyhan syndrome, dystonia, self-mutilation behavior, deep brain stimulation, connectivity

INTRODUCTION

Lesch-Nyhan disease is a rare, X-linked recessive genetic disorder of purine metabolism, that leads to characteristic neurodevelopmental abnormalities. It is characterized by a deficiency of the enzyme hypoxanthine-guanine phosphoribosyltransferase (HPRT), which is encoded by the HPRT1 gene, found on the X chromosome long-arm (1,2). It represents the most severe form of HPRT deficiency, typically associated with excessive uric acid production, generalized dystonia, lower limb–predominant weakness and spasticity (3). Self-injurious behavior, including compulsive self-mutilation, is highly prevalent and contributes to significant suffering for both patients and their families (1). Pharmacological treatment has limited efficacy in managing both the motor and neuropsychiatric symptoms of the disease. As a result, surgical approaches involving neuromodulatory techniques such as deep brain stimulation (DBS) have been proposed, with promising outcomes (4–6).

Since the advent of DBS, neuromodulatory techniques have largely supplanted ablative procedures. Neuromodulation offers several advantages, including reversibility and adjustability throughout the course of the disease. However, it also presents notable drawbacks, such

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Submitted: 25 June 2025
Accepted: 27 August 2025
Published: 13 September 2025

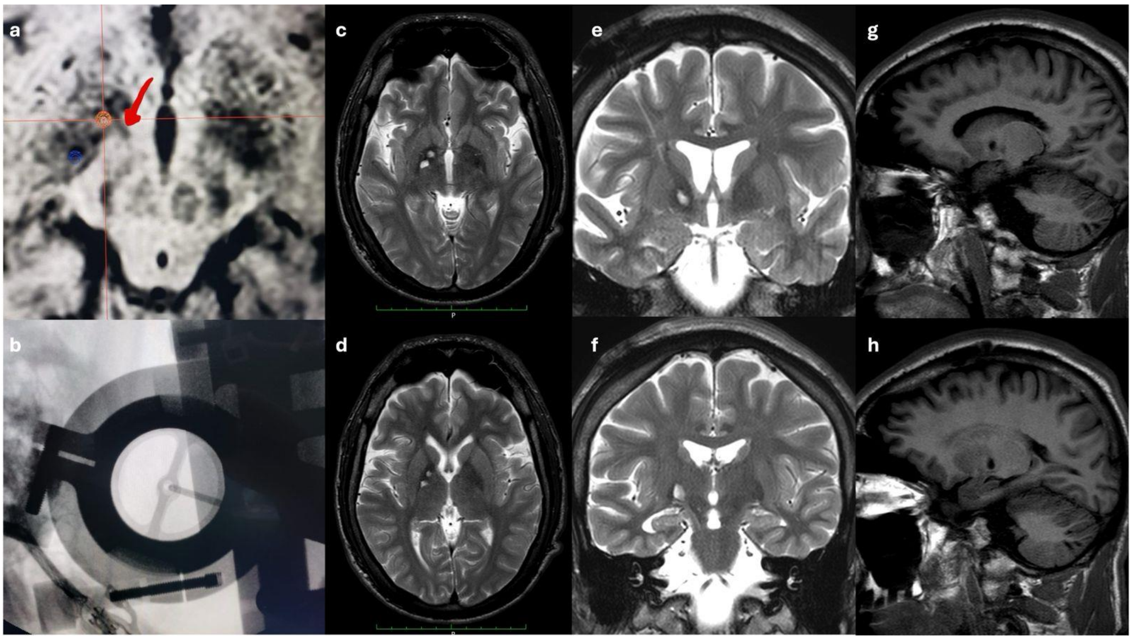

Figure 1 - Pre- and postoperative imaging. a) preoperative planning depicting the targeted region of interest within the anteromedial (am) (red) and posteroventral (pv) (blue) right Globus pallidus internus (GPi), where the Ansa Subthalamica, which connects the limbic areas of the subthalamic nucleus the GPi, is also seen (red arrow). b) intraoperative lateral x-ray showing the radiofrequency electrode at target. T2-weighted postoperative MRI scans revealing the am- and pv-GPi pallidotomies in axial (c and d) and coronal views (e and f), respectively. T1-weighted postoperative sagittal MRI scans revealing the am- (g) and pv-GPi (h) pallidotomies.

as the need for ongoing maintenance, periodic generator replacements, high costs, and the risk of complications

including infection and hardware malfunction (e.g., battery failure or lead fracture). These limitations are particularly relevant for patients with severe dystonia and limited socioeconomic resources, where restricted access to healthcare services may hinder the long-term management of an implanted device (7).

Currently, despite the availability of DBS in many reference centers, this is still not a reality in developing countries across the globe. Radiofrequency (RF) pallidotomy, on the other hand, is a well-established and accessible method, with a long history in the management of movement disorders (7–9).

Moreover, technological advancements such as the advent of high-focused ultrasound (FUS) have recently led to resurgence of interest in the application of ablative procedures in the management of movement and psychiatric conditions. Here, we report a severe case of a young patient diagnosed with LNS and his clinical evolution both in the psychiatric and motor domains, following combined anteromedial and posteroventral radiofrequency pallidotomy. Given that LNS is a rare disease and that the best neurosurgical treatment strategy is not well stablished, longitudinal data on its course following RF pallidotomy may provide valuable insights on clinical presentation, neural networks involved and management challenges.

METHODS

Stereotactic imaging and Surgical procedure

Standard magnetic resonance imaging (MRI) sequences were obtained on a 3.0T General Electric scanner during the preoperative assessment and stereotactic planning. On the day of the surgery, a stereotactic frame (Micromar, Brazil) was carefully fixed to the patients head under general anesthesia, and a volumetric stereotactic computed tomography acquired. The proposed surgical methodology follows the classical approach described in the literature for performing anteromedial and posteroventral pallidotomies (9). Target coordinates were calculated based on stereotactic atlases, with adjustments made according to the patient's individual neuroanatomy (Figure 1a).

Since motor symptoms were more severe on the left-hand side and the patient had preserved speech, decision was made to proceed with pallidotomy on his non-dominant (right) hemisphere.

Intraoperative neurophysiological monitoring included visual evoked potentials (VEP), continuous electromyography (EMG), electroencephalography (EEG), and EEG spectroscopy.

A RF probe (2 mm width, 5 mm exposed tip) was inserted into the predetermined targets. Pre-lesion electrophysiological potentials were recorded. Prior to performing the permanent RF ablation, test stimulation (at 5

DOI: 10.46900/apn.v7i3.316

Hz and 100 Hz, 500 ms pulse width) was conducted to assess proximity to the internal capsule and optic tract (10). A reversible test lesion was then applied for 60 seconds at 55°C, and evoked responses re-evaluated. Since no adverse effects were observed in motor or visual potentials, a permanent RF lesion was performed for 60 seconds at 80°C. This procedure was repeated at target (0 mm), as well as 2 mm above, along the craniocaudal axis, for each planned target (Figure 1b).

General anesthesia was reverted, the patient extubated and admitted to the intensive care unit (ICU) for postoperative monitoring. An immediate postoperative control CT scan did not show any signs of complications. The patient was discharged on postoperative day two. A follow-up MRI was performed to evaluate the extent of the RF lesion (Figure 1c-h).

Clinical Evaluation

The evaluation of patient outcomes pre- and post-operatively included assessments of dystonia and reduction in self-injurious behavior. Dystonia severity was monitored using the Burke-Fahn-Marsden Dystonia Rating Scale–Movement (BFMDRS-M) and Disability (BFMDRS-D) subscales. The overall percentage change in BFMDRS scores was calculated using the following formula:

[(Baseline score – Postoperative score) / Baseline score] × 100. To assess changes in self-injurious (SIB), stereotyped behavior (SB) and aggressive behavior (AB), the Behavior Problems Inventory (BPI) was used. Postoperative assessment of self-harm and aggression relied on changes in BPI scores and was supplemented by qualitative reports from caregivers during follow-up visits.

Connectivity lesion profile analysis

Although structural connectivity has been extensively used to correlate DBS results to areas connected to the VTAs (11–13), this method is not so popular to obtain information about networks involved in ablative surgeries. As we did not have access do DWI images of our patient, a normative connectome was employed to achieve the analysis. To accomplish that, postoperative MRI was normalized into MNI space using ANTs and a customized Python script was used to create ellipsoid ROIs given the diameters of the postoperative lesions. Those MNI-registered ROIs were imported in DSI studio and used as seeds, where a group connectome average template constructed from a total of 1021 subjects was used for the analysis. A multishell diffusion scheme was used, and the b-values were 990 ,1985 and 2980 s/mm2. The number of diffusion sampling directions were 90, 90, and 90, respectively. The in-plane resolution was 1.25 mm. The slice thickness was 1.25 mm. The diffusion data were reconstructed in the MNI space using q-space diffeomorphic reconstruction (14) to obtain the spin distribution function (15). A diffusion sampling length ratio of 2.5 was used, and the output resolution was 1 mm. The restricted diffusion was quantified using restricted diffusion imaging, and a deterministic fiber tracking algorithm (16) was used with augmented tracking strategies (17) to improve reproducibility. The anisotropy threshold was randomly selected between 0.5 and 0.7 Otsu threshold. The angular threshold was randomly selected from 45 degrees to 90 degrees. The step size was set to voxel spacing. Tracks with length shorter than 30.0 or longer than 200.0 mm were discarded. A total of 1000000 seeds were placed. Shape analysis was conducted to derive shape metrics for tractography (17). The Freesurfer DKT atlas was used to display cortical structures and the São-Paulo Würzburg Atlas of Neuroanatomy (SWAN) (18) histological atlas displayed the GPi.

CASE REPORT

We present the case of an adolescent male diagnosed with LNS, characterized by progressive generalized dystonia and severe self-injurious behavior since early childhood. He was referred to our pediatric neurosurgery clinic with mild lower limb spasticity and marked dystonia involving the trunk and extremities, occasionally escalating to severe retrocollis and opisthotonus. His clinical presentation included bilateral nephrocalcinosis, dystonic dyskinesia, orolingual and hand-to-face self-mutilation, compulsive self-injury necessitating physical restraints, emotional lability, dyskinetic speech, and compulsive swearing.

Due to persistent self-aggression and aggression toward caregivers, bilateral continuous physical restraint was required for safety. Multiple pharmacological regimens—including optimized doses of risperidone, baclofen, diazepam, and allopurinol—were trialed but achieved only limited control over both motor and psychiatric symptoms. Given the severity and refractory nature of his condition, the patient was indicated for radiofrequency pallidotomy, targeting both anteromedial and posteroventral regions of the internal globus pallidus.

RESULTS

A right-sided combined anteromedial and posteroventral RF pallidotomy was successfully performed. Following the surgical intervention, the patient continued to receive medical management, as well as physical rehabilitation and psychological assistance as previously, and was followed up for 48 months. Prior to surgical treatment he presented a BFMDRS motor and disability scores of 54 and 25, respectively.

DOI: 10.46900/apn.v7i3.316

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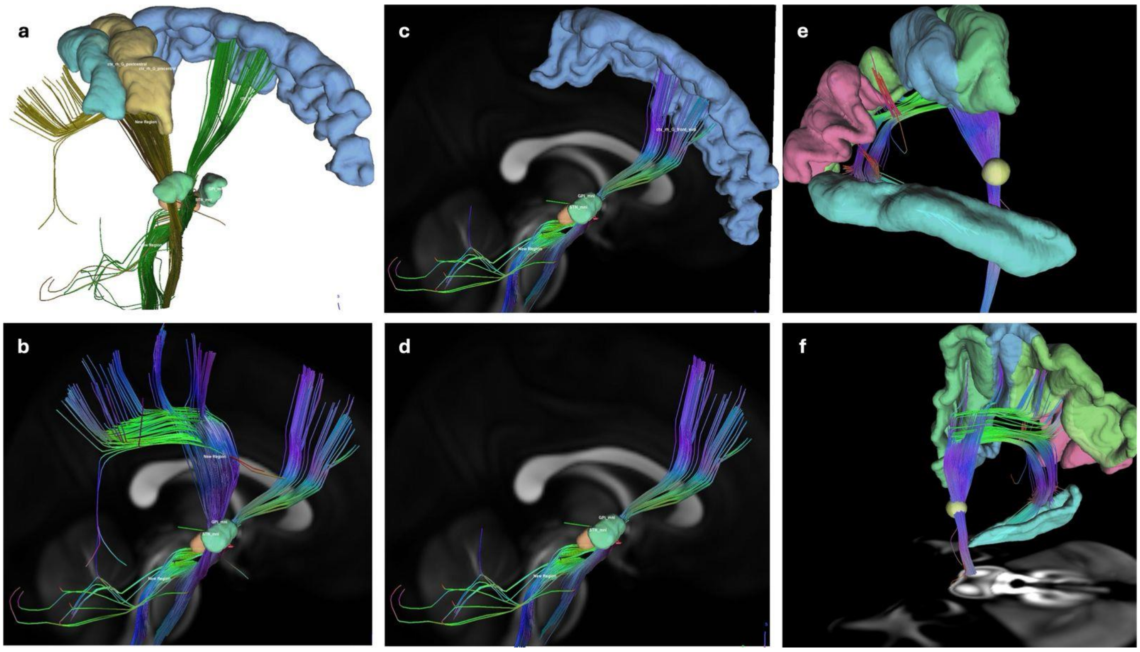

Figure 2- Structural connectivity distribution according to localisation of each region of interest (ROI), i.e. volume of the anteromedial (am) and posteroventral (pv) pallidal lesions, using the Freesurfer DKT atlas to display cortical structures and the São-Paulo Würzburg Atlas of Neuroanatomy (SWAN)(18) for subcortical structures. a and b) streamlines representing connections from am- and pv-GPi to the superior frontal gyrus and somatosensory cortex, respectively. The anteromedial GPi ROI was connected to frontal regions (frontal superior Gyrus) (c), with 750 streamlines (d), while the posteroventral tract was connected to somatosensory cortex (pre-central gyrus and post-central gyrus) (e) (lateral view), superior and inferior parietal and inferior temporal gyrus with 900 streamlines in total (f) (medial view).

Immediately following surgery, significant improvements in behavior and dystonic movements on the left-hand side (contralateral to the RF ablation) were achieved. Throughout neurological evaluation did not reveal any new onset neurological impairments. Interestingly, self-harm and aggression towards caregivers, as well as axial and dystonic movements of the left-hand side improved considerably, so that the left upper limb could be better trained for daily tasks and remain unrestrained by the first time in years. No short- or long-term complications related to the surgery were noted during the follow-up. Caregivers reported ongoing improvement in the patient's dystonic movements and left-hand function, supported by regular occupational and physiotherapy sessions. He gradually became more capable of participating in self-care activities such as hygiene, dressing, eating, and transferring. At last FU (48 months), the BFMDRS motor score improved 62% (20), mainly due to improvement on trunk, left upper and lower extremities. Nevertheless, the percentage change observed in disability score was limited to 16% (21). Regarding the scores evaluated by the Behavior Problems Inventory (BPI), an improvement in all scales was observed in the FU. SIB, SB and AB decreased in frequency (68%, 40% and 34%) and severity (47%, 20% and 43%), respectively. Interestingly, compulsive self-injurious behavior significantly decreased on the left-hand side. However, the right upper and lower limbs still required restraint due to persistent risk of self-harm. Connectivity analysis revealed that the anteromedial GPi ROI was mainly connected to frontal regions (frontal superior Gyrus), with 750 streamlines, while the posteroventral lesion area was connected to the somatosensory cortices (pre-central gyrus and post-central gyrus), superior and inferior parietal gyrus, and inferior gyrus with 900 streamlines in total (Figure 2).

DISCUSSION

Despite increased awareness regarding early diagnosis, the management of LNS remains challenging. Traditional therapeutic strategies have primarily focused on controlling hyperuricemia and motor symptoms (1,19). However, compulsive self-mutilation—often leading to tissue destruction around the lips and auto-amputation of the fingers—remains a major source of morbidity. These behaviors frequently necessitate the use of physical restraints and, in some cases, complete dental extraction for patient safety. For caregivers, the burden is substantial, and psychotropic medications have shown limited efficacy in alleviating these behavioral disturbances (1,5). Historically, stereotactic surgical procedures have been employed in an attempt to alleviate these symptoms, such as cingulotomy, amygdalotomy, dorsomedial thalamotomy (20), and also the posteromedial hypothalamotomy (10,21).

Self-injurious behavior and dystonia in LNS are thought to be associated with underlying dopaminergic dysregulation (2). However, both dopamine agonists and antagonists have shown inconsistent and generally unsatisfactory effects on

DOI: 10.46900/apn.v7i3.316

controlling self-injurious behavior and dystonia in these patients. Moreover, the precise relationship between HPRT deficiency, altered purine metabolism, and the behavioral phenotype of LNS remains incompletely understood (1,5,19).

Neuroimaging studies have shown reduced gray and brain white matter volume, and implicated basal ganglia dysfunction in the pathogenesis of motor symptoms in LNS. More recently, reductions in white matter integrity using whole brain fractional anisotropy have been observed in the corpus callosum, corona radiata, cingulum, interna capsule and superior longitudinal fasciculus, with greater degree of severity among LNS patients than in subjects with a milder variant of the disease (22). The prevailing hypothesis is that self-injurious behavior in LNS arises from dysfunction within the cortico-basal ganglia-thalamo-cortical circuitry, a network integral to motor control, emotional regulation, and adaptive behavior (4–6). Disruption at any level—whether structural, functional, or metabolic—within this circuit may result in the motor and behavioral manifestations characteristic of the syndrome.

Notably, the compulsive nature of self-mutilation and aggression seen in LNS differs from the explosive, reactive aggression described by Sano and colleagues in other conditions (21). Sano hypothesized that aggressive outbursts may result from a functional imbalance between the ergotropic (sympathetic) and trophotropic (parasympathetic) neural systems. Based on this theory, the rationale for performing stereotactic radiofrequency lesions in the posterior hypothalamus was to target the so-called "ergotropic triangle," which includes the dorsal longitudinal fasciculus of Schütz (21). This fasciculus was considered a key pathway connecting the sympathetic region of the hypothalamus with both supratentorial and infratentorial autonomic centers. The goal of posteromedial hypothalamotomy was to reduce sympathetic outflow and, in turn, mitigate the clinical expression of pathological rage (21). Interestingly, neuromodulation of this same area has been investigated in the management of other neuropsychiatric conditions, such as refractory pain syndromes, epilepsy and behavioral disorders (20,23,24).

The involvement of the globus pallidus and ventral striatum in the pathophysiology of compulsive self-harm is based on case reports documenting improvements in self-injurious behavior following GPi-DBS in LNS. Taira et al. were the first to report successful management of both dystonia and self-injurious behavior in a 19-year-old patient with LNS through bilateral DBS targeting the motor territory of the internal segment of the globus pallidus (GPi) (4). Building on this, Cif et al. explored the functional segregation of motor and behavioral circuits within the basal ganglia by implanting dual bilateral electrodes in both the anterior (limbic/prefrontal) and posterior (sensorimotor) regions of the GPi (6). Selective deactivation of the posterior (motor) electrodes resulted in re-emergence of dystonic symptoms while self-injurious behavior remained stable. Conversely, deactivation of the anterior (limbic) electrodes led to a worsening of self-harm behaviors without affecting motor function, suggesting functional dissociation within the pallidal circuitry.

Further evidence was provided by Abel et al., who observed potential lateralization of the neural pathways underlying dystonia and self-injury (25). In their report, a fracture in the right-sided DBS electrode led to exacerbation of both left-sided dystonia and self-injurious behavior, which improved following electrode revision, reinforcing the idea of laterality in symptom mediation. In line with this, following right anteromedial and posteroventral pallidotomies, our patient also presented lateralized improvement of dystonia and compulsive self-harm. Although single-case findings may not be generalizable to routine clinical practice, our results highlight distinct connectivity patterns associated with stimulation of specific subregions within the GPi. These observations are consistent with prior neuroanatomical and electrophysiological studies in both humans and animal models, which identify the GPi as a major output nucleus of the basal ganglia. Within this structure, anatomically segregated yet functionally interconnected circuits mediate motor, cognitive, associative, and limbic functions (5,6,26). In the present case, connectome analysis showed that while the sensorimotor pallidal region was strongly connected to pre- and postcentral gyrus, superior and inferior parietal, and inferior temporal gyri, the anteromedial GPi was imbedded in the limbic network. Other groups have shown improvement of obsessive-compulsive behavior in the context of Tourette's syndrome with am-GPi neuromodulation, likely suggesting upstream limbic neuromodulation via strong pallidal connections to the insula, prefrontal and orbitofrontal cortices (27,28). Tambirajoo et al. had previously shown in a case series of four LNS patients treated with pallidal DBS, that clinical improvement of self-harm behavior was not only dependent on the position of the active contact within the anteromedial GPi, but strongly correlated with the number of streamlines connecting the estimated VTA up- and downstream to distant cortical and subcortical limbic brain regions. Furthermore, a completely different connectivity profile was observed with stimulation of the posteroventral sensorimotor GPi (5). Therefore, targeting both the sensorimotor and limbic GPi, modulating different brain networks, seems to be central to achieving better motor and behavioral outcomes in LNS.

Some patients with dystonia are not suitable candidates for DBS for various reasons, as previously described (29).

Infection rates following DBS deep brain stimulation (DBS) in pediatric patients with dystonia have been reported to range from 9.3% to 21% in various case series (5,30). Tambirajoo et al. reported infection in three out of four LNS patients submitted to DBS for LNS (5). Age at surgery, the underlying indication for DBS, length of surgery, number of electrodes implanted might be related to increased risk (5,30,31). In the case of LNS specifically, other factors seem to contribute even further to higher complication rate, for instance, the presence of self-injurious behavior (e.g., manipulation of surgical wounds, both intentional and unintentional), severe physical disability, low body weight and poor nutritional status, and the hyperkinetic nature of generalized dystonic movements (5).

In the present case, the decision to proceed with an ablative procedure rather than DBS was based on the patient's psychiatric condition, which increases the risk of wound infection and the potential need for device removal. Furthermore, the need for close follow-up with regular evaluations at the DBS reference center, the long-term follow-up requirements for device maintenance and generator replacement posed a significant limitation. Other than that, within the Brazilian public health system (SUS), DBS is still restricted to very few centers across the country. Thus, since pallidotomy is a well-stablished technique and has demonstrated proven efficacy in the management of dystonia, and considering the factors enumerated above, radiofrequency ablation was considered the therapy of choice for the present patient (29,32–34).

Although improvements in BFMDRS scores might be relatively modest in these patients, notable functional and psychosocial benefits are often observed. These included enhanced sitting balance and postural control, return to school and social engagement with peers, increased comfort and emotional well-being, greater ease with personal care tasks such as washing and dressing, and a reduction in both the frequency and intensity of pain (35,36). Therefore, a comprehensive approach to outcome assessment is essential to fully capture the impact of DBS in children with LNS. Meaningful clinical improvements may still be achieved even in the absence of substantial changes in standard motor scales.

DBS provides several clear advantages when compared with ablative procedure, such as long-term possibility of system upgrade and technological improvements, reversibility and adjustability to the patient's needs, however the risk of related wound infection and hardware issues should be considered in LNS. Therefore, pallidotomy seems to be a valid alternative in the management of such complex indications. Future studies are required to evaluate the optimal surgical strategies according to individual patients' profiles in cases of LNS.

CONCLUSION

Combined anteromedial and posteroventral RF pallidotomy may be considered as an option for managing refractory dystonia and self-harm behavior in LNS patients, especially in cases where invasive neuromodulation with deep brain stimulation is not available or desirable for any reasons. A multi-disciplinary team-based approach is essential for patient selection and management, to support children and families, to achieve functional improvement and alleviate the overall disease burden for patients and caregivers. Patient and family members should be indulged regarding realistic expectations of symptom control and risk profile prior to neurosurgical interventions in the management of such challenging conditions.

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. According to institutional and national guidelines, ethics approval was not necessary for this study.

Consent to participate

The patient gave consent to use his information and images for publication.

Conflict 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 research received no specific grant from any funding agency in the public, commercial or not-for-profit sectors

Artificial intelligence

The authors affirm that no artificial intelligence tools were used in the writing, editing, or content generation of this manuscript. All work was conducted manually, based on thorough research and academic expertise.

CONTRIBUTIONS

-**Luciano Furlanetti**: Conceptualization, Data curation, Formal Analysis, Investigation, Writing – original draft, Writing – review & editing
-**Bernardo Assumpção de Monaco**: Conceptualization, Data curation, Writing – original draft

-**Fabio Okuda Furokawa**: Formal Analysis, Investigation, Methodology, Writing – review & editing
-**Guilherme Corsaletti Gregório:** Methodology, Writing – review & editing
-**Jessie Navarro**: Conceptualization, Writing – review & editing
-**Ana Tereza di Lorenzo Alho**: Conceptualization, Investigation, Writing – review & editingConceptualization, Writing – review & editing
-**Bianca Dalmaso**: Conceptualization, Visualization, Writing – review & editing
Eduardo Joaquim Lopes Alho: Conceptualization, Data curation, Formal analysis, Image reconstruction and processing, Investigation, Writing –original draft, Writing – review & editing

REFERENCES

1. Bell S, Kolobova I, Crapper L, Ernst C. Lesch-Nyhan Syndrome: Models, Theories, and Therapies. Mol Syndromol. 2016 Nov;7(6):302–11.
2. Saito Y, Takashima S. Neurotransmitter changes in the pathophysiology of Lesch-Nyhan syndrome. Brain Dev. 2000 Sep;22 Suppl 1:S122-131.
3. Fu R, Ceballos-Picot I, Torres RJ, Larovere LE, Yamada Y, Nguyen KV, et al. Genotype–phenotype correlations in neurogenetics: Lesch-Nyhan disease as a model disorder. Brain. 2014 May;137(5):1282–303.
4. Taira T, Kobayashi T, Hori T. Disappearance of self-mutilating behavior in a patient with lesch-nyhan syndrome after bilateral chronic stimulation of the globus pallidus internus. Case report. J Neurosurg. 2003 Feb;98(2):414–6.
5. Tambirajoo K, Furlanetti L, Hasegawa H, Raslan A, Gimeno H, Lin JP, et al. Deep Brain Stimulation of the Internal Pallidum in Lesch-Nyhan Syndrome: Clinical Outcomes and Connectivity Analysis. Neuromodulation. 2020 Jun 23.
6. Cif L, Biolsi B, Gavarini S, Saux A, Robles SG, Tancu C, et al. Antero-ventral internal pallidum stimulation improves behavioral disorders in Lesch-Nyhan disease. Mov Disord. 2007 Oct 31;22(14):2126–9.
7. Furlanetti L, Lin JP, Ashkan K. Globus pallidus internus deep brain stimulation in the management of movement disorders: Current evidence and future directions. In: International Review of Movement Disorders [Internet]. Elsevier; 2024 [cited 2025 Jun 16]. p. 99–146. Available from: https://linkinghub.elsevier.com/retrieve/pii/S266678782400005X
8. Hariz M. Pallidotomy: A “Phoenix the Bird” of Surgery for Parkinson’s Disease? Mov Disord Clin Pract. 2022 Feb;9(2):170–2.
9. Spiegel EA, Wycis HT. Thalamotomy and pallidotomy for treatment of choreic movements. Acta Neurochir (Wien). 1952;2(3–4):417–22.
10. Dos Santos RG, Mengai ACS, Da Silva LJ, Arruda JB. Tratamento Cirúrgico da Agressividade. jbnc. 2018 Mar 29;25(4):367–72.
11. Horn A, editor. Index. In: Connectomic Deep Brain Stimulation [Internet]. Academic Press; 2022 [cited 2024 Feb 13]. p. 561–71. Available from: https://www.sciencedirect.com/science/article/pii/B9780128218617099929
12. Baldermann JC, Schüller T, Kohl S, Voon V, Li N, Hollunder B, et al. Connectomic Deep Brain Stimulation for Obsessive-Compulsive Disorder. Biol Psychiatry. 2021 Nov 15;90(10):678–88.
13. Hollunder B, Ostrem JL, Sahin IA, Rajamani N, Oxenford S, Butenko K, et al. Mapping dysfunctional circuits in the frontal cortex using deep brain stimulation. Nat Neurosci. 2024 Mar;27(3):573–86.
14. Yeh FC, Tseng WYI. NTU-90: A high angular resolution brain atlas constructed by q-space diffeomorphic reconstruction. NeuroImage. 2011 Sep;58(1):91–9.
15. Fang-Cheng Yeh, Wedeen VJ, Tseng WYI. Generalized ${ q}$-Sampling Imaging. IEEE Trans Med Imaging. 2010 Sep;29(9):1626–35.
16. Yeh FC, Verstynen TD, Wang Y, Fernández-Miranda JC, Tseng WYI. Deterministic Diffusion Fiber Tracking Improved by Quantitative Anisotropy. Zhan W, editor. PLoS ONE. 2013 Nov 15;8(11):e80713.
17. Yeh FC. Shape analysis of the human association pathways. NeuroImage. 2020 Dec;223:117329.
18. Alho EJL, Alho ATDL, Grinberg L, Amaro E, Dos Santos GAB, da Silva RE, et al. High thickness histological sections as alternative to study the three-dimensional microscopic human sub-cortical neuroanatomy. Brain Struct Funct. 2018 Apr;223(3):1121–32.
19. Torres RJ, Puig JG, Jinnah HA. Update on the phenotypic spectrum of Lesch-Nyhan disease and its attenuated variants. Curr Rheumatol Rep. 2012 Apr;14(2):189–94.
20. Torres CV, Sola RG, Pastor J, Pedrosa M, Navas M, García-Navarrete E, et al. Long-term results of posteromedial hypothalamic deep brain stimulation for patients with resistant aggressiveness. J Neurosurg. 2013 Aug;119(2):277–87.
21. Sano K, Mayanagi Y. Posteromedial Hypothalamotomy in the Treatment of Violent, Aggressive Behaviour. In: Brihaye J, Calliauw L, Loew

F, Bergh R, editors. Personality and Neurosurgery [Internet]. Vienna: Springer Vienna; 1988 [cited 2025 Jun 22]. p. 145–51. Available from: http://link.springer.com/10.1007/978-3-7091-9005-0_28

22. Del Bene VA, Crawford JL, Gómez-Gastiasoro A, Vannorsdall TD, Buchholz A, Ojeda N, et al. Microstructural white matter abnormalities in Lesch–Nyhan disease. Eur J of Neuroscience. 2022 Jan;55(1):264–76.
23. Franzini A, Marras C, Tringali G, Leone M, Ferroli P, Bussone G, et al. Chronic high frequency stimulation of the posteromedial hypothalamus in facial pain syndromes and behaviour disorders. Acta Neurochir Suppl. 2007;97(Pt 2):399–406.
24. Benedetti-Isaac JC, Torres-Zambrano M, Vargas-Toscano A, Perea-Castro E, Alcalá-Cerra G, Furlanetti LL, et al. Seizure frequency reduction after posteromedial hypothalamus deep brain stimulation in drug-resistant epilepsy associated with intractable aggressive behavior. Epilepsia. 2015 Jul;56(7):1152–61.
25. Abel TJ, Dalm BD, Grossbach AJ, Jackson AW, Thomsen T, Greenlee JDW. Lateralized effect of pallidal stimulation on self-mutilation in Lesch-Nyhan disease. J Neurosurg Pediatr. 2014 Dec;14(6):594–7.
26. Horn A, Reich MM, Ewert S, Li N, Al-Fatly B, Lange F, et al. Optimal deep brain stimulation sites and networks for cervical vs. generalized dystonia. Proceedings of the National Academy of Sciences. 2022 Apr 5;119(14):e2114985119.
27. Shahed J, Poysky J, Kenney C, Simpson R, Jankovic J. GPi deep brain stimulation for Tourette syndrome improves tics and psychiatric comorbidities. Neurology. 2007 Jan 9;68(2):159–60.
28. Sachdev PS, Mohan A, Cannon E, Crawford JD, Silberstein P, Cook R, et al. Deep brain stimulation of the antero-medial globus pallidus interna for Tourette syndrome. PLoS ONE. 2014;9(8):e104926.
29. Centen LM, Oterdoom DLM, Tijssen MAJ, Lesman-Leegte I, Van Egmond ME, Van Dijk JMC. Bilateral Pallidotomy for Dystonia: A Systematic Review. Movement Disorders. 2021 Mar;36(3):547–57.
30. Kaminska M, Perides S, Lumsden DE, Nakou V, Selway R, Ashkan K, et al. Complications of Deep Brain Stimulation (DBS) for dystonia in children - The challenges and 10 year experience in a large paediatric cohort. Eur J Paediatr Neurol. 2017 Jan;21(1):168–75.
31. Koy A, Bockhorn N, Kühn AA, Schneider GH, Krause P, Lauritsch K, et al. Adverse events associated with deep brain stimulation in patients with childhood-onset dystonia. Brain Stimul. 2019 Oct;12(5):1111–20.
32. Guridi J, Lozano AM. A Brief History of Pallidotomy. Neurosurgery. 1997 Nov 1;41(5):1169–83.
33. Cersosimo MG, Raina GB, Piedimonte F, Antico J, Graff P, Micheli FE. Pallidal surgery for the treatment of primary generalized dystonia: Long-term follow-up. Clinical Neurology and Neurosurgery. 2008 Feb;110(2):145–50.
34. Cif L, Hariz M. Seventy years of pallidotomy for movement disorders. Movement Disorders. 2017 Jul;32(7):972–82.
35. Gimeno H, Tustin K, Selway R, Lin JP. Beyond the Burke-Fahn-Marsden Dystonia Rating Scale: deep brain stimulation in childhood secondary dystonia. Eur J Paediatr Neurol. 2012 Sep;16(5):501–8.
36. Perides S, Lin JP, Lee G, Gimeno H, Lumsden DE, Ashkan K, et al. Deep brain stimulation reduces pain in children with dystonia, including in dyskinetic cerebral palsy. Dev Med Child Neurol. 2020 Aug;62(8):917–25.

DOI: 10.46900/apn.v7i3.316