Surgical Neurology International

SNI: Stereotactic, a supplement to Surgical Neurology International

OPEN ACCESS

For entire Editorial Board visit : http://www.surgicalneurologyint.com

Editor
Antonio A. F. DeSalles, MD
University of California,
Los Angeles, CA, USA

Long-term follow-up of deep brain stimulation of peduncolopontine nucleus in progressive supranuclear palsy: Report of three cases

Domenico Servello, Edvin Zekaj, Christian Saleh, Claudia Menghetti, Mauro Porta

Departments of Neurosurgery and Neurology, IRCCS Galeazzi, Milan, Italy

E-mail: *Domenico Servello - servello@libero.it; Edvin Zekaj - ezekaj@yahoo.com; Christian Saleh - chs12us75010@yahoo.com; Claudia Menghetti - claudia.men@libero.it; Mauro Porta - mauroportamilano@gmail.com
*Corresponding author

Received: 04 December 13 Accepted: 04 April 14 Published: 05 September 14

This article may be cited as: Servello D, Zekaj E, Saleh C, Menghetti C, Porta M. Long-term follow-up of deep brain stimulation of peduncolopontine nucleus in progressive supranuclear palsy: Report of three cases. Surg Neurol Int 2014;5:S416-20.
Available FREE in open access from: http://www.surgicalneurologyint.com/text.asp?2014/5/9/416/140208

Copyright: © 2014 Servello D. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Background: Progressive supranuclear palsy (PSP) is a neurodegenerative disease due to mitochondrial dysfunction. The PSP syndrome presents generally with gait disorder, Parkinsonism, ophthalmoparesis and cognitive alteration. Few reports exist on deep brain stimulation (DBS) in patients with atypical Parkinsonism. The aim of our study was to evaluate further the potential role of DBS in PSP.

Case Description: We report three patients with PSP with long-term follow up undergoing DBS. Two patients had right peripedunculopontine nucleus (PPN) stimulation and one patient had simultaneous right PPN and bilateral globus pallidus internus DBS. DBS of the PPN alone or combined with globus pallidus internus (GPi) determined an improvement in gait and a reduction in falls sustained over time. Combined target stimulation (GPi-PPN) was correlated with better clinical outcome than single target (PPN) DBS for PSP.

Conclusions: Although few data on DBS for PSP exist, reported clinical results are encouraging. DBS might be considered as an alternative therapeutic option for patients with PSP presenting with relevant gait imbalance and frequent falls, who fail to respond to pharmacological treatment. Larger cohorts with longer follow-ups are needed to evaluate more exhaustively the efficacy of DBS in PSP.

Key Words: Axial symptoms, deep brain stimulation, peripedunculopontine nucleus, progressive supranuclear palsy

Access this article online

Website: www.surgicalneurologyint.com

DOI: 10.4103/2152-7806.140208

Quick Response Code:

INTRODUCTION

Progressive supranuclear palsy (PSP) is a neurodegenerative disease secondary to mitochondrial dysfunction characterized by neurofibrillary tangles accumulation and neuropil threads in subthalamic nucleus, pallidum, red nucleus, substantia nigra, striatum, pontine tegmentum, oculomotor nucleus, medulla, and dentate nucleus.

The PSP syndrome classically presents with gait disorder, cognitive alteration, Parkinsonism, and ophthalmoparesis (vertical gaze palsy). A plethora of PSP phenotypes have been described.[25,26] PSP subtypes show different responses to levodopa: A moderate response is present in PSP-Parkinsonism (PSP-P), while classical Richardson's syndrome has a poor response.[28] Also drugs acting at serotonergic, cholinergic, and noradrenergic

sites were tried.[8] Rivastigmine has some positive effect on cognitive deficit in PSP.[9] A small double-blind trial revealed that tricyclic antidepressants improved gait and rigidity.[20] Botulinum toxin was used in PSP to treat dystonia.[17,23] However, insufficient data does not allow any recommendation for a specific treatment in PSP. Few case-reports exist on deep brain stimulation (DBS) in patients with atypical Parkinsonism.[6,15,16,33] We report our experience with DBS in three patients with PSP.

Case 1

A 70-year-old male patient with a diagnosis of PSP presented with gait imbalance and frequent falls. Levodopa and ropironolo were tried but provided only partial benefit. The neurological evaluation prior to surgery revealed vertical gaze paralysis, dysarthria, dysphagia, and left sided dysmetria. Deambulation was solely possible with the help of a caregiver. In light of his gait imbalance and frequent falls, we proposed DBS surgery of the rostral pedunculopontine nucleus (PPN). The patient underwent electrode implantation (Medtronic, Model 3389, Minneapolis, MN, USA) in the right PPN. The PPN region was located lateral to the superior cerebellar peduncle, its decussation and central tegmental tract and medial to the lemniscal system.[32] The patient underwent volumetric brain T1 magnetic resonance imaging (MRI) and a MRI DPI sequence. Superior cerebellar peduncle and its decussation were directly visualized and the target was chosen lateral to these structures and medial to the lemniscal system.

Targeting occurred on T2-weigthed MRI at the rostral part of the PPN between the superior cerebellar peduncle decussation and the lemniscal system.[32]

Surgical procedure was uneventful. Two days after lead implantation, we performed a brain MRI [Figures 1-3], which confirmed correct lead position. We started with low frequency stimulation (35 Hz) that resulted in an improved postural stability. Progressively we increased the frequency of stimulation to 130 Hz with persistent clinical improvement. At one year follow-up, the patient reported a reduction in falls and an improvement in gait imbalance. The subjectively reported clinical improvement was associated with a 22% decrease on the progressive supranuclear palsy rating scale (PSPRS) [Table 1].

Case 2

A 68-year-old male patient presented with muscular hypertonus in the left superior limb of one year duration associated with dystonia in the left hand. Subsequently his clinical picture worsened with difficulty in deambulation and progressive gait enlargement. Neurological examination revealed further severe dysarthria and vertical gaze paralysis. The patient was able to walk only with bilateral sustain. In consideration of severe gait disturbances, DBS of the PPN was proposed. The patient underwent unilateral lead implantation (Medtronic, Model 3389, Minneapolis, MN, USA) in the right PPN [Figure 4]. The procedure was uneventful. Equally in this patient we started with low

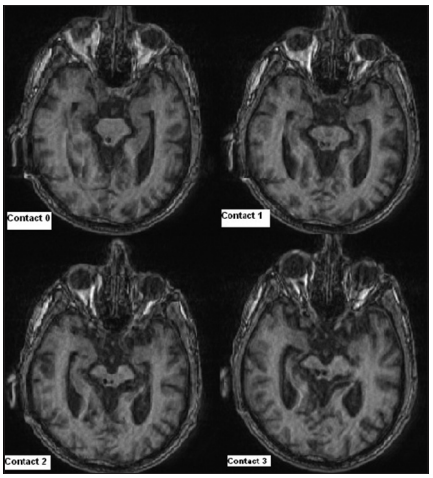

Figure 1: Patient 1, axial plane, showing all contacts

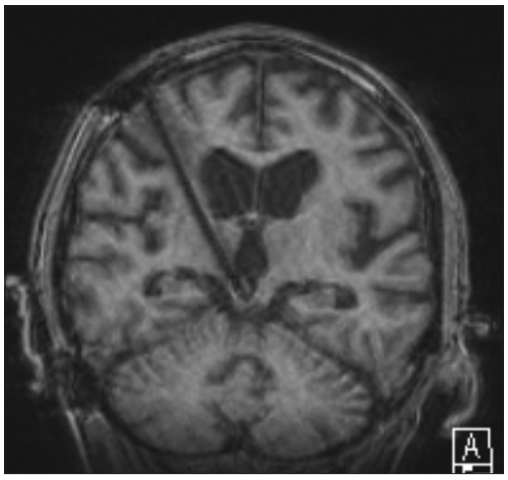

Figure 2: Patient 1, coronal plane, showing electrode trajectory

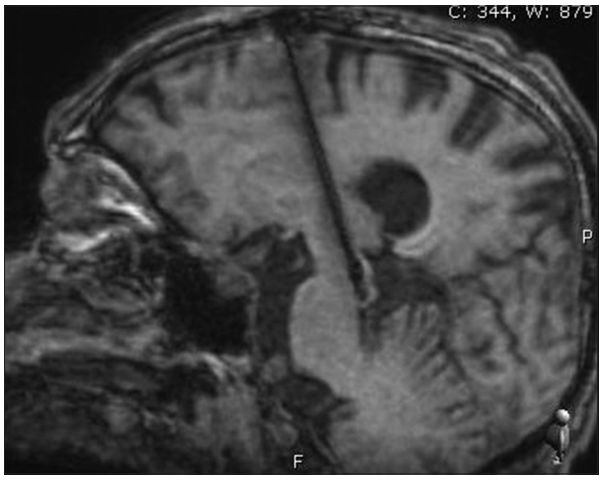

Figure 3: Patient 1, sagittal plane, showing electrode trajectory at the level of the inferior collicolli

frequency stimulation, which was progressively increased to high frequency stimulation, which resulted in gait improvement. The patient reported less assistance for daily activities. A 21% decrease on the PSPRS was noted at the 12 months follow-up visit [Table 1].

Case 3

A 66-year-old male presented with bradykinesia, ideomotor slowing, upward gaze palsy, and dystonia. In the previous months before admission at our department, a worsening of postural stability with frequent falls were observed. Dopaminergic therapy was poorly effective. Considering his strong dystonic component and difficulties in postural stability, the patient underwent DBS of the postero-ventral GPi and right PPN (Medtronic, Model 3389, Minneapolis, MN, USA). Implantation of both targets [Figures 5 and 6] occurred during the same procedure. At the one year follow-up visit his dystonia, gait, and postural stability had improved with a 36% reduction on the PSPRS [Table 1].

DISCUSSION

The PPN forms part of the rostral locomotor region of the brainstem.[3,4, 22] Experimental evidence suggests that it plays a central role in the initiation and maintenance of gait.[3,7,18,19] The classical clinical picture of PSP presents most frequently with a symmetric, akinetic-rigid syndrome, vertical supranuclear gaze palsy, frontal deficits, prominent postural instability, and falls.[10,11,28,29] PSP responds poorly to pharmacological therapy. Considering that postural imbalance and falls are the most disabling symptoms in PSP, DBS of the PPN is considered in pharmacological refractory cases. Preferably DBS should be applied in the early stages of the disease when cognitive function is preserved.

Several authors reported DBS to the rostral brainstem in Parkinsonian patients.[2,6,14-16,21,24,27] These studies reported variable clinical results. The heterogeneity in clinical outcome might be related to the topographic variability of the PPN and the degree of atrophy of the PPN and damage of interconnected basal ganglia structures.[5,30,31] Further methodological diversity, such as single versus multiple target stimulation, targeting methods and consequently different anatomical location of implanted electrodes in the rostral brainstem may explain the different clinical results.[1,2,13]

Table 1: Progressive supranuclear palsy rating scale (PSPRS)-IV scores pre-DBS, at 12 and 24 months

Patient	Target	PSPRS-VI pre DBS	PSPRS-VI at 12 months	PSPRS-VI at 24 months	% reduction at 12 months
No 1	R-PPN	18	14	14	22.2
No 2	R-PPN	15	11	-	21.4
No 3	R-PPN, bl GPi	14	9	-	35.7

PPN: Peripedunculopontine nucleus, DBS: Deep brain stimulation, R: Right, GPi: Globus pallidus internus, bl: bilateral, No: Number, PSPRS: Progressive supranuclear palsy rating scale

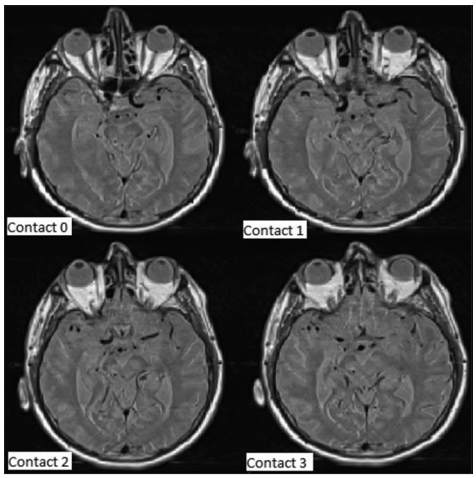

Figure 4: Patient 2, axial plane, showing all contacts

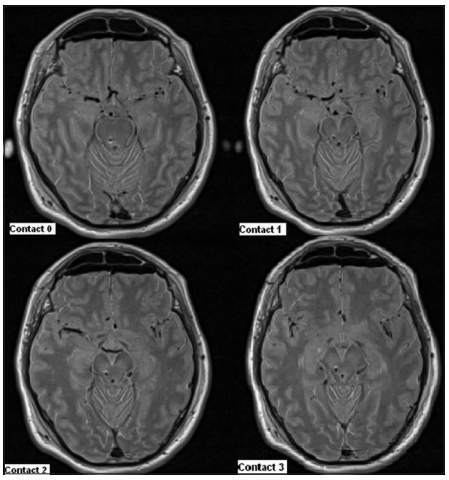

Figure 5: Patient 3, axial plane, showing all contacts

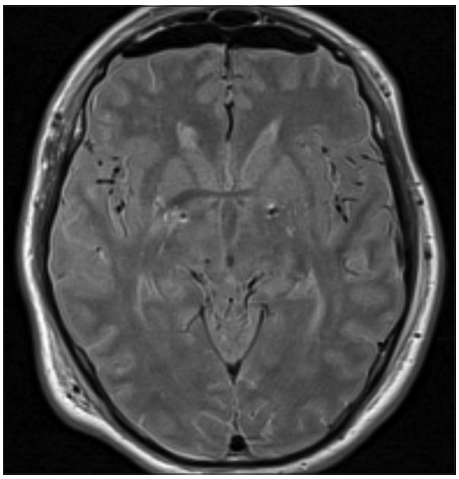

Figure 6: Patient 3 with bilateral posterventral GPi implantation

Based on the preliminary reports on DBS in PSP, we decided to perform DBS in three selected patients with PSP, who presented as major disabling symptoms gait imbalance and falls with mild cognitive deficits.

We have chosen unilateral stimulation, based on previous work of Moro *et al*.[16] and the extended experience of Mazzone *et al*.,[12,15] in which the authors obtained clinical improvement (i.e. falls, gait) with unilateral PPN stimulation. The site of implantation was chosen contralateral to the more compromised site of the body.

In all the three patients, a reduction of falls and an amelioration of postural balance were observed. The patients required less assistance for daily living activities. The clinical improvement was, however, not fully reflected in the evaluating scales. The mean PSPRS percentage decrease was of 26.3% (SD = 8.3) at the 12 months follow-up visit for the three patients. The diversity between the reported improvement and the PSPRS might be due to the phenomenological diversity of PSP, not fully captured by the PSPRS, and repeated scheduled postoperative evaluations are necessary to capture objectively the overall clinical improvement. That the greatest PSPRS percentage decrease (35.7%) was seen in the double implanted GPi-PPN patient is possibly due to the improvement of the concomitant amelioration of his dystonic state. It remains of course speculative in light of a single case, if this better clinical outcome seen in the GPi-PPN patient is reflection of an increased synergic effect of PPN and GPi secondary to stimulation, bearing in mind the strong connectivity between the basal ganglia and the PPN (5). An interesting observation was related to the stimulation parameters; we started with low frequency stimulation, which was increased progressively to 130 Hz without noticing a significant change in clinical presentation.

CONCLUSION

Our three cases support further the role of DBS of the PPN in improving postural stability and reduction of falls over an extended time period. However, more data on DBS in atypical Parkinsonism are needed to evaluate further the efficacy of neuromodulation in PSP.

REFERENCES

1. Albaugh DL, Shih YY. Neural circuit modulation during deep brain stimulation at the subthalamic nucleus for Parkinson's Disease: What have we learned from neuroimaging studies? Brain Connect 2014;4:1-14.
2. Brusa L, Iani C, Ceravolo R, Galati S, Moschella V, Marzetti F, *et al*. Implantation of the nucleus tegmenti pedunculopontini in a PSP-P patient: Safe procedure, modest benefits. Mov Disord 2009;24:2020-2.
3. Ferraye MU, Gerardin P, Debu B, Chabardes S, Fraix V, Seigneuret E, *et al*. Pedunculopontine nucleus stimulation induces monocular oscillopsia. J Neurol Neurosurg Psychiatry 2009;80:228-31.
4. Garcia-Rill E, Houser CR, Skinner RD, Smith W, Woodward DJ. Locomotion-inducing sites in the vicinity of the pedunculopontine nucleus. Brain Res Bull 1987;18:731-8.
5. Hardman CD, Halliday GM. The internal globus pallidus is affected in progressive supranuclear palsy and Parkinson's disease. Exp Neurol 1999;158:135-42.
6. Hardman CD, Halliday GM. The external globus pallidus in patients with Parkinson's disease and progressive supranuclear palsy. Mov Disord 1999;14:626-33.
7. Hazrati LN, Wong JC, Hamani C, Lozano AM, Poon YY, Dostrovsky JO, *et al*. Clinicopathological study in progressive supranuclear palsy with pedunculopontine stimulation. Mov Disord 2012;27:1304-7.
8. Kojima J, Yamaji Y, Matsumura M, Nambu A, Inase M, Tokuno H, *et al*. Excitotoxic lesions of the pedunculopontine tegmental nucleus produce contralateral hemiparkinsonism in the monkey. Neurosci Lett 1997;226:111-4.
9. Lang AE. Treatment of progressive supranuclear palsy and corticobasal degeneration. Mov Disord 2005;20 Suppl 12:S83-91.
10. Liepelt I, Gaenslen A, Godau J, Di Santo A, Schweitzer KJ, Gasser T, *et al*. Rivastigmine for the treatment of dementia in patients with progressive supranuclear palsy: Clinical observations as a basis for power calculations and safety analysis. Alzheimers Dement 2010;6:70-4.
11. Litvan I, Agid Y, Calne D, Campbell G, Dubois B, Duvoisin RC, *et al*. Clinical research criteria for the diagnosis of progressive supranuclear palsy (Steele-Richardson-Olszewski syndrome): Report of the NINDS-SPSP international workshop. Neurology 1996;47:1-9.
12. Mazzone P, Scarnati E, Garcia-Rill E. Commentary: The pedunculopontine nucleus: Clinical experience, basic questions and future directions. J Neural Transm 2011;118:1391-6.
13. Mazzone P, Sposato S, Insola A, Scarnati E. The deep brain stimulation of the pedunculopontine tegmental nucleus: Towards a new stereotactic neurosurgery. J Neural Transm 2011;118:1431-51.
14. Mazzone P, Sposato S, Insola A, Scarnati E. The clinical effects of deep brain stimulation of the pedunculopontine tegmental nucleus in movement disorders may not be related to the anatomical target, leads location, and setup of electrical stimulation. Neurosurgery 2013;73:894-906.
15. Mazzone P, Lozano A, Stanzione P, Galati S, Scarnati E, Peppe A, *et al*. Implantation of human pedunculopontine nucleus: A safe and clinically relevant target in Parkinson's disease. Neuroreport 2005;16:1877-81.
16. Mazzone P, Insola A, Sposato S, Scarnati E. The deep brain stimulation of the pedunculopontine tegmental nucleus. Neuromodulation 2009;12:191-204.
17. Moro E, Hamani C, Poon YY, Al-Khairallah T, Dostrovsky JO, Hutchison WD, *et al*. Unilateral pedunculopontine stimulation improves falls in Parkinson's disease. Brain 2010;133:215-24.
18. Muller J, Wenning GK, Wissel J, Seppi K, Poewe W. Botulinum toxin treatment in atypical parkinsonian disorders associated with disabling focal dystonia. J Neurol 2002;249:300-4.
19. Munro-Davies L, Winter J, Aziz TZ, Stein J. Kainate acid lesions of the pedunculopontine region in the normal behaving primate. Mov Disord 2001;16:150-1.
20. Nandi D, Jenkinson N, Stein J, Aziz T. The pedunculopontine nucleus in Parkinson's disease: Primate studies. Br J Neurosurg 2008;22 Suppl 1:S4-8.
21. Newman GC. Treatment of progressive supranuclear palsy with tricyclic antidepressants. Neurology 1985;35:1189-93.
22. Ostrem JL, Christine CW, Glass GA, Schrock LE, Starr PA. Pedunculopontine nucleus deep brain stimulation in a patient with primary progressive freezing gait disorder. Stereotact Funct Neurosurg 2010;88:51-5.
23. Pahapill PA, Lozano AM. The pedunculopontine nucleus and Parkinson's disease. Brain 2000;123:1767-83.
24. Piccione F, Mancini E, Tonin P, Bizzarini M. Botulinum toxin treatment of apraxia of eyelid opening in progressive supranuclear palsy: Report of two cases. Arch Phys Med Rehabil 1997;78:525-9.
25. Plaha P, Gill SS. Bilateral deep brain stimulation of the pedunculopontine nucleus for Parkinson's disease. Neuroreport 2005;16:1883-7.
26. Santacruz P, Uttl B, Litvan I, Grafman J. Progressive supranuclear palsy: A survey of the disease course. Neurology 1998;50:1637-47.
27. Steele JC, Richardson JC, Olszewski J. Progressive supranuclear palsy. A heterogeneous degeneration involving the brain stem, basal ganglia and cerebellum with vertical gaze and pseudobulbar palsy, nuchal dystonia and dementia. Arch Neurol 1964;10:333-59.
28. Stefani A, Lozano AM, Peppe A, Stanzione P, Galati S, Tropepi D, *et al*.

Bilateral deep brain stimulation of the pedunculopontine and subthalamic nuclei in severe Parkinson's disease. Brain 2007;130:1596-607.
29. Williams DR, de Silva R, Paviour DC, Pittman A, Watt HC, Kilford L, *et al*. Characteristics of two distinct clinical phenotypes in pathologically proven progressive supranuclear palsy: Richardson's syndrome and PSP-parkinsonism. Brain 2005;128:1247-58.
30. Williams DR, Holton JL, Strand K, Revesz T, Lees AJ. Pure akinesia with gait freezing: A third clinical phenotype of progressive supranuclear palsy. Mov Disord 2007;22:2235-41.
31. Yeh IJ, Tsang EW, Hamani C, Moro E, Mazzella F, Poon YY, *et al*. Somatosensory evoked potentials recorded from the human pedunculopontine nucleus region. Mov Disord 2010;25:2076-83.
32. Zrinzo L, Zrinzo LV, Massey LA, Thornton J, Parkes HG, White M, *et al*. Targeting of the pedunculopontine nucleus by an MRI-guided approach: A cadaver study. J Neural Transm 2011;118:1487-95.
33. Zrinzo L, Zrinzo LV, Hariz M. The pedunculopontine and peripeduncular nuclei: A tale of two structures. Brain 2007;130:e73.