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Clinical note

Deep brain stimulation for the alleviation of post-stroke neuropathic pain

Sarah L.F. Owen ^a, Alexander L. Green ^{b,*}, John F. Stein ^a, Tipu Z. Aziz ^b^a *University Laboratory of Physiology, University of Oxford, Oxford, UK*^b *Department of Neurological Surgery, Radcliffe Infirmary, Oxford, UK*

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Abstract

Our aim was to assess the efficacy of deep brain stimulation in post-stroke neuropathic pain. Since 2000, 15 patients with post-stroke intractable neuropathic pain were treated with deep brain stimulation of the periventricular gray area (PVG), sensory thalamus (Ventroposterolateral nucleus-VPL) or both. Pain was assessed using both a visual analogue scale and the McGill's pain questionnaire. VAS scores show a mean improvement of 48.8% (SD 8.6%). However, there is a wide variation between patients. This study demonstrates that it is an effective treatment in 70% of such patients.

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Keywords: Deep brain stimulation; Post-stroke pain; McGill pain questionnaire

1. Introduction

Intractable neuropathic pain affects approximately 10% of patients after a stroke (Greenberg et al., 2004). Typically, a burning hyperaesthesia and aching affect areas that are rendered numb. Such pain usually resists medical therapy leaving these patients with no symptom alleviation. In the UK, an estimated 28,000 people will suffer from this predicament.

Although motor cortex stimulation has been reported as a mode of therapy for this condition, the published literature quotes extremely variable results (Canavero and Bonicalzi, 2003; Carroll et al., 2000; Katayama et al., 1994; Tsubokawa et al., 1991). Therefore, deep brain stimulation has been our preferred mode of therapy since 1999. Here, we present the results of 15 post-stroke patients with neuropathic pain who were treated with deep brain stimulation.

2. Methods

Fifteen patients with a mean age of 58.6 years were selected for surgery (three female and 12 male). Five patients had cortical and 10 had subcortical strokes, of which eight were thalamic, one pontine, and one in the internal capsule. Average duration of pain prior to surgery was 5.2 years. The most disabling aspect of the pain syndrome was a burning hyperaesthesia in the area of numbness that affected seven of the 15 patients. Also described was a severe 'cramping' or 'crushing' sensation. Pre-operatively, each patient underwent a comprehensive neuropsychological assessment. Provided there were no medical or psychological contraindications, deep brain stimulation of the periventricular/periaqueductal grey areas (PVG/PAG) and sensory thalamus were offered. Both targets were chosen because the literature quotes both as being effective with no indication of the superiority of one target over another. Deep brain stimulation for neuropathic pain and this study were approved by our local (Oxford regional) ethics committee. Informed consent was obtained from all patients prior to participation in the study.

3. Recording of pain scores

Pre-operatively, and at 1 year, each patient recorded twice daily (am and pm) visual analogue score (VAS)

* Corresponding author. Address: Oxford Functional Neurosurgery, Radcliffe Infirmary, Woodstock Road, Oxford OX2 6HE, UK. Tel.: +44 1865 224221; fax: +44 1865 224786.

E-mail address: alex.green@physiol.ox.ac.uk (A.L. Green).

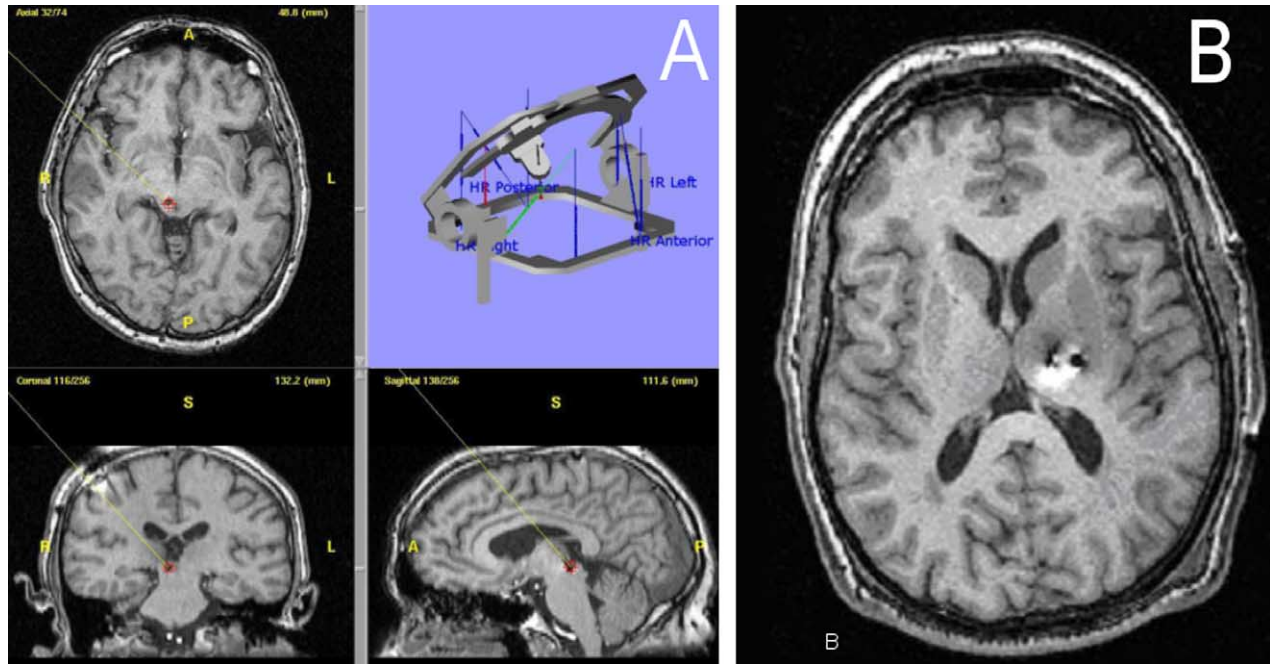


Fig. 1. (A) The screen view showing the planned trajectory and targeting of the PVG/PAG in three planes. (B) A POST-operative MRI showing the VPL electrode (lateral) and the wire leading to the PVG electrode (medial) which is located inferiorly.

of pain (scale of 1–10) in a pain diary over a period of 12 days. The 24 VAS scores were averaged to give a single pre-operative and post-operative figure. Pre- and post-operative VAS for each group were compared using a paired *t*-test with a two-tailed *P*-value of <0.05 taken as significant. Each patient also completed a McGill pain questionnaire (MPQ) on both occasions, in the presence of a specialist nurse. For analysis of data, we used the ranked pain rating index (PRI(R)) as described by Melzack (1975). In this method of scoring, each word in a category is assigned a number, depending on its severity. Using this method, we calculated overall pain rating index—PRI (R) (out of 78), sensory PRI(R) (out of 42), affective PRI(R) (out of 14), evaluative PRI(R) (out of 5) and miscellaneous PRI(R) (out of 17). Pre- and post-operative MPQ scores for each group were compared using the Wilcoxon signed ranks test for non-parametric data with a *P*-value of <0.05 taken as significant.

4. Surgical technique

All patients had a T-1 weighted axial MRI scan (2 mm-thick slices parallel to the AC–PC line) prior to surgery. For surgery, a CRW base ring was applied to the patients' head under local anaesthesia. A stereotactic CT scan was then performed and using the Radionics Image Fusion[®] and Stereoplan[®] programme, the MRI scan was volumetrically fused to the stereotactic CT scan. This technique has been used since 1995 to eliminate the errors of using MRI stereotaxy alone, which arise from the spatial distortions

intrinsic to magnetic fields. The co-ordinates for the PVG and VPL were then calculated. A double oblique trajectory (Fig. 1(a)) was used with an entry point just anterior to the coronal suture and laterality of approach dictated by ventricular width. A separate 2.7 mm twist drill skull perforation was made for each electrode. The VPL was located from 5 mm above and up to 5 mm below the AC–PC line, 5–8 mm posterior to the mid commissural point and approximately 12–14 mm lateral (Fig. 1(b)). Patients with strokes in the sensory thalamus were only implanted in the PVG/PAG. The proximal part of the electrode was located in the PVG/PAG 2–3 mm lateral to the wall of the third ventricle and 2 mm anterior to the level of the posterior commissure, and distally, the deepest part of the electrode lay in the superior colliculus (Fig. 2). After washing the patient's scalp with alcoholic chlorhexidine, a parasagittal posterior frontal scalp incision 3.0 cm from the midline was made contra-lateral to the side of pain. The VPL was implanted with a Medtronic 3387[®] electrode (Medtronic Inc, Minneapolis, USA) where stimulation induced paraesthesiae in the area of pain and the PVG/PAG with a Medtronic 3387[®] electrode where stimulation induced relief of pain or a sensation of warmth in the area of pain. In practice, capturing the whole area of pain can be challenging, particularly with hemi-body pain. Intraoperatively, we move the electrode proximal or distal, along the electrode track until we are able to cover the widest possible involved area with the middle two contacts. In general, the deepest electrode was noted to be in a satisfactory position if 'eye bobbing' was induced at intensity of stimulation at least twice that required for sensory effects. The electrodes

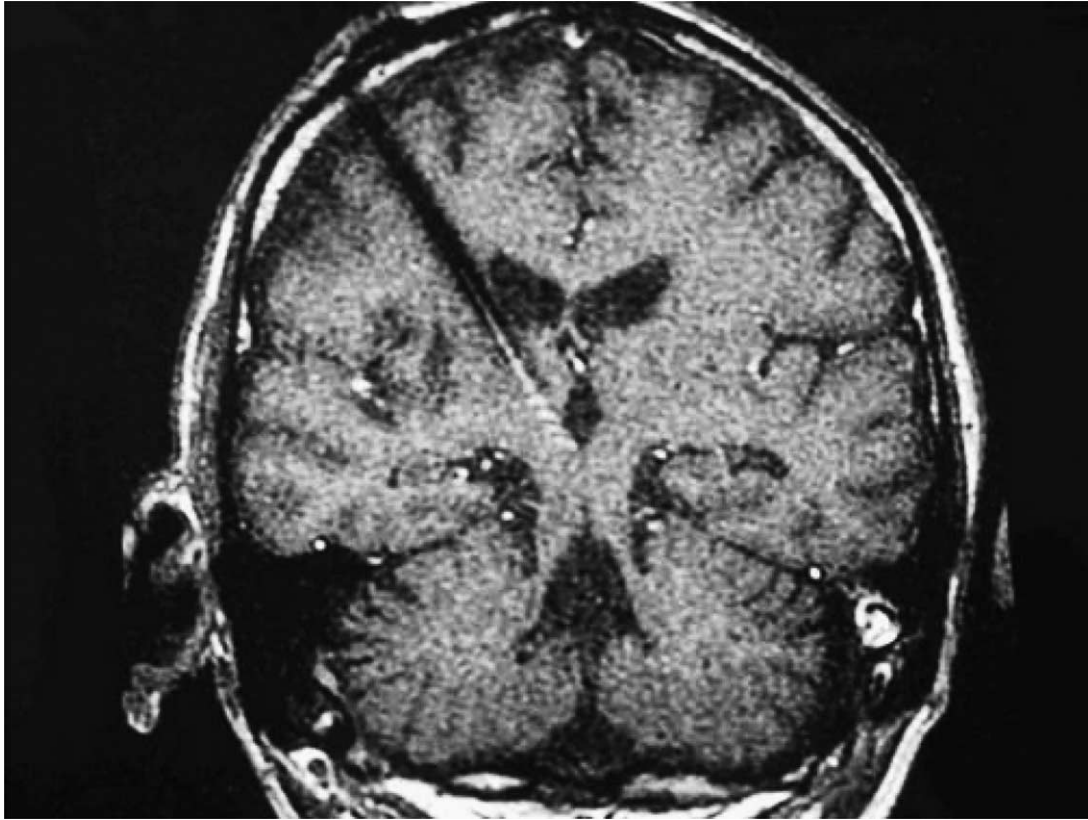


Fig. 2. View of the implanted PVG electrode with a T1 weighted MR scan.

were fixed to the skull with a miniplate[®] prior to externalisation.

In all patients, the electrodes were externalised for a week of trial stimulation. During this period, electrodes were trialled individually (1–2 days of each) to cover the area of pain and achieve maximum pain relief. After this period, those with two electrodes had 1–2 days of both electrodes being used. If the patients were satisfied with the degree of pain relief (from any of these combinations), full

implantation of a Medtronic pulse generator (Synergy[®], Medtronic, Minneapolis, USA) was performed the following week under general anaesthesia.

5. Results

During a trial period of 1 week following surgery, three patients did not feel there was significant pain relief to

Table 1
Patients that were fully implanted—location of stroke and DBS, as well as efficacy

Age/sex	Stroke location	Area of pain	Target	Best trial target	Final target used	Overall reduction in VAS/MPQ (%) at follow up
50 M	L Thalamus	R Hemi-body	PVG	(PVG)	(PVG)	74.3/41
63 M	R Thalamus	L Hemi-body	PVG	(PVG)	(PVG)	16/28
60 M	R Pons	L Leg, R face	PVG	(PVG)	(PVG)	41/39
66 M	R Thalamus	L Face and arm	PVG	(PVG)	(PVG)	35/50
74 M	R Internal capsule	L Hemi-body	PVG	(PVG)	(PVG)	17/22
46 F	L Cortex + thalamus	R Arm and leg	PVG	(PVG)	(PVG)	43/53
37 M	L Cortex	R Hemi-body	PVG/VPL	PVG	Both	76/40
54 M	R Parietal Cortex	L Arm and leg	PVG/VPL	PVG	Both (VPL off)	14/45
62 F	SAH (R Cortex)	L Hemi-body	PVG/VPL	PVG	Both (VPL off)	31/59
47 M	L Thalamus	R Hemi-body	VPL	(VPL)	(VPL)	41/31
60 F	Right MCA territory (Cortex)	Left Arm and leg	PVG/VPL	Both	Both	49/32
70 M	R Thalamus	L Hemi-body	PVG	(PVG)	(PVG)	43/19

L, left; R, right; PVG, periventricular grey; VPL, ventroposterolateral nucleus (of the thalamus); MPQ, McGill's pain questionnaire.

proceed to full implantation of the pacemaker, and the electrodes were removed under local anaesthesia. The 12 remaining underwent full implantation of the extension cables and the pacemaker (Synergy[®], Medtronic Inc). Although dual channel, all patients were implanted with a Synergy[®] because of the longer battery life. If one channel is used, a plug is used to close off the inactive channel. The patients were then reviewed 1 month later to optimise the settings for maximum pain relief and were reviewed 6-monthly thereafter.

Average follow up was 27 months (for simplification, 2-year pain scores were used in this study). Nine patients preferred chronic stimulation of the PVG, one in the VPL and two preferred both electrodes to be activated. The results are summarised in Tables 1 and 2. Overall, the reduction in VAS scores was 48.8% (SD 2.2, $P < 0.001$). The average reduction in the cortical strokes subgroup was

Table 2
Changes in pain scores for both the McGill pain questionnaire for each category and visual analogue scores (VAS)

MPQ category	Cortical strokes	Subcortical strokes	Total
<i>Sensory</i>			
Pre-op	17.60	23.86	21.25
Post-op	7.20	14.29	11.33
% Improvement	59	40.1	46.7
SD	7.8	5.0	6.8
P-value	0.04	0.062	0.004
<i>Affective</i>			
Pre-op	4.80	4.71	4.75
Post-op	2.40	3.14	2.83
% Improvement	50	33.3	40.4
SD	2.30	3.49	2.73
P-value	0.24	0.46	0.2
<i>Evaluative</i>			
Pre-op	3.60	2.86	3.17
Post-op	2.60	3.29	3.0
% Improvement	27.8	+ 13.1	5.4
SD	2.1	1.8	1.65
P-value	0.27	0.7	0.8
<i>Miscellaneous</i>			
Pre-op	7.0	6.29	6.58
Post-op	5.0	4.71	4.83
% Improvement	28.6	25.1	26.6
SD	3.6	3.25	3.45
P-value	0.28	1.16	0.10
<i>MPQ Total</i>			
Pre-op	33.4	37.71	35.92
Post-op	17.2	25.43	22.00
% Improvement	48.5	32.6	38.8
SD	8.6	9.9	13.20
P-value	0.06	0.16	0.017
<i>Mean VAS</i>			
Pre-op	8.4	7.8	8.1
Post-op	4.9	3.6	4.1
% Improvement	42	54	48.8
SD	2.7	1.4	2.2
P-value	0.023	<0.001	<0.001

SD, one standard deviation of the mean. P-value relates to the Wilcoxon signed ranks test comparing pre- and post-operative scores. MPQ, McGill's pain questionnaire. Significant changes are highlighted in bold type.

42% (SD 2.7, $P = 0.023$) and in the sub cortical stroke group was 54% (SD 1.4, $P < 0.001$). If burning hyperaesthesia was present this was markedly reduced. Analysis of the MPQ scores shows that the overall pain rating index (PRI(R)) reduced by 38% ($P < 0.05$, Wilcoxon) and that this reduction was mainly due to changes in the sensory category which showed an overall reduction of 46.7% ($P < 0.01$, Wilcoxon). These data suggest that there was a better reduction of pain in the cortical stroke group (48.5%, $P = 0.06$) than the subcortical stroke group (32.6%, $P = 0.16$), i.e opposite to the VAS results. However, the numbers in each group are small and it is therefore difficult to reach conclusions regarding differences between the groups. It is also important to point out that there is a large variation in improvements in the MPQ which ranged from -2% overall (i.e. slight worsening of scores) to a +91.3% improvement in one patient.

Of the 12 patients, seven stopped all analgesics (of these four were on opiates, three on Gabapentin[®]) and five changed from regular opiate analgesia to 'as required' non-opiates.

There was one complication in this series; a patient struck the top of his head against a lintel and fractured the extension lead. After surgical revision, pain relief was restored. We have found few side-effects from stimulation, but eye 'bobbing' is a common problem when stimulating the lowest part of the PVG electrode at high voltages.

6. Discussion

Combined stimulation of the PAG and sensory thalamus was first shown to be successful by Hosobuchi (1983). This prospective study demonstrates that deep brain stimulation of the PVG/PAG and sensory thalamus may have a useful role in the management of post-stroke central pain. In our experience, patients who symptomatically suffer from severe burning hyperaesthesia appear to respond best. In this series, the average pain relief is around 40–50% which is similar to the 50% relief often quoted as the bench mark for useful pain relief. However, pain relief varies markedly between patients and can be over 90%. The site of the stroke may be of relevance but as we have shown, the scoring system used may have a bearing on the exact figures. Also of note is that the majority of patients preferred the analgesic effects of PVG stimulation to VPL stimulation and these results therefore largely represent stimulation of the former.

One proposed disadvantage of deep brain stimulation is the onset of tolerance. In our experience it is not tolerance but that, once patients lose the intolerable burning hyperaesthesia, the background 'crushing', 'aching' sensation becomes more noticeable. Nevertheless, the effectiveness of the procedure can be confirmed in an N of one study (Green et al., 2004) in which the patient records pain scores and the stimulator is randomly turned on or off.

The mechanism of the effects is still unclear. There is some evidence to suggest that PVG/PAG stimulation has an inhibitory effect on the sensory thalamus (Nandi et al., 2003; Rinaldi, et al., 1991). However, the analgesic effects of deep brain stimulation can last for over 24 h after a period of stimulation. This may confound on/off studies (Green et al., 2004) but does support evidence that PVG/PAG stimulation results in the release of endogenous opiates (Hosobuchi et al., 1977; Rinaldi et al., 1991; Young et al., 1993).

Deep brain stimulation has been tried with success in the past, but due to overall poor results and poor patient recruitment into two trials in the 1980's this technique was largely abandoned (Burchiel, 2001). However, with the resurgence of functional surgery for movement disorders, the use of MRI scans for stereotactic target localisation, safer electrodes than those used in the early days (internalised stylets in particular), and more reliable pacemakers, this important indication should be revisited.

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