



# **Which patients with Dystonia benefit from Deep Brain Stimulation?- a meta-regression of individual patient outcomes**

Caroline Andrews, Iciar Aviles-Olmos, M I Hariz, T Foltynie

## **► To cite this version:**

Caroline Andrews, Iciar Aviles-Olmos, M I Hariz, T Foltynie. Which patients with Dystonia benefit from Deep Brain Stimulation?- a meta-regression of individual patient outcomes. *Journal of Neurology, Neurosurgery and Psychiatry*, 2010, 81 (12), pp.1383. <10.1136/jnnp.2010.207993>. <hal-00576255>

**HAL Id: hal-00576255**

**<https://hal.science/hal-00576255v1>**

Submitted on 14 Mar 2011

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



HAL Authorization

# **Which patients with Dystonia benefit from Deep Brain Stimulation?- a meta-regression of individual patient outcomes**

Caroline Andrews<sup>1</sup>, Iciar Aviles-Olmos<sup>2</sup>, Marwan Hariz<sup>2,3</sup>, Thomas Foltynie<sup>2</sup>

<sup>1</sup>Lysholm Department of Neuroradiology, National Hospital for Neurology & Neurosurgery, Queen Square, London WC1N 3BG.

<sup>2</sup>Unit of Functional Neurosurgery, Sobell Department of Motor Neuroscience, UCL Institute of Neurology, Queen Square, London WC1N 3BG.

<sup>3</sup>Department of Neurosurgery, University Hospital of Northern Sweden, Umea, Sweden.

Word count: 3718

MeSH headings; Dystonia, Stereotaxic surgery.

Corresponding author: Thomas Foltynie. Box 146, National Hospital for Neurology & Neurosurgery, Queen Square, London. WC1N 3BG.

Tel +44(0) 203 108 0026, Fax +44(0) 203 108 0142

Email: [T.Foltynie@ion.ucl.ac.uk](mailto:T.Foltynie@ion.ucl.ac.uk)

## **Abstract**

There is substantial variability in the responsiveness of dystonia patients to deep brain stimulation (DBS), presumably due to the multiple causes of dystonia. This article presents the results of an analysis of the combined published results of individual patient outcomes following DBS for all types of dystonia. From 157 papers reporting clinical outcomes of DBS for dystonia, individual quantitative data were available for 466 patients with all forms of dystonia. The sub-classification of these patients included 344 with primary forms of dystonia, 10 with myoclonus dystonia, 19 with heredo-degenerative dystonias and 93 patients that had DBS for secondary dystonia.

Patients with primary forms of dystonia, myoclonus dystonia, subtypes of heredo-degenerative dystonia and tardive dystonia have a greater than 50% mean improvement in dystonia severity following DBS. Among patients with primary generalised dystonia, multiple regression analysis showed that a shorter duration of symptoms ( $p=0.008$ ), a lower baseline severity score ( $p=0.024$ ) and DYT-1 positive status ( $p=0.002$ ) were all independently associated with a significantly higher percentage improvement from surgery. Patients with other forms of heredodegenerative and secondary dystonia have variable responses making prediction of response in future patients difficult.

The degree of dystonia response that justifies DBS is a highly subjective issue. Emphasis should be placed on both safety of surgical technique and an in depth evaluation of patients' own perception of their life before and after DBS by using validated quality of life measures, in addition to existing use of objective severity scales.

## INTRODUCTION

Dystonia is a common movement disorder, defined as ‘a syndrome of sustained muscle contraction usually producing twisting and repetitive movements or abnormal postures. Classification of dystonia is made according to three main features; the age of onset of symptoms, the distribution of the region of the body affected (focal, segmental or generalized) and the underlying etiology (Primary, Secondary, Dystonia-plus conditions, or Heredo-degenerative conditions). Patients with primary dystonia will present with no other neurological condition (with the exception of tremor) and will have no structural brain abnormalities or inborn errors of metabolism. About 10% of generalized dystonia starting in childhood or adolescence are linked to genetic mutations, the majority being caused by a GAG deletion in the DYT1 gene. Secondary dystonia results from other causes such as brain injury, drugs or toxins, or post encephalitis. Dystonia-plus conditions feature other neurological signs such as in the myoclonus-dystonia syndrome, but in these patients brain imaging is normal, no secondary cause is found, and genetic causes for these conditions have been identified. Dystonia is also seen in patients with a range of heredo-degenerative conditions in which neurological symptoms and signs such as parkinsonism, ataxia, bulbar failure or neuropathy can give clues to the underlying diagnosis. Surgical treatment for dystonia dates from the 1950s and 1960s. Irving Cooper reported that 69% of 227 patients with dystonia improved with thalamotomy, with marked improvement seen in 24% and mild to moderate improvement in 45%.[1] Further teams subsequently demonstrated the benefit of lesioning the globus pallidus internus (GPi) for the treatment of dystonia [2] and subsequently deep brain stimulation (DBS) of the GPi was evaluated for the treatment of dystonia. The original reports of successful outcomes following DBS for dystonia included patients with the primary generalised form that were positive for the DYT1 GAG deletion.[3]

Since then, multiple centres have used DBS as a treatment for patients with many other subtypes of dystonia insufficiently helped by oral medications or Botulinum toxin injections. While mean results have generally been encouraging, a wide range of outcomes have been reported.

Predictive factors of long term outcome have been sought in small series with hints that shorter disease duration is a statistically significant predictor of better long term outcome following DBS.[4] Whether patients positive for the DYT1 deletion have greater benefit has been unclear with some reports suggesting that the DYT1 mutation is a predictor of better outcome [5-7], whilst others have not found a significant difference between the DYT1+ve or DYT1-ve groups.[8,9] There is a lack of effective non-surgical treatment for patients with hereditary degenerative and secondary dystonias, therefore DBS has been trialled among widely varying subtypes of such patients; however the efficacy of DBS in the treatment of these patients is less clear.

In view of the substantial variability in the responsiveness of dystonia patients to DBS, we have reviewed the published literature and extracted the results of individual patient outcomes following DBS for dystonia. We have used these data in a meta-regression to re-analyse factors predictive of outcome following DBS for all types of dystonia.

## **METHODS**

### **Search strategy**

The PubMed database was searched for articles describing DBS for dystonia. MeSH headings used were “Dystonia” and “Stimulation”. Only articles written in English were reviewed and only publications reporting individual clinical outcome data were included in statistical analyses. Papers that reported summary mean outcomes following DBS for dystonia are reported alongside

the combined individual clinical outcome data. Where there were multiple serial publications from the same centre describing the same or overlapping patient groups, great care was taken to include data from any individual only once using their age at onset, age at surgery and baseline dystonia severity to distinguish them as individuals. Reports of patients with dystonia as a feature of Parkinson's disease were excluded. Dystonia subtypes were coded according to etiology- primary, dystonia plus, hereditary degenerative or secondary, then by subtype according to body distribution and or identified underlying cause.

### **Assessing the outcome of DBS for dystonia**

The scale most commonly used for rating severity of generalized dystonia is the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS). This comprises a clinician rated movement scale (120 point score) and patient rated disability scale (0 – 30 point score). For patients with cervical dystonia (an adult onset focal primary dystonia) the Toronto Western Spasmodic Torticollis Rating Scale (TWSTRS) is most commonly used with sub scores for severity, disability and pain. Whilst most studies have used BFMDRS and TWSTRS for measuring outcome, the Unified Dystonia Rating Scale (UDRS), the Abnormal Involuntary Movement scale, and the Tsui scale have also been utilized.

### **Statistical analysis**

From each paper documenting individual outcome data, the following information was noted: the dystonia subtype, gender, age at surgery, duration of symptoms, rating scale used, DBS target, pre-operative and post operative scores, duration of follow up, and whether assessment was open or blinded. The percentage improvement in dystonia severity was calculated for each patient. Microsoft Stata version 8 was used for all analyses. Multiple regression was performed to assess

whether percentage improvement in dystonia severity was associated with age at surgery, duration of symptoms, baseline severity, and surgical target. The centre, the duration of follow up, the rating scale used and whether the assessment was performed open or blinded were included as covariates in each model.

## **RESULTS**

The original Pubmed search revealed 1010 papers, of which 157 papers reported clinical outcomes of DBS for dystonia. From these papers, individual quantitative outcomes following DBS were available for 466 patients with all forms of dystonia. The sub-classification of these patients included 344 with primary forms of dystonia, 10 with myoclonus dystonia, 19 with heredo-degenerative dystonias and 93 patients that have had DBS for secondary dystonia. The number of patients in each sub-category together with the references from which the patient data was obtained are presented in Tables 1-3.

### **Primary Dystonia**

#### Primary generalised dystonia (PGD)

The search identified 209 patients that received DBS for primary generalised dystonia from 20 centres. The baseline features of these patients are presented in Table 1. The mean percentage improvement of the group as a whole was 60.7%, (inter-quartile range- 43.4% to 83.3%). Within this group, the 91 patients with DYT1 positive dystonia had the greatest percentage improvement. Multiple regression analysis (with adjustment for confounding covariates) showed that a shorter duration of symptoms ( $p=0.008$ ) (See also Figure 1), a lower baseline severity score ( $p=0.024$ ) and DYT-1 positive status ( $p=0.002$ ) (See also Figure 2) were all independently associated with a significantly higher percentage improvement from surgery. In a single patient

that had DBS of the subthalamic nucleus (STN) for idiopathic PGD, an overall improvement of 72.1% was observed.[10]

Additional patients have been published in other series but could not be included in the current analysis because of lack of individual data in the published manuscripts. Among 24 patients with generalised dystonia that received GPi DBS in a double blinded trial of DBS (the only double blind trial of DBS for primary generalized dystonia), there was a 41.9% mean reduction in dystonia severity.[8] A further series of 30 patients followed up for 2 years had a mean reduction in motor severity of 82.5%.[11] These authors demonstrated that the presence of fixed skeletal deformities and longer disease duration were both predictive of a lower percentage improvement following GPi DBS. A series of 24 primary generalised dystonia cases improved by a mean of 59% if DYT1 positive, and only 43% if DYT1 negative but this difference was not significant.[12]

### Spasmodic Torticollis

Individual outcome data were identified for 67 patients from 14 centres with isolated spasmodic torticollis treated with DBS. The mean improvement was 48% (SD 41%) but none of the variables entered into the regression model were associated with the magnitude of improvement from surgery. Sixty three patients had electrodes inserted in the GPi with a mean percentage improvement of 49.2%, whereas 4 patients had electrodes in the STN with improvement of only 34.9% .[10] Patients evaluated in a blinded fashion had a mean improvement of 33.3% compared to a mean improvement of 52.3% in those patients assessed in an open label fashion.

### Meige Syndrome



All 17 patients included in this analysis had GPi DBS, with a mean improvement of 64.3% (SD 29.5%). Compared with other patients with focal/ segmental dystonias, the patients with Meige syndrome were older, with a shorter duration of symptoms and a higher percentage response to treatment. The regression analysis confirmed that the only variable showing a trend towards association with improved percentage outcome from DBS was a shorter duration of symptoms ( $p=0.06$ ).

### Focal/ Segmental Dystonias

This subgroup of dystonia patients includes a mixture of phenotypes. The majority of published patients have not been tested for DYT-1 status. Patients had a mean improvement of 57.9% with the GPi target ( $n=37$ ), all with open label assessments. A single patient receiving STN DBS for this condition had a 23% improvement in symptoms [13] whereas a single report of ViM DBS had a 58.3% improvement.[14] An additional 16 patients with focal/segmental dystonia had GPi DBS as part of a blinded trial and showed a mean 52.6% reduction in dystonia severity but without individual data.[8] None of the variables entered into the regression model predicted the magnitude of improvement from surgery for patients with focal/segmental phenotypes.

### **Myoclonus Dystonia**

From 10 patients with myoclonus dystonia, a mean improvement of 58% was seen following GPi DBS (Table 1). Two case reports of VIM DBS for myoclonus-dystonia suggested improvement in myoclonus but not dystonia.[16,17]

### **Heredodegenerative dystonias**

Patients with Pantothenate Kinase-Associated Neurodegeneration (PKAN) had the greatest percentage improvement of the heredo-degenerative subcategory, all operated in the GPi (Table 2). The percentage response was not associated with age at surgery, duration of symptoms, or baseline severity. Some individuals with neuroacanthocytosis manifest both dystonia and chorea. Reports of GPi DBS in this condition suggest that dystonia may be improved but this may be at the expense of worsening of chorea.[18]

### **Secondary Dystonia conditions**

The number of patients with each secondary dystonia subtype is small (Table 3). Patients with tardive dystonia (n=41) had a 69% improvement in dystonia severity following DBS. A lower pre-operative score ( $p=0.04$ ) and shorter duration of symptoms ( $p=0.02$ ) both independently predicted improved percentage response. The 39 patients that had GPi DBS improved by 67.4% in comparison to 2 patients that had STN DBS improving by 92%.[19]

Patients with post-traumatic dystonia, dystonic cerebral palsy or post-encephalitic dystonia respond less well to DBS with only isolated rare exceptions [20,21]. The small number of patients with post anoxic dystonia have a higher mean percentage improvement but the variance in response is higher and is not related to age, duration of symptoms or baseline severity.

### **Quality of life**

The vast majority of studies measure the change in one of the validated dystonia severity scales to gauge outcome following DBS for dystonia. These scales are objective but the resulting scores do not necessarily reflect the patient's subjective perception of changes in their daily life or their quality of life (QoL). For example a minor improvement in neck posture, hardly detectable on the BFM movement subscale, may nevertheless have major importance in wheelchair comfort or

in swallowing, and indeed the converse can also apply. An alternative is therefore to measure quality of life which has been incorporated into several of the larger dystonia series.

Among 22 patients with primary generalised dystonia, significant improvements in general health, physical function and body pain were identified using the generic short form 36 (SF-36) scale. Mean scores did not deteriorate in any SF-36 domain and measures of cognition and mood were unchanged.[9] In the double blind trial of DBS for 40 patients with segmental or generalised dystonia, there was a significant improvement in the SF-36 physical composite score at 3 months.[22]

### **Adverse effects of DBS surgery for dystonia**

Not all published reports specifically document detailed adverse effects resulting from DBS for dystonia therefore no attempt to quantify their overall frequency is made here. There are multiple reports of lead migration and lead fracture [4,5,8,23-27] and one group have proposed that this complication is more common among dystonia patients than other patients undergoing DBS [28]. Other surgical adverse events do not seem to occur particularly more commonly in dystonia with only occasional reports of haemorrhage [27], infection [4,8,13,23,29-34], and misplaced electrodes.[27,35] Adverse effects specifically related to chronic GPi stimulation for dystonia include dysarthria [26,31,34,36,37,38] and parkinsonism [7,39-41] both of which seem to be reversible but sometimes at the expense of inadequate dystonia relief.

## **DISCUSSION**

This review has drawn together the published data describing the outcomes of DBS for the range of subtypes of dystonia, and presents the overall results of the combined dataset. The most impressive and consistent results are among patients with DYT-1 primary generalised dystonia

and patients with tardive dystonia. Because of the fairly recent introduction of DBS for dystonia, there is a lack of long term follow up, although four recent studies have reported on outcome at up to 7.5 and 10 years post DBS implantation [4,24,42,43] concluding that DBS can maintain a significant long-term benefit in responding patients.

Inevitably there are potential sources of bias in this type of review. Positive results from surgery are more likely to be reported than negative outcomes, and the vast majority of studies present data from open label assessments that are more likely subject to observer bias. Only two studies included in this review had blinded assessments of their patients (spasmodic torticollis [20,35] and secondary dystonia.[20] Indeed the quantitative outcomes following DBS for dystonia are considerably lower when patients are assessed in a blinded fashion. Despite these potential shortcomings, the data presented here represents the most comprehensive review of dystonia outcomes following DBS to date. DBS has been beneficial to the majority of dystonia patients highlighted in the literature although the percentage improvement rate is very variable.

#### *Primary Generalised Dystonia*

This dataset confirms that patients with PGD respond well to pallidal DBS. Patients with DYT1 positive dystonia respond better than those that are DYT1 negative or untested, although all PGD groups respond well overall, but with considerable inter-individual variability. Independent of DYT1 status, surgery performed at a younger age and with lower baseline severity is more likely to lead to a higher percentage improvement in symptoms of dystonia. While this trend is a useful guide, individual patients can confound this general trend for example a PGD patient experiencing only a 20% improvement in BFM despite disease duration of only 5 years, and another patient with an 85% improvement despite disease duration of 21 years.[5]

Analysis of further additional factors that might predict response to DBS was possible in a retrospective review of 40 PGD patients (included in this analysis) operated on in Montpellier, France with 2-8 year follow up. These authors created a multivariate model to evaluate which factors predicted response to DBS in PGD [42], and in addition to their data consistent with that presented here, found that increased anatomical and stimulated volumes of the GPi also predicted better outcomes. Several groups have attempted to look specifically at active electrode position within the GPi and relate this to outcome. Postero-ventral GPi stimulation has been found to provide the greatest overall effect, and has been considered superior for the arm and trunk.[7] However other series have found no correlation between active contact positions and post operative outcome.[9] The optimal programming parameters vary widely between patients and the interactions between the position of electrode contacts, pulse widths and mode of stimulation make comparisons difficult, although it has to be assumed that the optimal parameters have been chosen through an iterative process for each patient.

Further evaluation of factors predicting outcome following DBS for primary generalised dystonia were also performed as part of a 3 year study [9] that followed up 22 patients (included in this analysis), and demonstrated sustained benefit from the pallidal stimulation (58% mean improvement from baseline). Their patients who had little improvement tended to have severe tonic posturing, whereas the patients with the greatest improvements (>75%) had diffuse phasic hyperkinetic involuntary movements pre-operatively. In addition, most groups have found that those patients with fixed skeletal deformities do less well than those patients caught earlier in their disease progression, although may still improve from their baseline state and therefore benefit from treatment. In addition to fixed skeletal deformities, the development of secondary disability from e.g. cervical myelopathy further limits possible improvements.[44]

### *Spasmodic torticollis*

The most common of the adult onset, focal primary dystonias is spasmodic torticollis. The sternocleidomastoid muscles are innervated from both hemispheres with most of their supply coming ipsilaterally therefore bilateral surgery is required even for the most asymmetrical patients. The variance in response however is substantial and does not appear to be explained by age at surgery, duration of symptoms or baseline severity. Even at the same centre a range of improvement between 20 to 83% has been seen [31], despite post operative MRI confirming electrode positions and no correlation was found between location of electrode and magnitude of response.

Dystonia severity should not be the only measure of outcome following DBS. Among a single blind series [35], even patients with less than 30% improvement on motor score all improved in relation to their pain, disability and QoL. This study also investigated outcome predictors such as electrode location, surgical centre, surgical technique or type of dystonia (phasic, tonic or tremulous), but none appeared related. The only patient who deteriorated after DBS had good electrode placement.

### *Meige*

The current analysis confirms the findings of case reports suggesting that GPi DBS is a useful therapy for patients with Meige syndrome (Idiopathic cranial cervical dystonia).[45-47] In a series of patients with Meige syndrome that followed 6 patients for 6 months, most patients had meaningful clinical improvements by 4 to 6 weeks post implantation. Overall improvements were seen in blepharospasm, oromandibular dystonia and cervical dystonia. Speech and swallowing both showed a trend towards improvement.[39]

### *Myoclonus dystonia*

Although the number of published patients with myoclonus dystonia that have had DBS is small, the reports of good outcomes among these patients are consistent with our own experience. Both myoclonic features and dystonia can improve.

### *Heredodegenerative dystonia*

Patients with heredodegenerative dystonia are distinctive from other individuals with dystonia by the co-existence of other neurological deficits e.g. cognitive decline, seizures etc. There is no evidence that non-motor symptoms or the degenerative process itself are improved by DBS. However, improvement in pain as a result of DBS can allow lower medication doses which can have secondary beneficial effects.[48] Among these patients a vital pre-requisite in the decision regarding surgery is the identification of the degree of disability that they suffer purely due to dystonia.

### *Secondary dystonia*

The experience of GPi DBS in secondary dystonia has been limited, varied and less successful than in the idiopathic group. Conceptually it might be considered that patients with normal brain MRI have a reversible electro-physiological or neurochemical cause for their dystonia, whereas patients with abnormalities visible on conventional structural imaging may have an irreversible anatomical cause for their dystonia. The excellent response of patients with tardive dystonia is consistent with this. This concept is of course too simplistic in view of the diverse structural abnormalities in basal ganglia pathways that can all be associated with onset of dystonia added to the fact that the creation of lesions within basal ganglia structures can lead to resolution of dystonia.[6]

## **DBS of targets other than GPi**

### *Thalamus*

Thalamic DBS in dystonia, targeting various nuclei of the ventrolateral (VL) motor thalamus (Vim, ventral oral posterior (Vop), ventral oral anterior (Voa)) was tried initially as a treatment for dystonia based on the improvements in a minority of patients seen after thalamotomy. There has been no randomised comparison of GPi DBS versus Thalamic DBS for dystonia but the majority of centres have adopted the GPi target based on consensus experience. Among 12 patients that had thalamic DBS for a mixture of dystonia subtypes, three subsequently went on to have successful responses to GPi DBS because of insufficient benefit with thalamic DBS.[45]

Our view is that DBS of the VL thalamus should be restricted to those patients with marked tremor causing greater disability than dystonia, or in those patients with structural abnormality of the GPi (although the expectation of success in this group is lower).

### *Subthalamic Nucleus*

There is some experience of the STN as a target for dystonia patients especially in patients with damage to the GPi. Unilateral STN DBS in a patient with left hemidystonia secondary to a basal ganglia infarct led to improvement by 54.5% at 3 months.[49] Improvements in tardive and post traumatic hemidystonia have also been reported following STN DBS while 6 patients with other forms of secondary dystonia had minimal improvements.[50] The STN is still a novel target for DBS in dystonia patients so further studies will be needed to assess efficacy.

## **Conclusions**



DBS has been shown to be a safe effective surgical treatment for medically refractory dystonia with the postero-ventral sensori-motor GPi being the most favoured target site. Patients with primary forms of dystonia, and tardive dystonia respond well, particularly so when the surgery is performed at an earlier stage and among patients with lesser disability. Patients with DYT-1 positive dystonia respond better than DYT-1 negative cases although the DYT-1 negative group remains very heterogeneous. Patients with other forms of hereditary degenerative and secondary dystonia have variable responses making prediction of response in future patients difficult.

Differences in methodological approach, surgical technique, programming regimes and clinical presentation make determining outcome predictors in these subgroups even more challenging. A systematic and thorough approach to reporting all patient and technical variables needs to be implemented so that useful conclusions can be reached with accumulating reports. Additionally, emphasis should be put on in depth evaluation of patients' own perception of their life following DBS by using validated quality of life measures possibly including a qualitative approach.

Discussion with patients and their carers requires an honest explanation of the uncertainty of the usefulness of DBS, in particular for patients with hereditary degenerative and secondary dystonia subtypes. There is undoubtedly a placebo response and/or a clinician bias in evaluation following DBS, as evidenced by the excess benefits documented in open label follow up compared with blinded trials. The safety record of the centre should be an important factor which determines how much a potential improvement may justify the small surgical risks, especially as patients with dystonia frequently do not have alternative treatment options.

## **Acknowledgement**

This work was supported by the Parkinson's Appeal- registered charity **263064**

## Figure Legends

**Figure 1** Graph to show univariate relationship between duration of symptoms of dystonia and percentage improvement from DBS among patients with primary generalized dystonia together with regression line (Beta coefficient = -0.48, CI -0.82 to -0.16). In our multivariate analysis of patients with primary generalized dystonia, 13% of the variance in outcome was predicted by duration of symptoms, DYT1 status and baseline severity alone.

**Figure 2.** Mean percentage improvement following DBS for primary generalized dystonia patients with/without DYT1 mutation.

## Exclusive Licence

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non-exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd and its Licensees to permit this article (if accepted) to be published in Journal of Neurology, Neurosurgery & Psychiatry and any other BMJPG products to exploit all subsidiary rights, as set out in our licence

(<http://group.bmj.com/products/journals/instructions-for-authors/licence-forms>).

**Table 1. Published individual outcome data of patients with Primary forms of dystonia (and Myoclonus Dystonia) operated with DBS.**

**IQR-Interquartile range**

<b>Primary</b>	<b>Subtype</b>	<b>Numbers of Individual patient data</b>	<b>Age at surgery Mean (SD)</b>	<b>Duration of symptoms Mean (SD)</b>	<b>Pre-op Severity score Mean (SD)</b>	<b>Percentage improvement in motor/ severity score following DBS Mean (SD) IQR</b>	<b>References</b>
Generalised	DYT1 positive	91	22.6 (12.4)	13.4 (11.7)	53.8 (23.1)	67.5 (27.7) 53.3- 92.3	[4-7,9, ,25,27, 29,30,34,42,51-62]
Generalised	DYT1 negative	108	31.3 (16.2)	15.4 (11.1)	54.4 (23.6)	55.8 (26.6) 38.6- 79.3	[4-7,9,25,29, 30,34,42,51,52, 57-65]
Generalised	Unknown	10	36.9	17.0	57.5	51.9 (25.3)	[6,10,27,53,66]

			(16.1)	(12.8)	(22.7)	20.8- 71.4	
Focal	Writer's cramp	6	46.6 (17.4)	11.8 (9.3)	3.3 (0.5)	92 (12.9) 75-100	[67,68]
Focal	Spasmodic torticollis	67	50.0 (12.7)	10.7 (7.4)	24.9 (15.3)	48.3 (41.2) 26-78	[4,5,10,20, 27,31,35,37,41, 51,53,60,69,70- 73]
Focal/ segmental	Meige	17	56.1 (9.1)	8.5 (9.3)	21.9 (11.0)	64.3 (29.5) 55.5-82.2	[39-41,46,47, 53,74,75]
Focal/ segmental	Mixed Distribution	39	47.7 (15.6)	12.6 (7.2)	30.5 (16.1)	57.1 (24.0) 38.5- 79.3	[4,13,14,26,27, 55,60, 62,76- 79]
Focal/ segmental	Axial/ Camptocormia	6	48.7 (15.1)	12.4 (6.9)	30.3 (16.1)	66 (39.8) 33-87.5	[80-83]
<b>Dystonia plus</b>	Myoclonus dystonia	10	33.9 (18.6)	25.2 (19.4)	44.2 (49.6)	58 (19.2) 47.8- 73.9	[5,17,84-88]

**Table 2. Published individual outcome data of patients with Heredodegenerative forms of dystonia operated with DBS. IQR-Interquartile range. PKAN- Pantothenate kinase associated neurodegeneration. XDP- X-linked Dystonia parkinsonism. RDP- Rapid onset dystonia parkinsonism**

<b>Heredo- degenerative</b>	<b>Individual patient data</b>	<b>Age at surgery  Mean (SD)</b>	<b>Duration of symptoms  Mean (SD)</b>	<b>Pre-op Severity score  Mean (SD)</b>	<b>Percentage improvement in motor/ severity score following DBS  Mean (SD)  IQR</b>	<b>References</b>
PKAN	12	21.9  (12.2)	11.2  (7.6)	74.9  (29.7)	66 (21.9)  56.3-81.2	[27,32,48,89-92]
Lubag XDP	2	39.5  (7.8)	7.5  (9.2)	58.8  (26.5)	78	[93,94]

Lesch Nyhan	1	16	15	90	44	[95]
Dystonia Deafness	1	29	5	53	75	[96]
GM1 gangliosidosis	1	24	8	70	20	[97]
RDP	2	23.5 (0.7)	7 (7.1)	52.8 (3.9)	13	[98,99]

**Table 3. Published individual outcome data of patients with secondary forms of dystonia operated with DBS. IQR-Interquartile range.**

<b>Secondary subtype</b>	<b>Individual patient data</b>	<b>Age at surgery Mean (SD)</b>	<b>Duration of symptoms Mean (SD)</b>	<b>Pre-op Severity score Mean (SD)</b>	<b>Percentage improvement in motor/ severity score following DBS Mean (SD) IQR</b>	<b>References</b>

Tardive	41	47.3 (13.3)	5.9 (4.8)	36.2 (21.5)	69 (27.1) 57.9-90.4	[5,19- 21,27,36,51,57 100-106]
Cerebral palsy	22	30.3 (10.3)	29.1 (10.1)	49.7 (22.8)	24 (21.3) 7.6-31.8	[20,21,27,38,58, 61,107,108]
Post anoxic	9	38.6 (20.2)	21.4 (12.5)	48.2 (25.7)	45 (31.5) 24.7- 54.5	[20,21,50,51, 109,110]
Post encephalitic/ infectious/ encephalopathic	6	39.2 (23.4)	26.4 (12.9)	31.7 (20.1)	17 (37.7)	[6,20,21,58]
Post traumatic	5	40.6 (20.3)	10.4 (8.4)	40.4 (24.2)	32.6 (37.2)	[5,27,38,50,51]
Post haemorrhagic	2	64.5 (12.0)	7.0 (4.2)	32.3 (3.9)	42 (10.5)	[111]
Post radiation	1	29		10	90	[20]
Demyelinating	1	51	10	15	20	[5]

Basal ganglia calcification	1	14	12.5	59	73	[58]
Bilateral Striatal Necrosis	1	43	37	59	37	[112]
Unknown	3	44 (22.6)	11.5 (10.6)	28.2 (9.1)	42 (19.2)	[27,50,59]



## References

- 1 COOPER IS. 20-year followup study of the neurosurgical treatment of dystonia musculorum deformans. *Adv Neurol* 1976;14:423-52.
- 2 Lozano AM, Kumar R, Gross RE, Giladi N, Hutchison WD, Dostrovsky JO et al. Globus pallidus internus pallidotomy for generalized dystonia. *Mov Disord* 1997 November;12(6):865-70.
- 3 Coubes P, Roubertie A, Vayssiere N, Hemm S, Echenne B. Treatment of DYT1-generalised dystonia by stimulation of the internal globus pallidus. *Lancet* 2000 June 24;355(9222):2220-1.
- 4 Mehrkens JH, Botzel K, Steude U, Zeitler K, Schnitzler A, Sturm V et al. Long-term efficacy and safety of chronic globus pallidus internus stimulation in different types of primary dystonia. *Stereotact Funct Neurosurg* 2009;87(1):8-17.
- 5 Yianni J, Bain P, Giladi N, Auca M, Gregory R, Joint C et al. Globus pallidus internus deep brain stimulation for dystonic conditions: a prospective audit. *Mov Disord* 2003 April;18(4):436-42.
- 6 Eltahawy HA, Saint-Cyr J, Giladi N, Lang AE, Lozano AM. Primary dystonia is more responsive than secondary dystonia to pallidal interventions: outcome after pallidotomy or pallidal deep brain stimulation. *Neurosurgery* 2004 March;54(3):613-9.
- 7 Tisch S, Zrinzo L, Limousin P, Bhatia KP, Quinn N, Ashkan K et al. Effect of electrode contact location on clinical efficacy of pallidal deep brain stimulation in

- primary generalised dystonia. *J Neurol Neurosurg Psychiatry* 2007  
December;78(12):1314-9.
- 8 Kupsch A, Benecke R, Muller J, Trottenberg T, Schneider GH, Poewe W et al.  
Pallidal deep-brain stimulation in primary generalized or segmental dystonia. *N Engl J Med* 2006 November 9;355(19):1978-90.
  - 9 Vidailhet M, Vercueil L, Houeto JL, Krystkowiak P, Lagrange C, Yelnik J et al.  
Bilateral, pallidal, deep-brain stimulation in primary generalised dystonia: a  
prospective 3 year follow-up study. *Lancet Neurol* 2007 March;6(3):223-9.
  - 10 Kleiner-Fisman G, Liang GS, Moberg PJ, Ruocco AC, Hurtig HI, Baltuch GH et al.  
Subthalamic nucleus deep brain stimulation for severe idiopathic dystonia: impact on  
severity, neuropsychological status, and quality of life. *J Neurosurg* 2007  
July;107(1):29-36.
  - 11 Isaias IU, Alterman RL, Tagliati M. Deep brain stimulation for primary generalized  
dystonia: long-term outcomes. *Arch Neurol* 2009 April;66(4):465-70.
  - 12 Egidi M, Franzini A, Marras C, Cavallo M, Mondani M, Lavano A et al. A survey of  
Italian cases of dystonia treated by deep brain stimulation. *J Neurosurg Sci* 2007  
December;51(4):153-8.
  - 13 Novak KE, Nenonene EK, Bernstein LP, Vergenz S, Cozzens JW, Rezak M.  
Successful bilateral subthalamic nucleus stimulation for segmental dystonia after  
unilateral pallidotomy. *Stereotact Funct Neurosurg* 2008;86(2):80-6.
  - 14 Wohrle JC, Weigel R, Grips E, Blahak C, Capelle HH, Krauss JK. Risperidone-  
responsive segmental dystonia and pallidal deep brain stimulation. *Neurology* 2003  
August 26;61(4):546-8.

- 15 Azher SN, Jankovic J. Camptocormia: pathogenesis, classification, and response to therapy. *Neurology* 2005 August 9;65(3):355-9.
- 16 Kuncel AM, Turner DA, Ozelius LJ, Greene PE, Grill WM, Stacy MA. Myoclonus and tremor response to thalamic deep brain stimulation parameters in a patient with inherited myoclonus-dystonia syndrome. *Clin Neurol Neurosurg* 2009 April;111(3):303-6.
- 17 Trottenberg T, Meissner W, Kabus C, Arnold G, Funk T, Einhaupl KM et al. Neurostimulation of the ventral intermediate thalamic nucleus in inherited myoclonus-dystonia syndrome. *Mov Disord* 2001 July;16(4):769-71.
- 18 Guehl D, Cuny E, Tison F, Benazzouz A, Bardinet E, Sibon Y et al. Deep brain pallidal stimulation for movement disorders in neuroacanthocytosis. *Neurology* 2007 January 9;68(2):160-1.
- 19 Zhang JG, Zhang K, Wang ZC. Deep brain stimulation in the treatment of tardive dystonia. *Chin Med J (Engl )* 2006 May 5;119(9):789-92.
- 20 Pretto TE, Dalvi A, Kang UJ, Penn RD. A prospective blinded evaluation of deep brain stimulation for the treatment of secondary dystonia and primary torticollis syndromes. *J Neurosurg* 2008 September;109(3):405-9.
- 21 Katsakiori PF, Kefalopoulou Z, Markaki E, Paschali A, Ellul J, Kagadis GC et al. Deep brain stimulation for secondary dystonia: results in 8 patients. *Acta Neurochir (Wien )* 2009 May;151(5):473-8.
- 22 Mueller J, Skogseid IM, Benecke R, Kupsch A, Trottenberg T, Poewe W et al. Pallidal deep brain stimulation improves quality of life in segmental and generalized

- dystonia: results from a prospective, randomized sham-controlled trial. *Mov Disord* 2008 January;23(1):131-4.
- 23 Vidailhet M, Vercueil L, Houeto JL, Krystkowiak P, Benabid AL, Cornu P et al. Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. *N Engl J Med* 2005 February 3;352(5):459-67.
- 24 Loher TJ, Capelle HH, Kaelin-Lang A, Weber S, Weigel R, Burgunder JM et al. Deep brain stimulation for dystonia: outcome at long-term follow-up. *J Neurol* 2008 March 14.
- 25 Parr JR, Green AL, Joint C, Andrew M, Gregory RP, Scott RB et al. Deep brain stimulation in childhood: an effective treatment for early onset idiopathic generalised dystonia. *Arch Dis Child* 2007 August;92(8):708-11.
- 26 Sensi M, Cavallo MA, Quatrone R, Sarubbo S, Biguzzi S, Lettieri C et al. Pallidal stimulation for segmental dystonia: long term follow up of 11 consecutive patients. *Mov Disord* 2009 September 15;24(12):1829-35.
- 27 Starr PA, Turner RS, Rau G, Lindsey N, Heath S, Volz M et al. Microelectrode-guided implantation of deep brain stimulators into the globus pallidus internus for dystonia: techniques, electrode locations, and outcomes. *J Neurosurg* 2006 April;104(4):488-501.
- 28 Yianni J, Nandi D, Shad A, Bain P, Gregory R, Aziz T. Increased risk of lead fracture and migration in dystonia compared with other movement disorders following deep brain stimulation. *J Clin Neurosci* 2004 April;11(3):243-5.

- 29 Alterman RL, Miravite J, Weisz D, Shils JL, Bressman SB, Tagliati M. Sixty hertz pallidal deep brain stimulation for primary torsion dystonia. *Neurology* 2007 August 14;69(7):681-8.
- 30 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. *Clin Neurol Neurosurg* 2008 February;110(2):145-50.
- 31 Hung SW, Hamani C, Lozano AM, Poon YY, Piboolnurak P, Miyasaki JM et al. Long-term outcome of bilateral pallidal deep brain stimulation for primary cervical dystonia. *Neurology* 2007 February 6;68(6):457-9.
- 32 Mikati MA, Yehya A, Darwish H, Karam P, Comair Y. Deep brain stimulation as a mode of treatment of early onset pantothenate kinase-associated neurodegeneration. *Eur J Paediatr Neurol* 2009 January;13(1):61-4.
- 33 Bittar RG, Yianni J, Wang S, Liu X, Nandi D, Joint C et al. Deep brain stimulation for generalised dystonia and spasmodic torticollis. *J Clin Neurosci* 2005 January;12(1):12-6.
- 34 Borggraefe I, Mehrkens JH, Telegravciska M, Berweck S, Botzel K, Heinen F. Bilateral pallidal stimulation in children and adolescents with primary generalized dystonia - Report of six patients and literature-based analysis of predictive outcomes variables. *Brain Dev* 2009 April 28.
- 35 ZH, Doig-Beyaert K, Eliasziw M, Tsui J, Haffenden A, Suchowersky O. The Canadian multicentre study of deep brain stimulation for cervical dystonia. *Brain* 2007 November;130(Pt 11):2879-86.

- 36 Damier P, Thobois S, Witjas T, Cuny E, Derost P, Raoul S et al. Bilateral deep brain stimulation of the globus pallidus to treat tardive dyskinesia. Arch Gen Psychiatry 2007 February;64(2):170-6.
- 37 Jeong SG, Lee MK, Kang JY, Jun SM, Lee WH, Ghang CG. Pallidal deep brain stimulation in primary cervical dystonia with phasic type : clinical outcome and postoperative course. J Korean Neurosurg Soc 2009 October;46(4):346-50.
- 38 Woehrle JC, Blahak C, Kekelia K, Capelle HH, Baezner H, Grips E et al. Chronic deep brain stimulation for segmental dystonia. Stereotact Funct Neurosurg 2009;87(6):379-84.
- 39 Ostrem JL, Marks WJ, Jr., Volz MM, Heath SL, Starr PA. Pallidal deep brain stimulation in patients with cranial-cervical dystonia (Meige syndrome). Mov Disord 2007 October 15;22(13):1885-91.
- 40 Zauber SE, Watson N, Comella CL, Bakay RA, Metman LV. Stimulation-induced parkinsonism after posteroventral deep brain stimulation of the globus pallidus internus for craniocervical dystonia. J Neurosurg 2009 February;110(2):229-33.
- 41 Berman BD, Starr PA, Marks WJ, Jr., Ostrem JL. Induction of bradykinesia with pallidal deep brain stimulation in patients with cranial-cervical dystonia. Stereotact Funct Neurosurg 2009;87(1):37-44.
- 42 Vasques X, Cif L, Gonzalez V, Nicholson C, Coubes P. Factors predicting improvement in primary generalized dystonia treated by pallidal deep brain stimulation. Mov Disord 2009 April 30;24(6):846-53.

- 43 Cif L, Vasques X, Gonzalez V, Ravel P, Biolsi B, Collod-Beroud G et al. Long term follow up of DYT1 dystonia patients treated by Deep Brain Stimulation. *Mov Disord* 2010;in press.
- 44 Krauss JK, Lohr TJ, Pohle T, Weber S, Taub E, Barlocher CB et al. Pallidal deep brain stimulation in patients with cervical dystonia and severe cervical dyskinesias with cervical myelopathy. *J Neurol Neurosurg Psychiatry* 2002 February;(722):249-56.
- 45 Vercueil L, Pollak P, Fraix V, Caputo E, Moro E, Benazzouz A et al. Deep brain stimulation in the treatment of severe dystonia. *J Neurol* 2001 August;248(8):695-700.
- 46 Houser M, Waltz T. Meige syndrome and pallidal deep brain stimulation. *Mov Disord* 2005 September;20(9):1203-5.
- 47 Blomstedt P, Tisch S, Hariz MI. Pallidal deep brain stimulation in the treatment of Meige syndrome. *Acta Neurol Scand* 2008 March 7.
- 48 Castelnau P, Cif L, Valente EM, Vayssiere N, Hemm S, Gannau A et al. Pallidal stimulation improves pantothenate kinase-associated neurodegeneration. *Ann Neurol* 2005 May;57(5):738-41.
- 49 Tagliati M, Shils J, Sun C, Alterman R. Deep brain stimulation for dystonia. *Expert Rev Med Devices* 2004 September;1(1):33-41.
- 50 Zhang JG, Zhang K, Wang ZC, Ge M, Ma Y. Deep brain stimulation in the treatment of secondary dystonia. *Chin Med J (Engl )* 2006 December 20;119(24):2069-74.
- 51 Krause M, Fogel W, Kloss M, Rasche D, Volkmann J, Tronnier V. Pallidal stimulation for dystonia. *Neurosurgery* 2004 December;55(6):1361-8.

- 52 Vesper J, Klostermann F, Funk T, Stockhammer F, Brock M. Deep brain stimulation of the globus pallidus internus (GPI) for torsion dystonia--a report of two cases. *Acta Neurochir Suppl* 2002;79:83-8.
- 53 Lohrer TJ, Capelle HH, Kaelin-Lang A, Weber S, Weigel R, Burgunder JM et al. Deep brain stimulation for dystonia: outcome at long-term follow-up. *J Neurol* 2008 June;255(6):881-4.
- 54 Anheim M, Vercueil L, Fraix V, Chabardes S, Seigneuret E, Krack P et al. Early stimulation of DYT1 primary generalized dystonia prevents from its secondary irreversible complications. *Mov Disord* 2008 November 15;23(15):2261-3.
- 55 Nebel A, Reese R, Deuschl G, Mehdorn HM, Volkmann J. Acquired stuttering after pallidal deep brain stimulation for dystonia. *J Neural Transm* 2009 February;116(2):167-9.
- 56 Goto S, Yamada K, Shimazu H, Murase N, Matsuzaki K, Tamura T et al. Impact of bilateral pallidal stimulation on DYT1-generalized dystonia in Japanese patients. *Mov Disord* 2006 October;21(10):1785-7.
- 57 Magarinos-Ascone CM, Regidor I, Gomez-Galan M, Cabanes-Martinez L, Figueiras-Mendez R. Deep brain stimulation in the globus pallidus to treat dystonia: electrophysiological characteristics and 2 years' follow-up in 10 patients. *Neuroscience* 2008 March 18;152(2):558-71.
- 58 Zorzi G, Marras C, Nardocci N, Franzini A, Chiapparini L, Maccagnano E et al. Stimulation of the globus pallidus internus for childhood-onset dystonia. *Mov Disord* 2005 September;20(9):1194-200.



- 59 Diamond A, Shahed J, Azher S, Dat-Vuong K, Jankovic J. Globus pallidus deep brain stimulation in dystonia. *Mov Disord* 2006 May;21(5):692-5.
- 60 Hamani C, Moro E, Zadikoff C, Poon YY, Lozano AM. Location of active contacts in patients with primary dystonia treated with globus pallidus deep brain stimulation. *Neurosurgery* 2008 March;62(3 Suppl 1):217-23.
- 61 Tronnier VM, Fogel W. Pallidal stimulation for generalized dystonia. Report of three cases. *J Neurosurg* 2000 March;92(3):453-6.
- 62 Kupsch A, Klaffke S, Kuhn AA, Meissner W, Arnold G, Schneider GH et al. The effects of frequency in pallidal deep brain stimulation for primary dystonia. *J Neurol* 2003 October;250(10):1201-5.
- 63 Lenders MW, Vergouwen MD, Hageman G, van der Hoek JA, Ippel EF, Jansen Steur EN et al. Two cases of autosomal recessive generalized dystonia in childhood: 5 year follow-up and bilateral globus pallidus stimulation results. *Eur J Paediatr Neurol* 2006 January;10(1):5-9.
- 64 Kumar R, Dagher A, Hutchison WD, Lang AE, Lozano AM. Globus pallidus deep brain stimulation for generalized dystonia: clinical and PET investigation. *Neurology* 1999 September 11;53(4):871-4.
- 65 Blomstedt P, Hariz MI, Tisch S, Holmberg M, Bergenheim TA, Forsgren L. A family with a hereditary form of torsion dystonia from Northern Sweden treated with bilateral pallidal deep brain stimulation. *Mov Disord* 2009 November 4.
- 66 Katayama Y, Fukaya C, Kobayashi K, Oshima H, Yamamoto T. Chronic stimulation of the globus pallidus internus for control of primary generalized dystonia. *Acta Neurochir Suppl* 2003;87:125-8.

- 67 Fukaya C, Katayama Y, Kano T, Nagaoka T, Kobayashi K, Oshima H et al. Thalamic deep brain stimulation for writer's cramp. *J Neurosurg* 2007 November;107(5):977-82.
- 68 Cho CB, Park HK, Lee KJ, Rha HK. Thalamic Deep Brain Stimulation for Writer's Cramp. *J Korean Neurosurg Soc* 2009 July;46(1):52-5.
- 69 Chou KL, Hurtig HI, Jaggi JL, Baltuch GH. Bilateral subthalamic nucleus deep brain stimulation in a patient with cervical dystonia and essential tremor. *Mov Disord* 2005 March;20(3):377-80.
- 70 Kulisevsky J, Lleo A, Gironell A, Molet J, Pascual-Sedano B, Pares P. Bilateral pallidal stimulation for cervical dystonia: dissociated pain and motor improvement. *Neurology* 2000 December 12;55(11):1754-5.
- 71 Andaluz N, Taha JM, Dalvi A. Bilateral pallidal deep brain stimulation for cervical and truncal dystonia. *Neurology* 2001 August 14;57(3):557-8.
- 72 Goto S, Yamada K. Long term continuous bilateral pallidal stimulation produces stimulation independent relief of cervical dystonia. *J Neurol Neurosurg Psychiatry* 2004 October;75(10):1506-7.
- 73 Eltahawy HA, Saint-Cyr J, Poon YY, Moro E, Lang AE, Lozano AM. Pallidal deep brain stimulation in cervical dystonia: clinical outcome in four cases. *Can J Neurol Sci* 2004 August;31(3):328-32.
- 74 Foote KD, Sanchez JC, Okun MS. Staged deep brain stimulation for refractory craniofacial dystonia with blepharospasm: case report and physiology. *Neurosurgery* 2005 February;56(2):E415.

- 75 Hebb MO, Chiasson P, Lang AE, Brownstone RM, Mendez I. Sustained relief of dystonia following cessation of deep brain stimulation. *Mov Disord* 2007 October 15;22(13):1958-62.
- 76 Escamilla-Sevilla F, Minguez-Castellanos A, rjona-Moron V, Martin-Linares JM, Sanchez-Alvarez JC, Ortega-Morenoa A et al. Unilateral pallidal stimulation for segmental cervical and truncal dystonia: which side? *Mov Disord* 2002 November;17(6):1383-5.
- 77 Muta D, Goto S, Nishikawa S, Hamasaki T, Ushio Y, Inoue N et al. Bilateral pallidal stimulation for idiopathic segmental axial dystonia advanced from Meige syndrome refractory to bilateral thalamotomy. *Mov Disord* 2001 July;16(4):774-7.
- 78 Blahak C, Wohrle JC, Capelle HH, Bazner H, Grips E, Weigel R et al. Health-related quality of life in segmental dystonia is improved by bilateral pallidal stimulation. *J Neurol* 2008 February;255(2):178-82.
- 79 Low HL, Honey CR. Focal childhood-onset, action induced primary hip dystonia treated with pallidal deep brain stimulation. *Mov Disord* 2008 October 15;23(13):1926-8.
- 80 Zittel S, Moll CK, Hamel W, Buhmann C, Engel AK, Gerloff C et al. Successful GPi deep brain stimulation in a patient with adult onset primary axial dystonia. *J Neurol Neurosurg Psychiatry* 2009 July;80(7):811-2.
- 81 Sakas DE, Panourias IG, Boviatsis EJ, Themistocleous MS, Stavrinou LC, Stathis P et al. Treatment of idiopathic head drop (camptocephalia) by deep brain stimulation of the globus pallidus internus. *J Neurosurg* 2009 June;110(6):1271-3.

- 82 Nandi D, Parkin S, Scott R, Winter JL, Joint C, Gregory R et al. Camptocormia treated with bilateral pallidal stimulation: case report. *Neurosurg Focus* 2002 February 15;12(2):ECP2.
- 83 Fukaya C, Otaka T, Obuchi T, Kano T, Nagaoka T, Kobayashi K et al. Pallidal high-frequency deep brain stimulation for camptocormia: an experience of three cases. *Acta Neurochir Suppl* 2006;99:25-8.
- 84 Foncke EM, Bour LJ, Speelman JD, Koelman JH, Tijssen MA. Local field potentials and oscillatory activity of the internal globus pallidus in myoclonus-dystonia. *Mov Disord* 2007 February 15;22(3):369-76.
- 85 Magarinos-Ascone CM, Regidor I, Martinez-Castrillo JC, Gomez-Galan M, Figueiras-Mendez R. Pallidal stimulation relieves myoclonus-dystonia syndrome. *J Neurol Neurosurg Psychiatry* 2005 July;76(7):989-91.
- 86 Cif L, Valente EM, Hemm S, Coubes C, Vayssiere N, Serrat S et al. Deep brain stimulation in myoclonus-dystonia syndrome. *Mov Disord* 2004 June;19(6):724-7.
- 87 Kurtis MM, San LM, Yu Q, Goodman RR, Ford B, Raymond D et al. Clinical and neurophysiological improvement of SGCE myoclonus-dystonia with GPi deep brain stimulation. *Clin Neurol Neurosurg* 2009 November 4.
- 88 Jog M, Kumar H. Bilateral pallidal deep brain stimulation in a case of myoclonus dystonia syndrome. *Mov Disord* 2009 July 30;24(10):1547-9.
- 89 Shields DC, Sharma N, Gale JT, Eskandar EN. Pallidal stimulation for dystonia in pantothenate kinase-associated neurodegeneration. *Pediatr Neurol* 2007 December;37(6):442-5.

- 90 Krause M, Fogel W, Tronnier V, Pohle S, Hortnagel K, Thyen U et al. Long-term benefit to pallidal deep brain stimulation in a case of dystonia secondary to pantothenate kinase-associated neurodegeneration. *Mov Disord* 2006 December;21(12):2255-7.
- 91 Umemura A, Jaggi JL, Dolinskas CA, Stern MB, Baltuch GH. Pallidal deep brain stimulation for longstanding severe generalized dystonia in Hallervorden-Spatz syndrome. Case report. *J Neurosurg* 2004 April;100(4):706-9.
- 92 Isaac C, Wright I, Bhattacharyya D, Baxter P, Rowe J. Pallidal stimulation for pantothenate kinase-associated neurodegeneration dystonia. *Arch Dis Child* 2008 March;93(3):239-40.
- 93 Evidente VG, Lyons MK, Wheeler M, Hillman R, Helepolelei L, Beynen F et al. First case of X-linked dystonia-parkinsonism ("Lubag") to demonstrate a response to bilateral pallidal stimulation. *Mov Disord* 2007 September 15;(2212):1790-3.
- 94 Martinez-Torres I, Limousin P, Tisch S, Page R, Pinto A, Foltynie T et al. Early and marked benefit with GPi DBS for Lubag syndrome presenting with rapidly progressive life-threatening dystonia. *Mov Disord* 2009 August 15;(2411):1710-2.
- 95 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 October 31;(2214):2126-9.
- 96 Havrankova P, Jech R, Roth J, Urgosik D, Ruzicka E. Beneficial effect of deep brain stimulation of GPi in a patient with dystonia-deafness phenotype. *Mov Disord* 2009 February 15;24(3):465-6.

- 97 Roze E, Navarro S, Cornu P, Welter ML, Vidailhet M. Deep brain stimulation of the globus pallidus for generalized dystonia in GM1 Type 3 gangliosidosis: technical case report. *Neurosurgery* 2006 December;59(6):E1340.
- 98 Deutschlander A, Asmus F, Gasser T, Steude U, Botzel K. Sporadic rapid-onset dystonia-parkinsonism syndrome: failure of bilateral pallidal stimulation. *Mov Disord* 2005 February;20(2):254-7.
- 99 Kamm C, Fogel W, Wachter T, Schweitzer K, Berg D, Kruger R et al. Novel ATP1A3 mutation in a sporadic RDP patient with minimal benefit from deep brain stimulation. *Neurology* 2008 April 15;70(16 Pt 2):1501-3.
- 100 Trottenberg T, Volkmann J, Deuschl G, Kuhn AA, Schneider GH, Muller J et al. Treatment of severe tardive dystonia with pallidal deep brain stimulation. *Neurology* 2005 January 25;64(2):344-6.
- 101 Schrader C, Peschel T, Petermeyer M, Dengler R, Hellwig D. Unilateral deep brain stimulation of the internal globus pallidus alleviates tardive dyskinesia. *Mov Disord* 2004 May;19(5):583-5.
- 102 Franzini A, Marras C, Ferroli P, Zorzi G, Bugiani O, Romito L et al. Long-term high-frequency bilateral pallidal stimulation for neuroleptic-induced tardive dystonia. Report of two cases. *J Neurosurg* 2005 April;102(4):721-5.
- 103 Kefalopoulou Z, Paschali A, Markaki E, Vassilakos P, Ellul J, Constantoyannis C. A double-blind study on a patient with tardive dyskinesia treated with pallidal deep brain stimulation. *Acta Neurol Scand* 2009 April;119(4):269-73.

- 104 Cohen OS, Hassin-Baer S, Spiegelmann R. Deep brain stimulation of the internal globus pallidus for refractory tardive dystonia. *Parkinsonism Relat Disord* 2007 December;13(8):541-4.
- 105 Sako W, Goto S, Shimazu H, Murase N, Matsuzaki K, Tamura T et al. Bilateral deep brain stimulation of the globus pallidus internus in tardive dystonia. *Mov Disord* 2008 October 15;23(13):1929-31.
- 106 Eltahawy HA, Feinstein A, Khan F, Saint-Cyr J, Lang AE, Lozano AM. Bilateral globus pallidus internus deep brain stimulation in tardive dyskinesia: a case report. *Mov Disord* 2004 August;19(8):969-72.
- 107 Gill S, Curran A, Tripp J, Melarickas L, Hurran C, Stanley O. Hyperkinetic movement disorder in an 11-year-old child treated with bilateral pallidal stimulators. *Dev Med Child Neurol* 2001 May;43(5):350-3.
- 108 Vidailhet M, Yelnik J, Lagrange C, Fraix V, Grabli D, Thobois S et al. Bilateral pallidal deep brain stimulation for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study. *Lancet Neurol* 2009 August;8(8):709-17.
- 109 Ghika J, Villemure JG, Miklossy J, Temperli P, Pralong E, Christen-Zaech S et al. Postanoxic generalized dystonia improved by bilateral Voa thalamic deep brain stimulation. *Neurology* 2002 January 22;58(2):311-3.
- 110 Constantoyannis C, Kagadis GC, Ellul J, Kefalopoulou Z, Chroni E. Nucleus ventralis oralis deep brain stimulation in postanoxic dystonia. *Mov Disord* 2009 January 30;24(2):306-8.

- 111 Hamasaki T, Yamada K, Kuratsu J. Hemidystonia secondary to thalamic hemorrhage treated with GPi stimulation. *Mov Disord* 2008 September 15;23(12):1762-6.
- 112 Aniello MS, Martino D, Petruzzella V, Eleopra R, Mancuso M, Dell'Aglia R et al. Bilateral striatal necrosis, dystonia and multiple mitochondrial DNA deletions: case study and effect of deep brain stimulation. *Mov Disord* 2008 January;23(1):114-8.



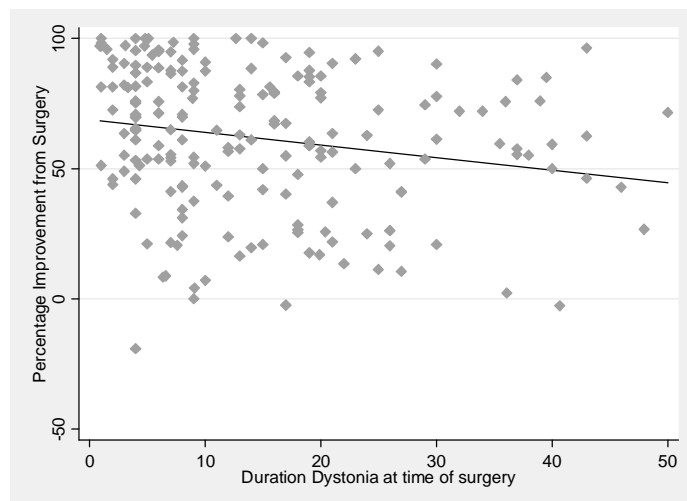


Figure 1.

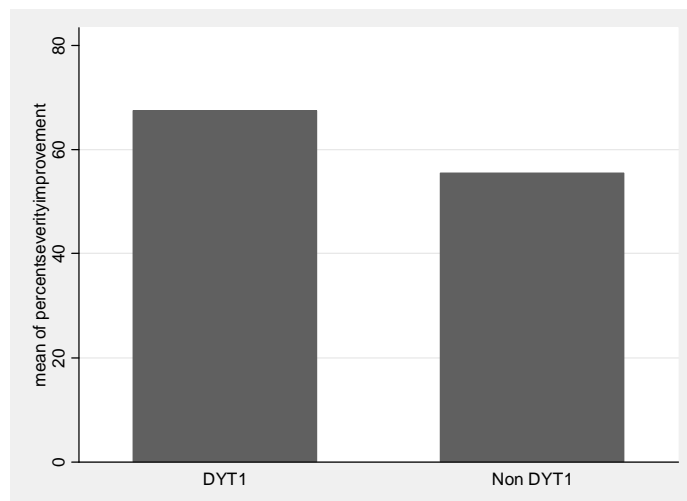


Figure 2.