King's Research Portal

DOI:

[10.1016/j.ejpn.2016.07.024](https://doi.org/10.1016/j.ejpn.2016.07.024)

Document Version

Peer reviewed version

[Link to publication record in King's Research Portal](#)

Citation for published version (APA):

Kaminska, M., Perides, S., Lumsden, D. E., Nakou, V., Selway, R., Ashkan, K., & Lin, J-P. (2016). Complications of Deep Brain Stimulation (DBS) for dystonia in children – the challenges and 10 year experience in a large paediatric cohort. *European Journal of Paediatric Neurology*. <https://doi.org/10.1016/j.ejpn.2016.07.024>

Citing this paper

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

General rights

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

Take down policy

If you believe that this document breaches copyright please contact librarypure@kcl.ac.uk providing details, and we will remove access to the work immediately and investigate your claim.

Accepted Manuscript

Complications of Deep Brain Stimulation (DBS) for dystonia in children – the challenges and 10 year experience in a large paediatric cohort

Dr Margaret Kaminska, MD, Sarah Perides, BSc, Daniel E. Lumsden, PhD, Vasiliki Nakou, MD, Richard Selway, FRCS, Keyoumars Ashkan, MD, Jean-Pierre Lin, MRCP(UK), PhD

PII: S1090-3798(16)30130-1

DOI: [10.1016/j.ejpn.2016.07.024](https://doi.org/10.1016/j.ejpn.2016.07.024)

Reference: YEJPN 2106

To appear in: *European Journal of Paediatric Neurology*

Received Date: 23 May 2016

Revised Date: 20 July 2016

Accepted Date: 25 July 2016

Please cite this article as: Kaminska M, Perides S, Lumsden DE, Nakou V, Selway R, Ashkan K, Lin J-P, Complications of Deep Brain Stimulation (DBS) for dystonia in children – the challenges and 10 year experience in a large paediatric cohort, *European Journal of Paediatric Neurology* (2016), doi: 10.1016/j.ejpn.2016.07.024.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Title: Complications of Deep Brain Stimulation (DBS) for dystonia in children – the challenges and 10 year experience in a large paediatric cohort

Authors: Margaret Kaminska ^{1*} MD, Sarah Perides ¹ BSc, Daniel E Lumsden ¹ PhD, Vasiliki Nakou MD, Richard Selway² FRCS, Keyoumars Ashkan² MD, Jean-Pierre Lin¹ MRCP(UK), PhD

¹Complex Motor Disorders Service, Evelina London Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, London, UK

²Department of Neurosurgery, King's College Hospital NHS Foundation Trust, London, UK

*Corresponding Author

Dr Margaret Kaminska, Complex Motor Disorder Service, Evelina Children's Hospital, Guy's and St Thomas' NHS Foundation Trust, Westminster Bridge Road, London, UK, SE1 7EH

Telephone Number: 020 7188 8533

Fax Number: 020 7188 0851

Margaret.kaminska@gstt.nhs.uk

Key words: dystonia, DBS, pallidal stimulation, complications, children

Highlights:

- Lower than previously reported infection rates following DBS for movement disorders in children were identified and no increased susceptibility for patients younger than 7 years.
- We report relatively high incidence of technical problems with electrodes and extensions and in particular recharging.
- Presentation of heterogeneous phenotypes requires an experienced team to manage and prevent complications.

The paper confirms that DBS in young children is safe and can be offered.

Abstract:

Deep brain stimulation (DBS) has been increasingly used for primary and secondary movement disorders in children and young people. Reports of hardware related complications have been sparse for this population and from small cohorts of patients. We report DBS complications from a single large DBS centre with 10 year experience. Data was collected as a prospective audit and additionally from a questionnaire on recharging of the stimulators. 129 patients with a minimum 6 months follow up were identified, mean age 10.8 y (range 3.0 – 18.75), mean follow up 3.3y (range 0.5 – 10.3), weight 10.4-94.2kg, 126 new implants (92 Activa RC) and 69 revisions for reasons other than infection. 26 patients were 7y or younger. Surgical site infections (SSI) rates were 10.3% for new implants and revisions, lower 8.6% for new Activa RC and even lower, 4.7%, for new Activa RC in patients under 7y (1/21). SSI occurred within first 6 months and necessitated total system removal in 86% of those infected. Electrode/extension problems were recorded in 18.4% of patients, fracture in 4.6% malfunction in 7.7%, short extension 3.8% and electrode migration in 2.3%. Other complications involved clinically silent intracranial bleed in 1 patient, skin erosions (2.3%), unexpected switching off in 18.7% of Soletra/Kinetra and 3.4% of Activa RC, transient seroma at IPG site in postoperative period (8%). Of the 48 returned recharging questionnaires, 38% of families required recharger replacement and 23% experienced frequent problems maintaining connection during recharging. However, 83% of responders considered recharging not at all or only a little care burden. We identified lower than previously reported DBS infection rates particularly for patients under 7 years, but relatively high incidence of technical problems with electrodes, extensions and in particular recharging. This has to be considered when offering DBS for children with movement disorders.

Introduction:

Dystonia in childhood is most frequently of a secondary aetiology, is unlikely to remit spontaneously^{1 2} and negatively affects a child's life including activity and participation³. Expression of dystonia on the background of a maturing central nervous system potentially leads to alteration of response to pharmacological agents^{4 5}. Multiple medications have been used in childhood dystonia without robust evidence and resulting in side effects in two thirds of patients⁶.

Deep Brain Stimulation has been increasingly used in the management of childhood dystonias. Favourable responses to DBS in primary dystonias have been well documented^{7 8 9 10 11 12} and there is growing evidence supporting its use in secondary dystonias, however with more modest effects^{13 14 15}.

Complications of DBS in paediatric populations have been sparsely reported in small cohorts of patients. We aim to report complications and discuss challenges of DBS for children from a single large paediatric centre with 10 year experience.

Methods:

Surgery:

All DBS surgeries were performed under general anaesthesia as a one-stage procedure. In the first three years single channel Soletra and double channel Kinetra stimulators were implanted (Medtronic). Once a rechargeable Activa RC stimulator (Medtronic) became available in December 2008 it has been offered preferentially. A Leksell frame was used in all cases, with finger tightening of screws in the very young

patients. DBS electrodes were implanted bilaterally through frontal incisions and burr holes into posteromedial globus pallidus interna (GPI) in the majority of patients. Two patients with hemidystonia had unilateral implants (first - unilateral GPI and thalamus, second – unilateral GPI). Three patients had electrodes implanted in subthalamic nucleus (STN) bilaterally due to severe damage of globus pallidus, we reported previously early outcome of STN DBS in the first of these patients¹⁶. There were two patients with two pairs of electrodes in GPIs, one with additional pair implanted at revision and another with four electrodes implanted at initial procedure. All new DBS patients underwent direct anatomical targeting using pre-operative high-resolution proton density and T1 weighted volume stereotactic brain MRI scans. Medtronic Framelink software was used to calculate the coordinates of the target. Post operative stereotactic CT scan was performed in all patients to confirm electrode placement. Intra-operative impedance or microelectrode¹⁷ recordings were also used to improve localisation of the target. Accuracy of the electrodes placement has been validated retrospectively on the fused in frame preoperative MRI and postoperative CT¹⁸. All electrodes used were Medtronic 3389.

Patients with *de novo* implants received a 7-day prophylactic course of intravenous antibiotic (cefuroxime unless specific indications for a different antibiotic) following new implants. For battery replacement procedures 24-48 hours intravenous antibiotic prophylaxis was used initially, and from June 2010 the protocol was unified to 7-day course for new implants and all revision procedures.

When changing neurostimulators from Soletra and Kinetra to Activa RC an adaptor was used to enable connection of the existing extensions to Activa RC. The adaptor was positioned behind the neurostimulator to avoid interference with recharging¹⁹.

For Activa RC stimulators all families (children and caregivers where relevant) received an information session on recharging the stimulator prior to surgery and individual

practical training during the postoperative 7 days admission until they felt confident with the stimulator maintenance. Families were advised to recharge stimulator initially daily to ensure the process became a routine care and to maintain high battery charge – 75 to 100%.

Data collection and analysis:

Patients undergoing DBS surgery in our paediatric centre during 10 years between May 2005 and October 2015 were prospectively monitored for surgery related complications. Cases with a minimum of 6 months follow up were entered for further analysis.

Additionally a questionnaire on recharging technique, frequency, duration and any related difficulties was applied to the patients with rechargeable stimulators on the with a minimum 6 months follow up.

Patients'/caregivers' responses were recorded during clinic appointments or over the telephone or filled questionnaires were returned via email.

Simple percentage analysis was used.

Results:

Patients and procedures – Figure 1:

138 paediatric patients with DBS were under our care between June 2005 and October 2015. 129 patients had a follow up of minimum 6 months, of these 126 had *de novo* implants in our centre and 3 patients had original implants elsewhere. There were 69 revision procedures not related to infection, mainly battery changes.

Mean age at the DBS implant was 10.8 y (range 3.0 – 18.75) and 26 patients were younger than 7years. Mean follow up was 3.3y (range 0.5 – 10.3). Patients' weight ranged between 10.4 and 94.2kg.

Within new implants 32 received Soletra and Kinetra stimulators, 92 Activa RC and 2 patients had Activa PC. 22 patients had Soletra and Kinetra stimulators replaced with Activa RC over the course of the study period. When the rechargeable stimulator became available, although we strongly encouraged this type of implant, few patients had a non-rechargeable stimulators implanted due to their/family preference.

29 patients were transitioned to the adult services, 1 patient was lost to follow up. 10 patients died due to underlying natural history of the diagnosis at time points unrelated to surgery (Table 1). The exception was a patient (case 4 Table 1) with Aicardi-Goutieres Syndrome type 6 who died within 24 hours post DBS electrode revision after an initial normal post-operative recovery – post mortem examination failed to identify cause of death and specifically there was no evidence of an intracranial bleed.

Surgical site infections:

Surgical site infection rate was 8.6% for new Activa RC implants. Overall surgical site infection rate was 10.3% for all new implants and 10.1% for revisions. A lower rate (7.6%) was recorded for patients under 7y at the time of implant (2/26) and even lower rate of 4.7% in a group of patients under 7y with new Activa RC implants (1/21). All surgical site infections occurred within the first 6 months after surgery. Treatment with prolonged courses of antibiotics was unsuccessful in 86% of patients with surgical site infections following new implants and revisions, necessitating eventually total removal of the DBS system.

Other hardware related complications:

A clinically insignificant small intracranial bleed was detected on postoperative CT at the site of one electrode in one patient (0.8%) and a self - resolving small CSF collection on the scalp in one patient. Overall, 8% of patients developed self - resolving seromas in the postoperative period, primarily at the battery site.

Three patients (2.3%) developed skin erosions eventually leading to full system explantation in all. One patient developed an unusual granuloma 4 years after the DBS implant and another developed late infection following trauma and haematoma at the stimulator site two years after the surgery.

18.4% of patients experienced problems with electrode leads and extensions: short/tight extension was observed in 3.8%, electrode migration in 2.3%, electrode/extension fracture in 4.6% and electrode/extension malfunction in 7.7%. Electrode/extension malfunction was defined as high impedance on at least one contact in monopolar settings ($>4000\ \Omega$ for Kinetra and Activa; $>2000\ \Omega$ for Soletra) or significant fluctuations of therapy current (minimum 50% fluctuations on different measurements of the same therapy settings) including very low current drain.

Two patients (1.5%) remain with the DBS switched off due to perceived intolerable side effects of stimulation, low mood (abulia) relative to previous smiling, likely partially dyskinetic, and ebullience in one and increased rigidity in another.

The IPG was unexpectedly (not related to battery depletion) switched off in 18.7% of patients with Soletra and Kinetra and in 3.4% of patients with Activa RC.

Status dystonicus following disruption of DBS was observed in 6 patients (4.6%) after IPG was switched off unexpectedly in 2 cases, electrode fracture in 1 and system removal in 3.

Complications related to recharging:

Shielded battery syndrome¹⁷ preventing recharging of the neurostimulator due to anterior position of adaptor or rotational flipping over of Activa RC occurred in two cases following replacement of Kinetra with an Activa RC stimulator. With the adaptation of surgical technique no more such cases were observed. Two overweight patients (1.7%) required Activa RC repositioning due to difficulty recharging.

Questionnaire on recharging:

We obtained 48 completed recharging questionnaires (Fig 2). Parents and carers were responsible for recharging of the stimulators in 69 % and patients themselves in 29%. The stimulators were recharged every day or every 2-3 days in the majority of cases (79%) during quiet activities (69%) and the recharging session was shorter than 1 hour in 73%.

Various methods were used to maintain connection between the battery and recharger with the recharger held by hand in most (48%) and original belt or harness used only in 14%.

77% of families have never or only sometimes experienced difficulty maintaining connection, however 14% had difficulty most or all the time.

The recharger had to be replaced due to malfunction in 38% of cases, and twice in 6%. The battery was reported to be fully discharged (battery flat) at least once in 23% including 13% more than once.

83% of responders considered recharging of DBS stimulator as 'not at all' or 'only a little' of a care burden.

Discussion:

Surgical site infections and erosions:

We identified 8.6% infection rate for new Activa RC implants in comparison to a higher 10.3% for all new implants in the whole cohort and 10.1% for revision procedures. This is in line with reports of 1.2-15% from adult cohorts^{20 21 22 23}. Higher infection rates 9.3 – 21% have been reported in paediatric cohorts or case series^{24 25 26 27 28 29 30}. Although Olaya et al³¹ reported no complications in case series of 9 patients, Air et al²⁷ reported a 57% infection rate in patients younger than 10y. Keen et al²⁶ suggested that young children may have increased infection risk after reporting a 40% rate in a small group of 5 patients aged 8-17y.

This is in contrast to our finding of only 7.6% in our patients under 7 y and even lower (4.7%) if they had new Activa RC implant. We postulate that lower rate of infections in Activa RC new implants group can be related to its smaller size and favourable shape resulting in easier accommodation of an implant, but a growing experience of the centre in relation to surgery and perioperative care may also be an important factor.

Staphylococcus aureus was the most common infection-site culture and despite different antibiotic regimens and partial system removal in some cases, 86% of infected systems were eventually totally removed. A majority (58%) of patients had very localised symptoms, comprising delayed wound healing with purulent discharge without fever or raised inflammatory markers. However, one patient with severe cerebral palsy and malnutrition developed sepsis necessitating intensive care support and urgent system removal. Another child with severe PKAN (PANK-2 positive) disease had DBS implanted directly from PICU for status dystonicus precipitated by unsuspected acute Hepatitis A which was diagnosed 3 weeks after DBS implant with the onset of jaundice and acutely deranged liver function tests, complicated by nephrotic syndrome. This immunocompromise resulted in a brain abscess along left DBS lead requiring DBS removal with minimal residual scarring.

Another seven patients developed cellulitis with significantly elevated inflammatory markers.

None of these had permanent sequelae due to DBS infection.

Three patients presented with skin erosion (two over the IPG positioned in the upper chest, one on the scalp) at 11, 42 and 22 months after surgery respectively without signs of infection and negative or inconclusive microbiology results. All of these cases were severely malnourished with body-weights below the 0.4th centile which we believe contributed to this complication. Our practice has changed since and the stimulators are implanted in the abdomen particularly in patients with low weight.

Electrode leads and extension problems

Complications related to electrodes and extensions were not uncommon in our cohort (18.4%). This is higher than reported in the literature^{20 21 22 23 28} although 14% lead fractures were recorded in a series of 14 patients²⁹. In our series, particularly frequent were electrode/extension fractures and malfunction (12.3%). In one case an electrode fracture presented as deterioration of dystonia without typical very high impedances. Nevertheless, we recommend that the therapy and electrode impedances should be measured during every programming session and particularly when deterioration of symptom control is noted. An X-ray should be performed in cases of high impedance or significant fluctuations of impedance and current or unexplained deterioration of dystonia to exclude an electrode or extension fracture.

Recharging

Rechargeable Activa RC stimulators have been almost exclusively implanted in our centre since December 2008 (Fig 1) due to its small size, important for our population of

patients, and to reduce the frequency of battery replacement³². Increased risk of implant infection related to higher number of surgical revisions, including IPG replacement, has been reported^{33 34}.

Economic savings can be expected from implantation of rechargeable vs non-rechargeable IPG³⁵ alongside with a high patient satisfaction from rechargeable stimulators^{36 37}.

Indeed, the majority of patients/carers in our cohort (84%) indicated that recharging was 'not at all' or 'only a little' care burden. However, a third of families required a recharger replacement and a fifth had frequent difficulty maintaining connection between the recharger and the battery. As previously reported³⁷ the majority of carers did not use the harness or belt supplied by the manufacturer as they were not suitable either due to patient small size or severe dystonic/dyskinetic movements.

Unexpected IPG switching off, not related to battery failure, occurred in 18.7% of children with Soletra and Kinetra neurostimulators falling to 3.4% in patients with Activa RC implants. This is despite of the fact that a patient control device was offered routinely to all patients with rechargeable stimulators, thus increasing possibility of neurostimulator accidental switching off by patient/carers while patient control device was not supplied for patients with Soletra and Kinetra.

Interestingly 23% of rechargeable stimulators were reported by questionnaire responders (11/48) to be fully discharged at least once. This warrants closer inspection of device usage history at each review point and active reminding about the necessity of recharging. Nonetheless we have not experienced Activa RC permanent battery failure to date.

Deterioration of dystonia in the post-operative period

Dyskinetic storms can emerge in patients with Parkinson Disease and STN DBS postoperatively^{38 39}. Similarly we observed in some cases significant deterioration of dystonia or dyskinesia in the postoperative period requiring transient escalation of

medical treatment. This predominantly occurred in younger children with a more severe background dystonia and may have been related to many factors such as stress of surgery and hospital admission, fear, pain, difficulty communicating needs, constipation, vomiting and intolerance of DBS settings. This has not been included in the data collection therefore it is not possible to give quantitative, but only qualitative description. We have introduced routine morphine infusions (Nurse Controlled Analgesia) for a minimum of the first 12 hours postoperatively and proactively managed pain, constipation, feeding, vomiting with improved patient comfort and experience. Nonetheless change of DBS settings (mainly reduction of voltage and/or pulse width) and escalation of medication for dystonia was still necessary in some.

Status dystonicus after disruption of DBS

Sudden discontinuation of DBS may result in return of dystonia^{39 40 41}. This may occur as a consequence of the system switching off unexpectedly, battery failure, electrode/extension fracture or malfunction. Symptoms can return gradually or lead to severe deterioration including status dystonicus in short order. In our cohort 4.6 % of patients developed difficult-to-treat or refractory status dystonicus after disruption of stimulation and many had milder, more gradual deterioration. Re-institution of DBS where possible led to resolution of symptoms or significantly helped in the management. Our observation is that severe status dystonicus with active DBS is very rare in patients other than suffering from PKAN and even in these cases treatment is much more difficult when DBS is discontinued. However, we have not formally analysed our cohort to ascertain the incidence of status dystonicus or severe exacerbation of dystonia when receiving active stimulation.

Limitations

We reported hardware related complications from a large paediatric cohort, however this cohort is not as large as in some adult studies.

DBS for children with dystonia was a relatively new experience at the beginning of data collection, with limited reports on complications available and emergence of new complications with time. This might have resulted in delayed recognition of some problems e.g. electrode malfunction when impedances were high on two vs more contacts. Our patients inevitably move on to the adult services, which are more local to them as opposed to our service accepting referrals often from a great distance. It has an impact on the length of follow up e.g. a patient receiving DBS at 16 years of age will likely leave our service after 2 years.

Conclusions:

DBS in children may be unduly delayed because of concerns of a greater complication risks in young children. We show here that device infection remains the most significant adverse event although with much lower rates than in previously reported small sample case-series of children under 10 years. In particular we do not show increased susceptibility in young patients below 7 years of age. This implies that medical and surgical experience is important in teams delivering DBS to children. This information also supports a practice of safe early DBS in an attempt to mitigate or forestall inevitable co-morbidities such as functional musculoskeletal deformities⁴² and adverse drug reactions⁶ but perhaps even more importantly to capitalise on the activity – dependent plasticity of the developing brain as discussed by Ismail, Fatemi and Johnston (EJPN Special Edition on Neuromodulation).

DBS in children and young people, although helpful in the management of movement disorders, can be associated with frequent other hardware related complications. Adverse events related to electrode and extension malfunction are common and most often require surgical intervention. Although rechargeable stimulator is well - accepted

by most of the patients, the maintenance can be challenging particularly in young/small-sized patients with severe involuntary movements and those with learning or developmental delay. A small, skull-mounted neurostimulator, avoiding wires crossing the neck into the chest or abdomen, and a longer lifespan or better suited recharging equipment would be a very welcome development.

Disclosure:

Dr Margaret Kaminska received unrestricted educational grants from Medtronic to attend conferences.

Mr Keyoumars Ashkan received educational grants and honoraria from Medtronic, St Jude and Boston scientific companies.

Dr Jean-Pierre Lin has received a Guy's and St Thomas' Charity New Services and Innovation Grant (G060708), grants from The Dystonia Society (UK), and Action Medical Research (GN2097). Dr Lin is a consultant for Medtronic and has received unrestricted educational grants for courses and to attend conferences.

References:

- ¹ Bressman SB. (2004) Dystonia genotypes, phenotypes, and classification. *Adv. Neurol.* 94: 101-7.
- ² Lin, J., Lumsden, D., Gimeno, H. and Kaminska, M. (2014). The impact and prognosis for dystonia in childhood including dystonic cerebral palsy: a clinical and demographic tertiary cohort study. *Journal of Neurology, Neurosurgery & Psychiatry*, 85(11), pp.1239-1244.
- ³ Lumsden, D., Gimeno, H., Tustin, K., Kaminska, M. and Lin, J. (2015). Interventional studies in childhood dystonia do not address the concerns of children and their carers. *European Journal of Paediatric Neurology*, 19(3), pp.327-336.
- ⁴ Mink JW. (2013) Special concerns in defining, studying, and treating dystonia in children. *Mov. Disord.* 28: 921-5.
- ⁵ Roubertie A, Mariani LL, Fernandez-Alvarez E, Doummar D, Roze E. (2012) Treatment for dystonia in childhood. *Eur. J. Neurol.* Vidailhet M, Vercueil L, Houeto JL, et al.: Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. *NEJM* 2005; 352: 459-67
- ⁶ Lumsden, D., Kaminska, M., Tomlin, S. and Lin, J. (2016). Medication use in childhood dystonia. *European Journal of Paediatric Neurology*.

- ⁷ Kumar, R., Dagher, A., Hutchison, W., Lang, A. and Lozano, A. (1999). Globus pallidus deep brain stimulation for generalized dystonia: Clinical and PET investigation. *Neurology*, 53(4), pp.871-871.
- ⁸ Vidailhet M, Vercueil L, Houeto JL, et al.: Bilateral deep-brain stimulation of the globus pallidus in primary generalized dystonia. *NEJM* 2005; 352: 459–67
- ⁹ Kupsch A, Benecke R, Muller J, et al.: Pallidal deep-brain stimulation in primary generalized or segmental dystonia. *NEJM* 2006; 355: 1978–90
- ¹⁰ Volkmann J, Wolters A, Kupsch A, et al.: Pallidal deep brain stimulation in patients with primary generalised or segmental dystonia: 5-year follow-up of a randomised trial. *Lancet Neurol* 2012; 11: 1029–38
- ¹¹ Coubes, P., Vayssiere, N., El Fertit, H., Hemm, S., Cif, L., Kienlen, J., Bonafe, A. and Frerebeau, P. (2002). Deep Brain Stimulation for Dystonia. *Stereotactic and Functional Neurosurgery*, 78(3-4), pp.183-191.
- ¹² Lumsden, D., Kaminska, M., Gimeno, H., Tustin, K., Baker, L., Perides, S., Ashkan, K., Selway, R. and Lin, J. (2013). Proportion of life lived with dystonia inversely correlates with response to pallidal deep brain stimulation in both primary and secondary childhood dystonia. *Dev Med Child Neurol*, 55(6), pp.567-574.
- ¹³ Katsakiori, P., Kefalopoulou, Z., Markaki, E., Paschali, A., Ellul, J., Kagadis, G., Chroni, E. and Constantoyannis, C. (2009). Deep brain stimulation for secondary dystonia: results in 8 patients. *Acta Neurochir*, 151(5), pp.473-478.
- ¹⁴ Vidailhet, M., Yelnik, J., Lagrange, C., Fraix, V., Grabli, D., Thobois, S., Burbaud, P., Welter, M., Xie-Brustolin, J., Braga, M., Ardouin, C., Czernecki, V., Klinger, H., Chabardes, S., Seigneuret, E., Mertens, P., Cuny, E., Navarro, S., Cornu, P., Benabid, A., LeBas, J., Dormont, D., Hermier, M., Dujardin, K., Blond, S., Krystkowiak, P., Destée, A., Bardinet, E., Agid, Y., Krack, P., Broussolle, E. and Pollak, P. (2009). Bilateral pallidal deep brain stimulation for the treatment of patients with dystonia-choreoathetosis cerebral palsy: a prospective pilot study. *The Lancet Neurology*, 8(8), pp.709-717.
- ¹⁵ Koy, A., Hellmich, M., Pauls, K., Marks, W., Lin, J., Fricke, O. and Timmermann, L. (2013). Effects of deep brain stimulation in dyskinetic cerebral palsy: A meta-analysis. *Movement Disorders*, 28(5), pp.647-654.
- ¹⁶ Chakraborti, S., Hasegawa, H., Lumsden, D., Ali, W., Kaminska, M., Lin, J. and Ashkan, K. (2013). Bilateral subthalamic nucleus deep brain stimulation for refractory total body dystonia secondary to metabolic autopathology in a 4-year-old boy with infantile methylmalonic acidemia. *Journal of Neurosurgery: Pediatrics*, 12(4), pp.374-379.
- ¹⁷ McClelland, V., Valentin, A., Rey, H., Lumsden, D., Elze, M., Selway, R., Alarcon, G. and Lin, J. (2016). Differences in globus pallidus neuronal firing rates and patterns relate to different disease biology in children with dystonia. *Journal of Neurology, Neurosurgery & Psychiatry*, pp.jnnp-2015-311803.
- ¹⁸ Lumsden, D., Ashmore, J., Charles-Edwards, G., Lin, J., Ashkan, K. and Selway, R. (2013). Accuracy of stimulating electrode placement in paediatric pallidal deep brain stimulation for primary and secondary dystonia. *Acta Neurochir*, 155(5), pp.823-836.
- ¹⁹ Chelvarajah, R., Lumsden, D., Kaminska, M., Samuel, M., Hulse, N., Selway, R., Lin, J. and Ashkan, K. (2012). Shielded Battery Syndrome: A New Hardware Complication of Deep Brain Stimulation. *Stereotactic and Functional Neurosurgery*, 90(2), pp.113-117.
- ²⁰ Coubes, P., Vayssiere, N., El Fertit, H., Hemm, S., Cif, L., Kienlen, J., Bonafe, A. and Frerebeau, P. (2002). Deep Brain Stimulation for Dystonia. *Stereotactic and Functional Neurosurgery*, 78(3-4), pp.183-191.
- ²¹ Falowski, S., Ooi, Y. and Bakay, R. (2015). Long-Term Evaluation of Changes in Operative Technique and Hardware-Related Complications With Deep Brain Stimulation. *Neuromodulation: Technology at the Neural Interface*, 18(8), pp.670-677.
- ²² Oh, M., Abosch, A., Kim, S., Lang, A. and Lozano, A. (2002). Long-term Hardware-related Complications of Deep Brain Stimulation. *Neurosurgery*, 50(6), pp.1268-1276.
- ²³ Fenoy, A. and Simpson, R. (2014). Risks of common complications in deep brain stimulation surgery: management and avoidance. *Journal of Neurosurgery*, 120(1), pp.132-139.
- ²⁴ Zorzi G1, Marras C, Nardocci N, Franzini A, Chiapparini L, Maccagnano E, Angelini L, Caldiroli D, Broggi G. Stimulation of the globus pallidus internus for childhood-onset dystonia. *Mov Disord*. 2005 Sep;20(9):1194-200.

- ²⁵ Alterman RL, Tagliati M: Deep brain stimulation for torsion dystonia in children. *Childs Nerv Syst* 23:1033–1040, 2007
- ²⁶ Alterman RL, Tagliati M: Deep brain stimulation for torsion dystonia in children. *Childs Nerv Syst* 23:1033–1040, 2007
- ²⁷ Keen, J., Przekop, A., Olaya, J., Zouros, A. and Hsu, F. (2014). Deep brain stimulation for the treatment of childhood dystonic cerebral palsy. *Journal of Neurosurgery: Pediatrics*, 14(6), pp.585-593.
- ²⁸ Air EL, Ostrem JL, Sanger TD, Starr PA: Deep brain stimulation in children: experience and technical pearls. Clinical article. *J Neurosurg Pediatr* 8:566–574, 2011
- ²⁹ Ghosh PS, Machado AG, Deogaonkar M, Ghosh D: Deep brain stimulation in children with dystonia: experience from a tertiary care center. *Pediatr Neurosurg* 48:146–151, 2012
- ³⁰ Petrossian, M., Paul, L., Multhaupt-Buell, T., Eckhardt, C., Hayes, M., Duhaime, A., Eskandar, E. and Sharma, N. (2013). Pallidal deep brain stimulation for dystonia: a case series. *Journal of Neurosurgery: Pediatrics*, 12(6), pp.582-587.
- ³¹ Koy, A., Weinsheimer, M., Pauls, K., Kühn, A., Krause, P., Huebl, J., Schneider, G., Deuschl, G., Erasmí, R., Falk, D., Krauss, J., Lütjens, G., Schnitzler, A., Wojtecki, L., Vesper, J., Korinthenberg, R., Coenen, V., Visser-Vandewalle, V., Hellmich, M. and Timmermann, L. (2016). German registry of paediatric deep brain stimulation in patients with childhood-onset dystonia (GEPESTIM). *European Journal of Paediatric Neurology*.
- ³² Olaya, J., Christian, E., Ferman, D., Luc, Q., Krieger, M., Sanger, T. and Liker, M. (2013). Deep brain stimulation in children and young adults with secondary dystonia: the Children's Hospital Los Angeles experience. *Neurosurgical Focus*, 35(5), p.E7.
- ³³ Lumsden DE, Kaminska M, Tustin K, Gimeno H, Baker L, Ashkan K, Selway R, Lin JP. Battery life following pallidal deep brain stimulation (DBS) in children and young people with severe primary and secondary dystonia. *Childs Nerv Syst*. 2012 Jul;28(7):1091-7
- ³⁴ Pepper, J., Zrinzo, L., Mirza, B., Foltynie, T., Limousin, P. and Hariz, M. (2013). The Risk of Hardware Infection in Deep Brain Stimulation Surgery Is Greater at Impulse Generator Replacement than at the Primary Procedure. *Stereotactic and Functional Neurosurgery*, 91(1), pp.56-65.
- ³⁵ Thrane, J., Sunde, N., Bergholt, B. and Rosendal, F. (2014). Increasing Infection Rate in Multiple Implanted Pulse Generator Changes in Movement Disorder Patients Treated with Deep Brain Stimulation. *Stereotactic and Functional Neurosurgery*, 92(6), pp.360-364.
- ³⁶ Rizzi, M., Messina, G., Penner, F., D'Ammando, A., Muratorio, F. and Franzini, A. (2015). Internal Pulse Generators in Deep Brain Stimulation: Rechargeable or Not?. *World Neurosurgery*, 84(4), pp.1020-1029.
- ³⁷ Waln, O. and Jimenez-Shahed, J. (2013). Rechargeable Deep Brain Stimulation Implantable Pulse Generators in Movement Disorders: Patient Satisfaction and Conversion Parameters. *Neuromodulation: Technology at the Neural Interface*, 17(5), pp.425-430.
- ³⁸ Kaminska M, Lumsden DE, Ashkan K, Malik I, Selway R, Lin J-P: Rechargeable Deep Brain Stimulators (DBS) in the management of paediatric dystonia: well tolerated with a low complication rate. *Stereotact Funct Neurosurg* 2012;90:233–239
- ³⁹ Herzog, J., Pinsker, M., Wasner, M., Steigerwald, F., Wailke, S., Deuschl, G. and Volkmann, J. (2007). Stimulation of subthalamic fibre tracts reduces dyskinesias in STN-DBS. *Movement Disorders*, 22(5), pp.679-684.
- ⁴⁰ Morishita, T., Foote, K., Burdick, A., Katayama, Y., Yamamoto, T., Frucht, S. and Okun, M. (2010). Identification and management of deep brain stimulation intra- and postoperative urgencies and emergencies. *Parkinsonism & Related Disorders*, 16(3), pp.153-162.
- ⁴¹ Grips, E., Blahak, C., Capelle, H., Bazner, H., Weigel, R., Sedlacek, O., Krauss, J. and Wöhrle, J. (2006). Patterns of reoccurrence of segmental dystonia after discontinuation of deep brain stimulation. *Journal of Neurology, Neurosurgery & Psychiatry*, 78(3), pp.318-320.
- ⁴² Cif, L., Ruge, D., Gonzalez, V., Limousin, P., Vasques, X., Hariz, M., Rothwell, J. and Coubes, P. (2013). The Influence of Deep Brain Stimulation Intensity and Duration on Symptoms Evolution in an OFF Stimulation Dystonia Study. *Brain Stimulation*, 6(4), pp.500-505.
- ⁴³ Lumsden, D., Gimeno, H., Elze, M., Tustin, K., Kaminska, M. and Lin, J. (2016). Progression to musculoskeletal deformity in childhood dystonia. *European Journal of Paediatric Neurology*, 20(3), pp.339-345.

	Diagnosis	Age at surgery in years	Age of death in years	DBS in situ Y/N	comments
1	PKAN*	4.25	8.8 4 years after DBS removed	N	DBS implanted for status dystonicus requiring PICU. Acute Hepatitis A diagnosed 3 weeks later complicated by nephrotic syndrome. This immunocompromise resulted in brain abscess along left lead requiring DBS removal. No residual scarring. DBS re-implant declined by the family. Patient died while on holiday abroad due to unexplained haematemesis.
2	PKAN*	7.9	12.6	Y	Patient died in sleep at the end stage of disease.
3	PKAN*	10.5	18	Y	Patient died at the end stage of disease.
4	Aicardi-Goutieres Syndrome	6.6	10.5	Y	Died within 24 hours after DBS electrode replacement, respiratory arrest, examination post mortem did not reveal the cause of death.
5	Aicardi-Goutieres Syndrome	3.3	9.2 1 year after DBS removed	N	DBS removed due to infection following revision.
6	Glutaric Aciduria type 1	10.6	14.3	Y	DBS inserted as a palliative measure but non-rechargeable battery not replaced, therefore stimulation ceased. Patient died with full palliative care support.
7	PKAN*	16.4	18.5	N	DBS implanted in

			11 months after DBS removed		advanced stage of disease in patient with tracheostomy colonised with Pseudomonas and MRSA. System removed due to infection. Patient died with full palliative care support.
8	PKAN*	14.3	18.1	Y	Patient found dead at the end stage of disease in the residential care centre with neck hyperextended. Further details unknown.
9	PKAN*	10.2	11.2	Y	Patient died due to aspiration pneumonia.
10	Undiagnosed secondary dystonia/chorea	12.5	15.2 5 months after DBS removed	N	DBS removed due to infection following new implant. Dystonia deteriorated significantly requiring dramatic escalation of medications.

*Pantothenate Kinase Associated Neurodegeneration

Table 1: Patients deaths

Table 2: DBS in children - hardware related complications

Complication	% of patients
Surgical site infections new implants (all)	10.3
new implants Activa RC	8.6
new implants under 7 y	7.6
new implants under 7y Activa RC	4.7
Surgical site infections - revisions	10.1
Skin erosion	2.3
Seroma	8
Intracranial bleeding (asymptomatic)	0.8
CSF collection on a scalp	0.8
Electrode/extension problems (all)	18.4
fracture	4.6
malfunction	7.7
migration	2.3
Short/tight extension	3.8
Battery switched off unexpectedly Soletra/Kinetra	18.7
Battery switched off unexpectedly Activa RC	3.4
Status dystonicus following sudden cessation of DBS	4.6
Recharging of stimulator:	
Shielded battery syndrome (Kinetra replaced with Activa RC)	14 (2 of 14 patients)
Battery repositioned for difficulty recharging in overweight patients	2
Significant difficulty maintaining connection during recharging	23
Recharger replaced at least once	38
Battery flat at least once	23

Figure 1:

- a) Patients and implanted new stimulators
 b) Patients and follow up

a)

b)

Figure 2:**Results of survey on recharging of the DBS battery (48 patients)**