An Open-Label Prospective Pilot Trial of Nucleus Accumbens Deep Brain Stimulation for Children with Autism Spectrum Disorder and Severe, Refractory Self-Injurious Behaviour: Study Protocol

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Study Protocol

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Abstract

Background

Children and youth with Autism Spectrum Disorder (ASD) may manifest self-injurious behaviours (SIB) that may become severe and refractory with limited pharmacologic or behavioural treatment options. Here, we present the protocol of a prospective, mixed-methods study to assess the safety and efficacy of deep brain stimulation (DBS) of the nucleus accumbens (NAcc) for children and youth with ASD and severe, refractory SIB.

Methods

This is a prospective, single-center, single-cohort, open-label, non-randomized pilot trial of 6 patients. Participants will be recruited through specialized behavioural clinics with persistent severe and refractory SIB following standard and intensive interventions. Following NAcc-DBS, participants will be enrolled in the study for 12 months. The primary objectives of the study are safety and feasibility, assessed by rate of recruitment and identification of factors impacting adherence to follow-up and study protocol. Treatment efficacy will be assessed by changes in the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS), the Behaviour Problems Index (BPI), the Inventory of Statements about Self-Injury (ISAS) and the Repetitive Behaviour Scale-Revised (RBS-R) questionnaires. Additional clinical outcomes will be assessed, including measures of participant and caregiver quality of life, actigraph measurements, and positron emission tomography (PET) changes following DBS.

Discussion

This study will be the first to evaluate the effect of DBS of the NAcc on a pediatric population in a controlled, prospective trial. Secondary outcomes will improve the understanding of behavioural, neuro-imaging and electrophysiologic changes in children with ASD and SIB treated with DBS. This trial will provide an estimated effect size of NAcc-DBS for severe refractory SIB in children with ASD in preparation for future comparative trials.

Trial Registration

Registration on ClinicalTrials.gov was completed on June 12 of 2019 with the Identifier: NCT03982888. https://clinicaltrials.gov/ct2/show/NCT03982888

Background

Autism spectrum disorder (ASD) is a clinical diagnosis based on a set of heterogeneous neurodevelopmental conditions. ASD is characterized by difficulties in social interaction and communication, and repetitive restricted behaviours and interests according to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V).(1) ASD has a worldwide prevalence of 1%, an estimated 1 in 68 births in the United States in 2014 by the Centre for Disease Control and Prevention, and a greater prevalence in males than females.(2–4)

The behavioural comorbidities of ASD include aggressive behaviour (up to 68%)(5, 6) and repetitive self-injurious behaviour (up to 50%).(7, 8) In children with ASD and self-injurious behaviours (SIB), over 75% of children will have persistence of these behaviours into adulthood, sometimes resulting in severe harm and even death.(5, 9–11) SIB can be defined as repetitive “behaviour which produces physical injury to the individual’s own body” with several different subclassifications.(12) Pharmacologic agents, such as antipsychotics (e.g. risperidone, aripiprazole), and selective serotonin reuptake inhibitors (e.g. fluoxetine) show evidence for treating irritability but not specifically reducing self-injury.(13–17)

Applied behaviour analysis, based on operant methodology, offers an evidence-based method to assess and treat SIB. Functional analysis identifies the function of the behaviour and shows what conditions self-injury are associated with and what stimulus conditions maintain it.(18) It is hypothesized that social consequences, such as escape from demands or selective attention, mediate 20–25% of SIB through automatic reinforcement.(12, 19) Subtypes of automatic reinforcement show differential responses to reinforcement-based interventions and may have implications on the biological bases of SIB and biobehavioural research. This may also give us insight into the role of neuromodulation as a feasible intervention for SIB.

Neuromodulation, through deep brain stimulation (DBS), may present novel treatment options for this population when other treatments are not effective or tolerated. DBS is a precise neuromodulation strategy for targeting pathological brain circuity,(20) albeit with incompletely understood mechanisms of action. DBS involves implantation of electrodes (often two with one on each side of the brain) into deep brain targets and delivery of an electrical current through these electrodes via an impulse generator implanted in the chest. The indication for DBS in pediatric populations is primarily for dystonia, notably inherited dystonia without nervous system pathology.(21) In children with refractory disease processes, DBS has been previously utilized for novel indications, such as select cases of Tourette’s syndrome, obsessive-compulsive disorder (OCD), and epilepsy with varying levels of success.(22–26) In the course of DBS treatment for dystonia and Tourette’s syndrome in adult patients with comorbid SIB, reduction in the frequency or full cessation of SIB has been reported.(27, 28) DBS of several targets has previously been employed to treat SIB, including in six patients under the age of 20 with ASD (Table 1). These targets include the basolateral amygdala,(29) globus pallidus internus,(30) posterior hypothalamus (31) and the nucleus accumbens (NAcc).(32)

Table 1
Literature Review of DBS for the Treatment of SIB & ASD

(33)Author	Age, Sex	Behaviour	DBS Target (programming)	Pre-DBS Score	Post-DBS Score
Sturm 2012 (29)	13M	Self-aggression	Basolateral Amygdala (120 µs, 130 Hz, 2- 6.5V)	Restraints do not prevent skin lesions and life threatening self-injury	Restraint of the wrists suffices and is well tolerated
Stocco 2014 (30)	19F	Self-picking	Globus Pallidus Internus (120 µs, 80 Hz, 3.3 V)	JHMRS 46	JHMRS 4
Stocco 2014 (30)	17M	Punching of arms and legs, biting	Globus Pallidus Internus (120 µs, 100 Hz, 2.5 V) + Anterior limb of internal capsule (210 µs 100 Hz 2.0 V)	JHMRS 67	JHMRS 19
Benedetti-Isaac 2015 (34)	27M	Aggressive behaviour towards self	Posterior Hypothalamus (90 µs, 185 Hz, 2.7 V)	OAS 9	OAS 1
Benedetti-Isaac 2015 (34)	16M	Self-aggression	Posterior Hypothalamus (90 µs, 185 Hz, 2.8 V)	OAS 8	OAS 8 (temporary improvement at 1 month)
Segar 2015 (35)	24F	Biting hands, picking skin	Nucleus accumbens (90 µs, 130 Hz, 8 V)	GAF 20	GAF 50–60
Park 2016 (32)	13M	Self-mutilation, face-hitting causing fractures	Nucleus accumbens (90 µs, 130 Hz, 3–5 V)	CGI-S 6 ABC 106 CY-BOCS 22 K-ARS 54 SRS 101	CGI-S 4 ABC 40 CY-BOCS 7 K-ARS 36 SRS 98
Kakko 2019 (33)	19M	Aggression, self-mutilation, lacerations	Globus Pallidus Internus		Self-destructive behaviour ceased
Doshi 2019 (36)	42F	Hitting, violent outbursts	Nucleus accumbens (60 µs, 130 Hz, 2.6 V)	YBOCS 19 HDS 20 HAS 30 SCQ 26	YBOCS 5 HDS 15 HAS 18 SCQ 16

ABC, Antecedent Behaviour Consequence; CGI-S, Clinical Global Impairment-Severity; CY-BOCS, Children's Yale-Brown Obsessive Compulsive Scale; DBS, deep brain stimulation; GAF, global assessment of functioning; HAS, Hamilton Anxiety Scale; HDS, Hamilton Depression Scale; JHMRS, John's Hopkins motor stereotypy rating scale; K-ARS, Korean ADHD Rating Scale; OAS, Overt Aggression Scale; SCQ, Social Communication Questionnaire; SRS, Social Responsiveness Scale

The NAcc of the ventral striatum receives projections from the orbitofrontal cortex and sends hierarchical information via spiraling striatonigrostriatal projections to the dorsal striatum.(37, 38) Volumetric studies of the striatum suggest that an imbalance of the ventral-dorsal striatal circuity may underlie SIB.(39, 40) Likewise, the amygdala, a previous target for SIB in children also projects widely to the striatum, with weaker connectivity patterns in children with ASD.(41) The NAcc also possesses widespread projections to the dopaminergic receptors of the ventral tegmental area.(37) Other pathologies, such as OCD, addiction and alcoholism, have been treated with NAcc-DBS.(42–45) When the NAcc is targeted for DBS, the anterior limb of the internal capsule (ALIC) can be stimulated simultaneously to augment behavioural changes related to attention and sensorimotor control.

Study Design

We present a protocol for a single-center, single-cohort, open-label, non-randomized prospective pilot trial of NAcc-DBS for refractory and severe SIB in children with ASD. The trial is currently open for recruitment at the Hospital for Sick Children (HSC) in Toronto.

Goals and Objectives

The primary objective of the study is to assess feasibility and safety, measured by recruitment rate, identification of factors impacting follow-up and protocol adherence, and successful implantation. Secondary objectives include change in frequency or severity of SIB following surgery, measured regularly by caregiver-reported questionnaires over the course of one year. Additional clinical outcomes include changes quality of life for the patient and their caregiver(s), repetitive motion characteristics as measured with actigraphy, metabolic changes seen through positron emission tomography (PET), and changes on electrophysiologic data. This is the first prospective trial of DBS for children with SIB and represents the first assessment of a potential surgical treatment for patients with extremely limited therapeutic options.

Methods/design

This is a prospective, single-center, open-label, non-randomized study of six patients at HSC. The aim is to evaluate the feasibility and safety of DBS of the NAcc for medically-refractory, repetitive self-injurious behaviours in children with ASD. Electrophysiological parameters are optimized in the 12-month follow-up to study and manage possible side effects.

Ethics & Registry

This research involves human participants and is performed in accordance with the Delcaration of Helsinki. This trial was approved by the Hospital for Sick Children Research Ethics Board, approval number 1000060282. Registration on ClinicalTrials.gov was completed in June of 2019 with the Identifier: NCT03982888. Patient recruitment and continuation in the study is considered by a safety monitoring board at HSC. Written informed consent to participate in the trial is acquired from the child or adolescent when able, or the parent or legal guardians. If the child or adolescent is unable to provide consent, assent is sought.

Enrollment and Surgery

Potential participants are recruited from specialized behavioural clinics. Potential participants are reviewed by the investigators with respect to inclusion and exclusion criteria (Table 2). Eligible patients are discussed in a multidisciplinary meeting of the surgical, psychiatric and medical teams. There are no changes to the participants' medications or behaviour therapies after enrollment prior to surgery. Any changes to medications following surgery are noted, including changes to dosages and indication for change.

Table 2: Study Inclusion & Exclusion Criteria

Inclusion Criteria
1. Female or Male patients between age 7-18 2. Diagnosis of Autism Spectrum Disorder (as defined by the DSM-5). The treating physicians at each individual clinic will be responsible for diagnosis. All children screened for entry into the study will be re-diagnosed by a clinician prior to entry. 3. Failure or non-eligibility of medical therapy with ongoing repetitive self-injurious behaviours, at 6 months or more after instigation of therapy. Failure is defined as a lack of improvement in self-injurious behaviours, as documented by objective evidence, including caregiver logs or clinician assessment, if the clinician has documented a baseline status prior to instigation of the medical therapy. 4. The child has undergone rigorous, gold-standard Functional Behaviour Assessment including functional analysis, leading to treatment lasting a minimum of six months, without significant change from baseline. 5. Diagnosis of secondary stereotypies, based on clinical assessment of the treating physicians with evidence of self-injury, documented in the patient records. The definition of self-injury is contextual, but requires current, previous or potential manifestation of physical injury to the child. 6. The child is at risk of permanent injury as a result of self-injurious behaviours. 7. Parents or legal guardians, including caregivers, informed and able to give written consent. 8. Able to comply with all testing, follow-ups and study appointments and protocols for 12 months following the end of the duration of the study.
Exclusion Criteria
1. Substance dependence or abuse in the last 6 months, excluding caffeine and nicotine 2. Any contraindication to MRI or PET scanning 3. Likely to relocate away from the study site or move during the study's one-year duration 4. Presence of cardiac arrhythmias, coagulopathy or other cardiac, respiratory, renal or endocrine conditions that will result in significant risk from a surgical procedure. 5. Pregnancy 6. Unable to communicate adequately in English in order to complete the baseline and follow-up questionnaires.

Participants are assessed by the anesthesia service, neuropsychology team, and receive a magnetic resonance image (MRI) and optional fluorodeoxyglucose (FDG) PET scan. On the day of surgery, a Leksell stereotactic frame is applied under general anesthesia. The patient receives a head computed tomography (CT) scan that is merged to the pre-operative MRI and planned targets. Stereotactic coordinates are calculated and verified to target the NAcc with the goal to include the ALIC in the trajectory of the DBS electrode (Figure 1B&C). In the operating room, a curvilinear incision anterior to the coronal suture is made to place the DBS electrodes stereotactically. Thresholds for side effects are recorded intraoperatively. Electrodes

are placed with fluoroscopic confirmation and a pulse generator is connected and implanted in the infraclavicular region under the same anesthetic.

Patients undergo a postoperative MRI to confirm the position of the electrodes. After the surgery, they are monitored in the hospital for 3-5 days and discharged with the stimulator off. Patients start DBS programming at 4-6 weeks after surgery and visit the joint neurosurgery, neurology DBS clinic at HSC. There is regular monitoring for the development of behavioural, motor, and psychiatric effects from stimulation. During weeks 2-6, there are weekly follow-ups to address any potential complications. The full schedule of events is presented in Table 3.

Sample Size and Recruitment

In this prospective, controlled trial, six patients are selected to determine safety and initial efficacy, as it typical for most DBS early phase trials. There is no control group, and each patient will serve as a comparator for primary outcome measures.

		Study Period							
		Enrollment	Surgery	Follow-up					Post-Trial
Timepoint		Week -8 +/- 4 weeks	Baseline W0	Weekly (W1-6) +/- 1 day	Every 4 W (W8-56) +/- 3 days	Week 12 +/- 1 week	Week 26 +/- 2 weeks	Week 52 +/- 2 weeks	W >52
ırollment	Eligibility screen	X							
	Informed Consent for Trial	X							
	Demographics Questionnaire	X							
	Anesthetic Evaluation	**X**							
	Informed Surgical Consent	**X**							
-Hospital eatment & Care	Deep Brain Stimulation leads and IPG insertion		**X**						
	Programming				**X**	**X**	**X**	**X**	**Every 6 months or as indicated**
maging	MRI	**X (or earlier)**	**X**						
	CT		**X**						
	FDG-PET (optional)	X						X	
stionnaires	Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS)	X				X	X	X	
	Inventory of Statements about Self-Injury (ISAS)	X				X	X	X	
	Behavior Problems Inventory (BPI)	X				X	X	X	
	Repetitive Behaviour Scale-Revised (RBS-R)	X				X	X	X	
	Quality of Life Scale 9Peds QL	X				X	X	X	
	Aberrant Behaviour Checklist	X				X	X	X	
Other sessments	Neurosurgery Evaluation			X (virtual)	X (virtual)	**X**	**X**	**X**	**Annual follow-up**
	Neuropsychology Evaluation	**X**					X	X	As needed
	Actigraphy (Optional)	X				X		X	
	Self-Injury Log	X		X	X	X	X	X	

Table 3: Follow-up Schedule for trial participants. Bolded cells show standard of care for all pediatric DBS patients.

Feasibility and Safety

The trial will be determined feasible if there is >20% recruitment rate. This will provide additional information regarding decision-making for experimental surgical trials. Any deviance to study protocol or inability to complete clinical questionnaires will be documented with an attempt to understand patient barriers.

Safety of the intervention will be carefully monitored with weekly phone calls to participants for the first six weeks. Parents are cautioned and reminded about the signs of infection or sudden changes in neurologic function prior to discharge from hospital.

Clinical Outcome Measures

This trial will conduct pre-post analyses to compare frequency and severity of SIB in children and youth with ASD before and after DBS intervention. Clinical outcomes are measured by the change between baseline and 1-year in the following scales: Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS),(46, 47) the Behavior Problems Inventory (BPI),(48) the Inventory of Statements about Self-Injury (ISAS)(49) and the Repetitive Behaviour Scale-Revised (RBS-R).(50) Secondary clinical outcomes are measured using the Quality of Life Scale 9Peds QL version 4, Aberrant Behaviour Checklist,(51, 52) and caregiver logs of repetitive self-injurious behaviours.

Patients and caregivers complete scales prior to the intervention and also at week 12, week 26, and week 52. Baseline assessments are completed prior to surgery. Efficacy is determined by the within-subject percent change in the primary outcome scores at 1 year (week 52) following surgery compared to baseline.

Additional outcomes include changes in motor patterns based on actigraphy. Actigraphy is the continuous measurement of an individuals' movement using a device worn similarly to a watch (Axivity AX3 and Axivity AX6).(53, 54) The Axivity device can quantify movements and has been validated to detect specific behaviours, such as hand flapping, of patients with ASD with 94.6% accuracy.(55) Children have an actigraph placed on their nondominant wrist 4 weeks prior to the surgery for a total of 2 weeks of recordings. During specific follow-up visits (weeks 12, 26, and 52), the children have the option to wear the actigraph for 2-week intervals. Markers of stereotypies include maximum and minimum value amplitudes, variance, peak to peak, and entropy fast fourier transform, to be analyzed using MATLAB (Mathworks, Natick, MA).(53, 55)

Children enrolled in the trial may receive a FDG-PET scan prior to surgery, and 12 months after surgery. PET scanning is optional and for research purposes only, which will be disclosed to

all participants. PET scans of pediatric patients with anorexia who received NAcc-DBS has demonstrated the reversal of metabolic abnormalities, such as hypermetabolism in the frontal lobes, hippocampus, and lentiform nucleus.(56) The FDG-PET of participants in the present study may similarly demonstrate changes of metabolism in the brain following NAcc-DBS.

Follow-up

Evaluation and assessments occur at approximately 22 time points from pre- to 1-year post-surgery (Table 3). Participants are followed weekly after surgery by the medical team between weeks 0-6, and monthly after 8 weeks. There are two required MRI scans that fall under the standard of care, two optional FDG-PET scans, and 3 possible two-week periods of actigraph recordings. Surveys for the primary clinical outcomes and secondary outcomes are administered once prior to the surgery and three times following surgery. DBS programming starts at approximately 4-6 weeks and reassessment and stimulation changes are planned for weeks 12, 26, and 52 unless there are adverse effects, for which there will be additional programming visits. Ongoing follow-up for safety and DBS programming will occur at HSC until participants turn 18 years old, at which point they will be transitioned to adult care.

Data Management & Statistical Analysis

Patient information will be kept strictly confidential at all times, and all files related to this study will be password protected and kept on a password protected computer. Patient and caregivers will complete surveys and questionnaires online via a secure email link or on paper. The research team will check the content and completion of the forms monthly. All data will be kept for 25 years following the conclusion of the trial.

This is not a blinded study and all investigators and patients are aware of treatment. There is not blinded stimulation-off or stimulation-on periods after DBS implantation. Change in SIB and adverse effects will be analyzed longitudinally using comparative statistics. Repeated measures ANOVA and mixed-effects linear regression are used for analysis of clinical measures and changes over the course of 12 months. All efforts are made to reduce missing data with retrospective review and multiple imputation will be employed for unfound data.

Discussion

The current paper presents a single-cohort, open-label, non-randomized, prospective pilot trial for the first controlled study of DBS of the NAcc for severe, refractory SIB in children and youth with ASD. This study is

important to understand treatment response and safety as well as unforeseen barriers to recruitment and follow-up.

SIB has a high prevalence in several genetic disorders, such as Lesch-Nyhan disease and Fragile X syndrome, suggesting the pathophysiology of SIB may at least in part be rooted in neurobiological as well as neurodevelopmental etiologies.(6) Conversely, environmental triggers, such as novel sensory stimuli or changes in routine, often trigger the onset of episodes of SIB.(57) In patients with ASD, SIB frequency has a direct correlation with ASD severity.(58) The phenotype of SIB in patients with ASD shares similar features to phenotypic behaviours in other psychiatric conditions affecting children and adults, including OCD, attention-deficit hyperactivity disorder, and Tourette's syndrome.(59) These conditions may be comorbid and share a common behavioural phenotype characterized by repetition, rigidity, invariance and sometimes inappropriateness.(39, 59) Improved understanding of neural circuitry and effective DBS treatment options for one indication may enrich the understanding of the related diagnoses and their neurobiological pathophysiology.

DBS is a minimally invasive surgical option for patients with refractory SIB. It is reversible, adjustable and has a well-tolerated safety profile. Although increasingly offered to children for expanding indications, it is often considered an experimental therapy in this context. A proposed ethical framework to guide the conduct of DBS in children has been proposed, to which this study adheres.(60) The principles of this framework include viewing outcomes in a developmentally relevant context, cautiously applying adult data, and weighing the timing of the procedure.(60)

Adult data and experience regarding DBS are not directly applicable to children. As one example, most children will have surgery under general anesthesia, which may preclude microelectrode recordings. Second, stimulation settings are often adopted from adult literature, yet long-term effects for children are not yet fully understood.(23) Third, indications and decisions regarding timing for intervention are complicated in children as treatment decisions are made within the context of childhood development and disease natural history. For example, the natural history of Tourette's syndrome is often to remit as children develop and therefore the indications for DBS in children are as-of-yet unknown.(61, 62) Finally, complications including infection, lead migration or wire fractures are probably higher in children,(21) and side effects of DBS on the developing brain require further study. Moreover, these hardware-related adverse events may manifest differently in children and youth with ASD and repetitive or compulsive SIB, relative to other pediatric cohorts.

Strengths and limitations

This is a prospective, pilot trial of six patients and analyses of clinical outcomes will be limited by the small cohort. The results of this trial should inform larger clinical trials of multiple institutions. Furthermore, there is a lack of consensus regarding the ideal clinical assessment tool to measure the severity and frequency of SIB events. The use of the CY-BOCS, ISAS and the RBS-R questionnaires incorporates several aspects of SIB such as repetitive movements, degree of harm, and impact on functional activities.

Conclusion

This trial has primary objectives to assess the feasibility and safety of DBS for SIB in children with ASD. Clinical outcomes are composed of the change in CY-BOCS, ISAS and the RBS-R questionnaires. Additional outcomes

include measures of participant and caregiver quality of life, actigraph measurements, PET changes, and electrophysiologic data. These data will inform the design and conduct of future investigations in this vulnerable population to deliver novel effective therapies.

List Of Abbrevations

ALIC	anterior limb of internal capsule
ASD	autism spectrum disorder
CGI-S	Clinical Global Impairment-Severity
CT	computed tomography
CY-BOCS	Children's Yale-Brown Obsessive-Compulsive Scale
DBS	deep brain stimulation
DSM-V	Diagnostic and Statistical Manual of Mental Disorders, 5th edition
FDG	flurodeoxyglucose
GAF	global assessment of functioning
HAS	Hamilton Anxiety Scale
HDS	Hamilton Depression Scale
HSC	Hospital for Sick Children
ISAS	Inventory of Statements about Self-Injury
JHMRS	John's Hopkins motor stereotypy rating scale
K-ARS	Korean ADHD Rating Scale
MRI	magnetic resonance image
NAcc	nucleus accumbens
OAS	Overt Aggression Scale
OCD	obsessive-compulsive disorder
PET	positron emission tomography
RBS-R	Repetitive Behavioural Scale-Revised
SCQ	Social Communication Questionnaire

SIB	self-injurious behaviour
SRS	Social Responsiveness Scale
Y-BOCS	Yale-Brown Obsessive-Compulsive Scale

Declarations

Ethics approval and consent to participate

- This trial was approved by the Research Ethics Board at the Hospital of Sick Children, with protocol number 1000060282.
- Consent to participate in the trial is acquired from parent or legal guardians and assent is sought from the child or adolescent.

Consent for publication

- Not applicable

Availability of data and materials

- The datasets generated and/or analysed during the current study are not publicly available due to patient privacy given the small cohort but are available from the corresponding author on reasonable request.

Competing interests

- F. is a consultant for Abbott, Ceregate, Ipsen, Medtronic, Boston Scientific, and AbbVie Inc. He has received research support from Medtronic, Boston Scientific, University of Toronto, Michael J. Fox Foundation for Parkinson's Research, Dystonia Medical Research Foundation, and honoraria for serving as a speaker from Abbott, UCB, Medtronic, Paladin, Sunovion, Ipsen, Boston Scientific, AbbVie Inc.
- There are no other declarations of COI.

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Authors' contributions

- This study was conceived by GMI, with clinical implementation by SB, CG, AF, AR and AL.
- The manuscript was written by HY, with significant contributions by LS, SB, AR, AL and AVK.
- Inclusion criteria and selection of outcome measures influenced by GMI, HY, AR, AL, AVK
- All authors read and approved the final manuscript.

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Figures

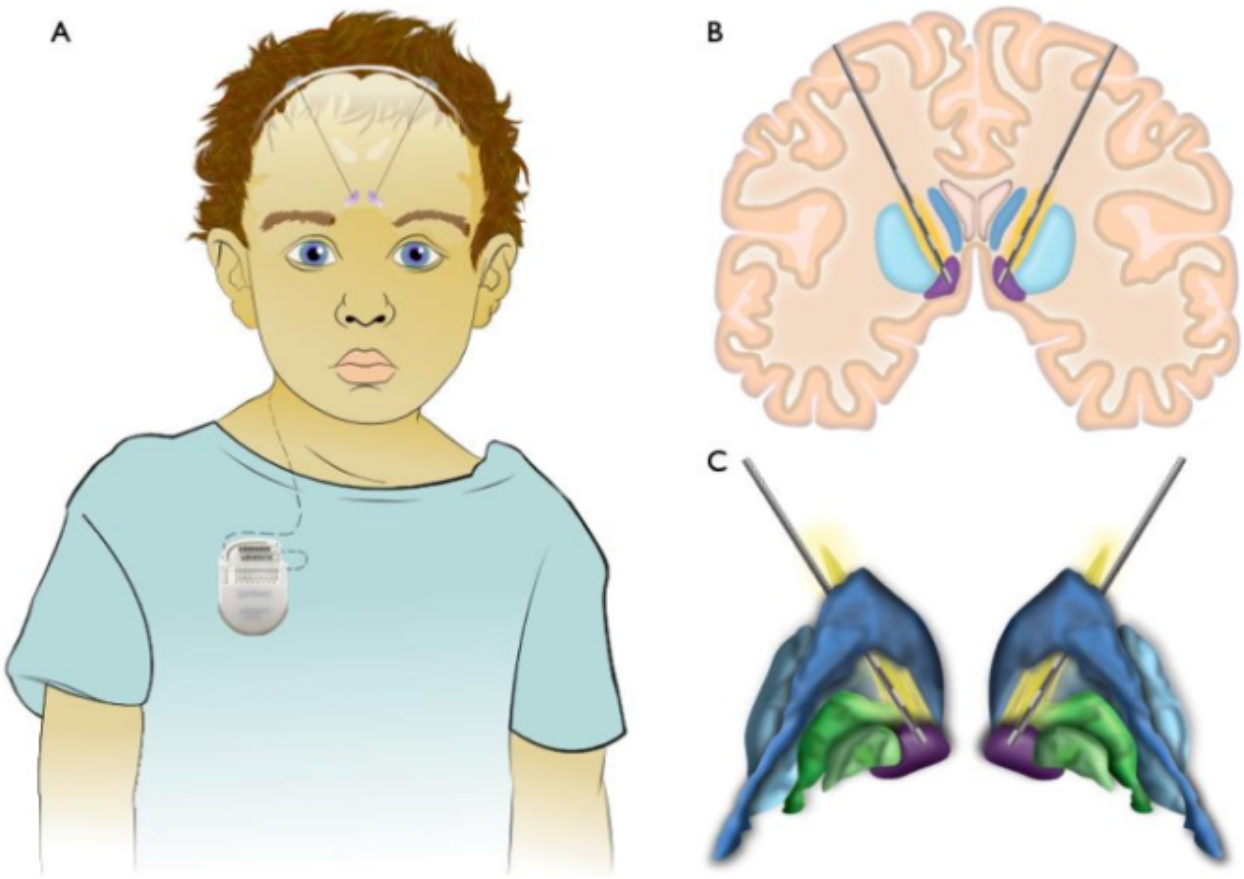

Figure 1

DBS for children, targeting the NAcc. A: DBS extension wires for children are placed with greater length to allow for growth. B: Coronal representation of DBS lead trajectory, passing through the ALIC and targeting the NAcc. C: 3D representation of DBS lead trajectory. NAcc (purple), ALIC (yellow), caudate (dark blue), putamen (light blue), globus pallidus (green).

Supplementary Files

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