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Feasibility and optimization of *a novel, cranially-mounted deep brain stimulation* device for children with epilepsy – the CADET Pilot study

Dear editor,

Deep brain stimulation (DBS) is increasingly used for the treatment of severe, drug-resistant neurological conditions. In childhood-onset epilepsy, early intervention is particularly urgent as this is associated with improved cognitive function and quality of life [1]. It is therefore imperative to conduct clinical studies of DBS specifically in pediatric patients to investigate its impact on seizure burden, development and long-term quality of life (QoL) [2]. However, children are not simply 'small adults', and pediatric DBS is limited by current adult-centric technologies that are not optimized to the clinical, developmental, and practical needs of children [3,4]. Devices for children need to be robust to physical growth and avoid limiting children in what activities (e.g. sports) they can partake in – presenting challenges for traditional devices implanted in the chest with vulnerable leads tunnelled through the neck. Device longevity and futureproofing are key concerns; in particular, a rechargeable battery is required so that research and monitoring features such as brain activity recording can be enabled without affecting long-term therapy delivery, and wireless upgrades so that the latest therapy algorithms can be implemented without requiring device replacement. For experimental device trials, there needs to be a clear plan for *lifelong* follow-up care. Finally, developmental and behavioural differences associated with severe epilepsy present unique device usage challenges.

Here we report on a *first-in-child* and *first-in-epilepsy* study of a novel investigational device with design features attuned to the needs of pediatric patients. The *CADET* (*Children's Adaptive Deep brain stimulation for Epilepsy Trial*) *Pilot* study (NCT05437393) was a UCL-Sponsored prospective single-arm medical device clinical investigation (Fig. 1A) using the *Picostim*® DBS system (Amber Therapeutics), investigating the *safety* and *feasibility* of centromedian thalamic (CMT) DBS in a population with *Lennox Gastaut syndrome* (LGS) [5]. The *Picostim* has a cranially mounted implanted pulse generator (IPG; Fig. 1B), which makes it growth-compatible and reduces risks of lead fracture and device-related discomfort. The system is non-invasively rechargeable, minimising the need for frequent IPG replacements. The device ran the *DyNeuMo-1* firmware but can be wirelessly upgraded post-operatively to enable neural signal sensing during active stimulation, long-term neural activity monitoring and closed-loop therapy algorithms [6–8]. *CADET Pilot* was designed to inform protocol development of a larger clinical device investigation (*CADET Trial*) statistically powered to evaluate the *efficacy* of the therapy as well as the feasibility of closed-loop seizure-responsive therapy [9].

The primary outcomes of *CADET Pilot* were *safety* (adverse events) and *feasibility* of the study and therapy (patient recruitment, study completion, and recharge compliance). Secondary outcomes were seizure frequency reduction (via 30-day diaries and 48h EEG monitoring), ratings of seizure severity, QoL and neurodevelopment, and the ability to record thalamic local field potentials (LFPs). Eligible children (Table S1) with LGS underwent device implantation and continuous high-frequency DBS (130Hz; 90 ms; 4.5mA; bipolar) for six months. Four children were enrolled - three children completed the full study protocol (7–12 years; Table S2), while one participant withdrew pre-implantation due to spontaneous seizure improvement. The device and cranial implantation of the IPG (Fig. 1B) were well tolerated and no neurological harm was observed. Six adverse events were reported, of which two were serious but only one— a wound infection and subsequent breakdown at the IPG site — was procedure-related (and not device-related).

Recharge compliance and device ergonomics emerged as critical considerations for pediatric use. Integrating recharging into daily or weekly routines was an important adjustment for participating families. Participant 3 had microcephaly and experienced inefficient charging due to difficulty maintaining contact between the charging puck and cranially mounted IPG. A custom-engineered recharging headset (Fig. 1C) dramatically improved the number of recharging sessions achieving full charge from 6.2% to 72.6% and greatly benefited caregiver experience (Table S3). Two participants experienced unintentional interruption of therapy (19/158 days and 4/180 days, respectively) due to stimulation not being reactivated after full battery depletion. This was mitigated through enabling automatic therapy re-activation and further device training.

For all time points, 48h video-EEG recordings were obtained, CMT LFPs were recorded successfully (including one seizure; Fig. 1D), and completed seizure diaries were returned (Fig. 1E). At six months, all participants demonstrated clinically meaningful reductions in seizure frequency, ranging from 25.6% to 47.4% on carer diaries and 20.7% to 40.9% on 48-h EEG analysis (Fig. 1F). One participant showed a notable decline in daytime seizures specifically (82.8%, Fig. 1E–F). No consistent effects were observed on seizure severity, QoL or impact of epilepsy rating scales (Fig. 1F). All three patients continue to receive therapy with the device via the MHRA's *exceptional use* framework.

Overall, *CADET Pilot* provides evidence for the *safety* and *feasibility* of DBS research with the *Picostim* system in pediatric epilepsy - no participants withdrew for study- or intervention-related reasons, and no prohibitive safety or device concerns emerged. All trial time points were successfully completed indicating strong family engagement, though device recharging proved an important challenge leading to two instances of unintended therapy cessation. This was mitigated through iterative adaptations in consultations between carers, clinicians and academic and industrial collaborators, which will be carried forward into *CADET Trial*. This emphasizes the importance of the clinical-academic-industrial partnership for the pediatric epilepsy context:

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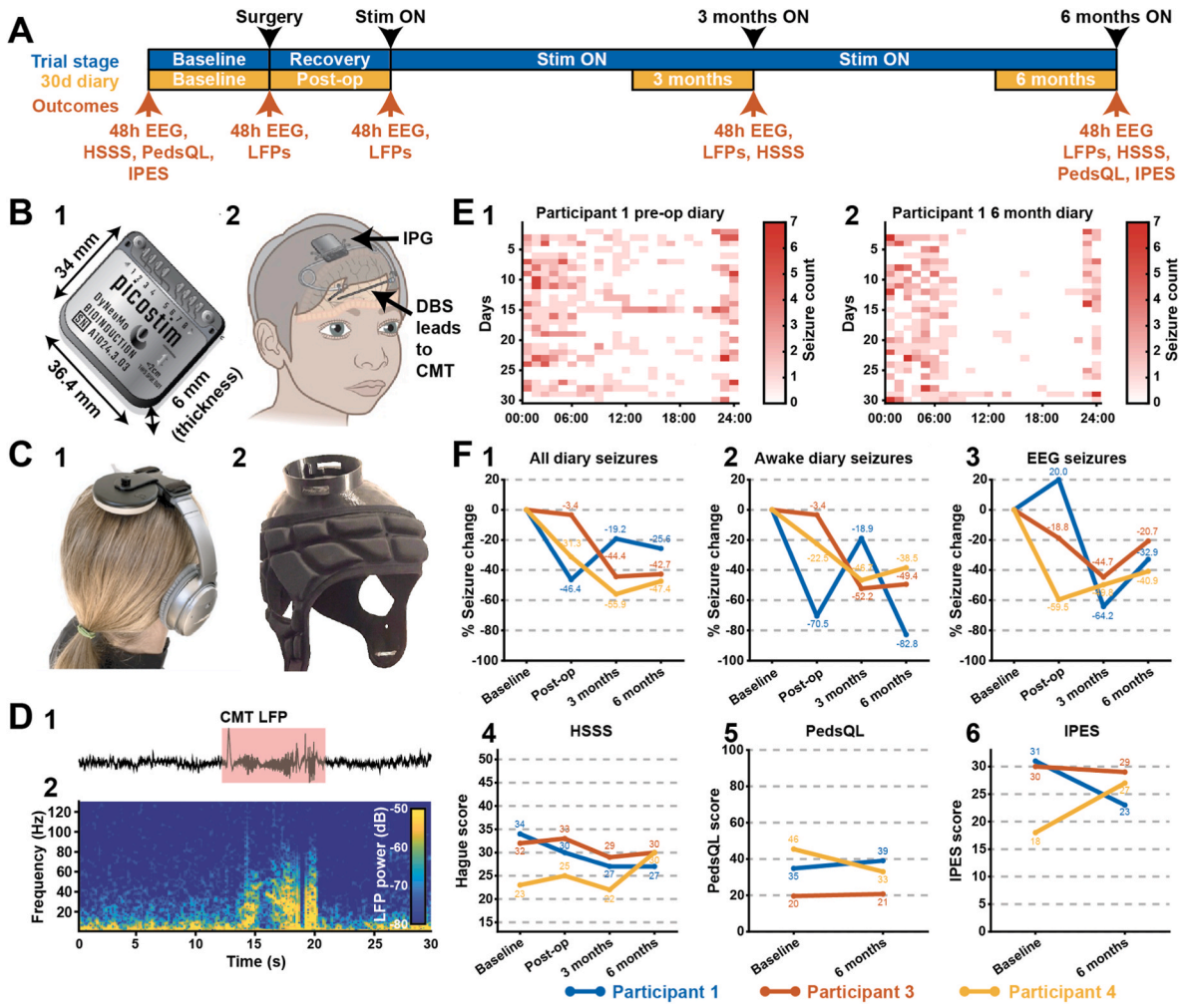

Fig. 1. Feasibility and optimization of *a novel, cranially-mounted deep brain stimulation (DBS)* device for children with epilepsy – the CADET Pilot study. A: Timeline of the *CADET Pilot Study*. **B:** The investigational device used in the CADET Project, the *Picostim® Deep Brain Stimulation (DBS) System* (*Amber Therapeutics, previously Bioinduction Limited*). The implantable components include an implanted pulse generator (IPG; **B1**)) and two leads, each with four stimulation contacts. The IPG is implanted in a craniectomy site in the parietal bone (**B2**). The leads are implanted to the centromedian nucleus of the thalamus (CMT) via bilateral frontal bone craniostomies. **C:** Recharging performance using the baseline head mount (**C1**) was improved after using the customized, 3-D printed recharging headmount (**C2**). **D:** CMT local field potentials (LFPs) were successfully streamed from the device during all planned time points. An example is shown of a seizure recorded from an LFP of the CMT in a follow-up visit (red box), indicating feasibility of adaptive (seizure-responsive) therapy in *CADET Trial*. **E:** The 30-day seizure diary for participant 1 is shown at baseline (**E1**) and in the sixth month of stimulation (**E2**). **F:** The secondary outcomes are shown for all three participants, including all seizure events recorded on parent-recorded diaries relative to baseline (**F1**), awake seizure events recorded on parent-recorded diaries relative to baseline (**F2**), clinical seizures recorded on 48-hr home video EEG relative to the baseline EEG session (**F3**), seizure severity measured using the *Hague Seizure Severity Score (HSSS)*, quality of life measured using the *Pediatric Quality of Life Inventory (PedsQL)* and *Impact of Pediatric Epilepsy Scale (IPES)*. Post-op. = postoperative; 3-/6 months = 3-/6 months after starting stimulation; Stim. = stimulation.

continual tailoring of DBS treatment is likely to be required in a population where anatomical variability and behavioural disturbance are common. While our sample size precludes formal statistical inference, the observed seizure reductions provide early evidence of therapeutic potential. The observed differential effects on daytime and night-time seizures might warrant time-of-day dependent therapy (supported by the *Picostim*), but could present a challenge for diary-recorded seizure counts if continual overnight monitoring by a carer is not available. Successful capture of a seizure signature in CMT LFP supports the feasibility of the planned sub-study on closed-loop therapy in *CADET Trial*.

The *CADET Pilot Study* represents an important milestone in neuromodulation for pediatric epilepsy, demonstrating safe implantation, stimulation, and chronic use of the *Picostim*, and iterative, patient-centred refinement that lays the groundwork for further DBS research in children. C*ADET Trial*, the phase III clinical trial statistically powered to establish efficacy will commence imminently.

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CRediT authorship contribution statement

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests. VSM, JJvR, KL and JEF have been paid consultants or employees at *Amber Therapeutics*. JJvR has received speaker fees from *Medtronic*. VSM was a paid intern at *Medtronic*. HH has been paid as a consultant by *Renishaw*, *Medtronic* and *LivaNova*. KL is funded through an *MRC iCASE studentship* (partly funded by *Amber Therapeutics*). TD is a founder and chief engineer of *Amber Therapeutics*, is the non-executive chairman of *MintNeuro*, and a non-executive director at *Onward Medical*.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.brs.2026.103149.

References

[1] Braun KPJ, Cross JH. Pediatric epilepsy surgery: the earlier the better. Expert Rev Neurother 2018;18(4):261–3.

[2] Piper RJ, Ibrahim GM, Tisdall MM. Deep brain stimulation for children with generalized epilepsy. Neurosurg Clin N Am 2024;35(1):17–25.

[3] Piper RJ, Fleming J, Valentín A, et al. Neurostimulation devices for children: lessons learned [Internet]. Lancet Child Adolesc. Health 2022;6(6):359–61.

[4] Kheder A. Growing up modulated: paediatric neuromodulation needs a new ethical framework. Lancet Child Adolesc. Health 2026;10(1):5–7.

[5] Piper RJ, Tisdall MM. Children's adaptive deep brain stimulation for epilepsy trial (CADET): pilot (CADET pilot). ClinicalTrials.gov; 2023. Available from: https://clinicaltrials.gov/ct2/show/NCT05437393.

[6] Zamora M, Toth R, Morgante F, et al. DyNeuMo Mk-1: design and pilot validation of an investigational motion-adaptive neurostimulator with integrated chronotherapy. Exp Neurol 2022;351:113977.

[7] Toth R, Zamora M, Ottaway J, et al. DyNeuMo Mk-2: an investigational circadian-locked neuromodulator with responsive stimulation for applied chronobiology. Conf Proc IEEE Int Conf Syst Man Cybern 2020;2020:3433–40.

[8] Benjaber M, Zamora M, Toth R, et al. A clinical grade neurostimulation implant for hierarchical control of physiological activity. bioRxiv 2025;22:2025–10.21.683630. https://doi.org/10.1101/2025.10.21.683630.

[9] Piper RJ, Tisdall M. The children's adaptive deep brain stimulation for epilepsy trial (CADET). 2025. Available from: https://clinicaltrials.gov/study/NCT06924086.

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