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Stereoelectroencephalography in the very young: Case report

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ABSTRACT

Stereoelectroencephalography (SEEG) is an increasingly popular invasive monitoring approach to epilepsy surgery in patients with drug-resistant epilepsies. The technique allows a three-dimensional definition of the epileptogenic zones (EZ) in the brain. It has been shown to be safe and effective in adults and older children but has been used sparingly in children less than two years old due to concerns about pin fixation in thin bone, registration accuracy, and bolt security. As such, most current series of pediatric invasive EEG explorations do not include young participants, and, when they do, SEEG is often not utilized for these patients. Recent national survey data further suggests SEEG is infrequently utilized in very young patients. We present a novel case of SEEG used to localize the EZ in a 17-month-old patient with thin cranial bone, an open fontanelle, and severe drug-resistant epilepsy due to tuberous sclerosis complex (TSC), with excellent accuracy, surgical results, and seizure remission.

Introduction

Stereoelectroencephalography (SEEG) is an increasingly popular invasive EEG monitoring approach that allows three-dimensional definition of the epileptogenic zones (EZ) in the brain [1–3]. It has been shown to be safe and effective in adults and older children but has been sparsely used in children less than two years old due to concerns about pin fixation in thin bone, registration accuracy, and bolt security [2–4]. As such, most current series of pediatric invasive EEG explorations do not include young participants, and, when they do, SEEG is often not utilized for these patients [1,4–16]. Recent national survey data further suggests SEEG is infrequently utilized in very young patients [17]. We present a novel case of SEEG used to localize the EZ in a 17-month-old patient with thin bone, an open fontanelle, and severe drug-resistant epilepsy due to tuberous sclerosis complex (TSC), with excellent accuracy, surgical results, and seizure remission.

Clinical Presentation.

A 17-month-old girl with developmental delay and TSC with a heavy, multilobar, bilateral tuber burden and a large left-sided subependymal giant cell astrocytoma (SEGA) was referred for surgical management of her epilepsy after 11 months of medical management with worsening seizure control and functional decline. She had 27 radiographically distinct tubers – 12 in the left hemisphere, and 15 in the right – ranging from 9 to 36 mm in width. She had 3 distinct seizure semiologies: a cluster associated with rightward head movement, right arm and right leg myoclonic jerks, and behavior arrest that occurred many times daily. A cluster of abrupt myoclonic head movements followed by head atonia occurred infrequently. In addition, a previous frequently encountered semiology that had resolved consisted of a glazed look with open mouth followed by slow leftward head turning and left gaze and head drop. Overall seizure frequency was reported as 2–16 times per day. Scalp EEG (Fig. 2a) revealed left-sided seizures primarily involving F3 and F7 regions at onset, suggesting a left frontotemporal focus or foci. Clinical onset was minutes into the electrographic seizure. The seizures appeared electrographically similar whether the clinical manifestation involved rightward head turn with right-sided movements, a head drop with atonia, or both together. In this patient, the region electrographically implicated in the EZ was contained within her large SEGA, which abutted cortical areas, as well as multiple frontal and temporal tubers of various size and depth (Fig. 1). At the time of neurosurgical evaluation her epilepsy had worsened resulting in significant functional and neurological regression. Previously she had been babbling and sitting unsupported, but these abilities had been recently lost. Additionally, her right hand was fisted, and she had completely stopped using it. At this point, twice daily she was taking 30 mg/kg/day of

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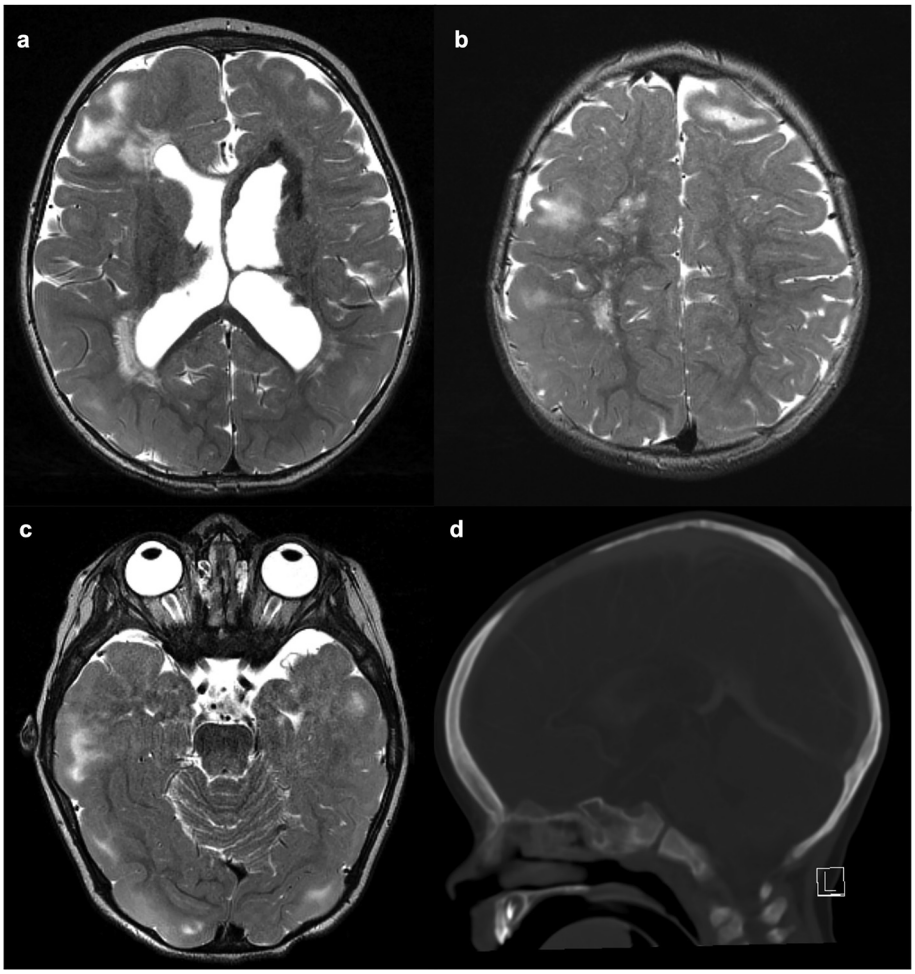

Fig. 1. Axial T2 MRI demonstrating a portion of the patient's tubers. Surgical decision-making was influenced by presence of multiple tubers in the left frontal lobe, right frontal lobe, and left temporal lobe (a-c). Sagittal CT demonstrating open anterior fontanelle (d).

levetiracetam, 130 mg/kg/day of vigabatrin, 5 mg/kg/day of zonisamide, and 2.5 mg of clobazam. She was weaning off physiologic doses of prednisolone. She was also on 2 mg daily of everolimus, which had resulted in a slight reduction in the size of her SEGA. Previously she had also taken sirolimus and failed topiramate.

Given the severity of her epilepsy and developmental decline despite medical management, especially with consistent focal seizure onset, the recommendation was surgical management following localization of the EZ with SEEG. Multiple approaches to invasive monitoring and excision were considered. As this was a very young patient with a heavy tuber burden and at high risk for additional seizures and surgery throughout her life, it was considered critical to limit any resection to the minimum necessary to halt her current seizure type and facilitate developmental progress. In order to monitor deep, medial tubers, multiple lobes, and determine which tuber or tubers were responsible for her current seizures, while avoiding a large craniotomy in a patient who may need future craniotomies, SEEG was recommended.

Operative technique

The patient was placed in a Mayfield frame with pediatric pins. Pins were placed in the left mastoid bone, occipital bone, and the anterior aspect of the right superior temporal line, and slowly tightened to forty pounds per square inch of pressure, taking care to watch for any local deformation of the skull, but none was appreciated. The Mayfield was affixed to the ROSA® robot (Zimmer Biomet, Warsaw, Indiana) and contactless laser registration of the face was performed using a preoperative CT scan with contrast as a reference scan (Fig. 3a). Excellent registration accuracy was achieved. Of note, this patient's anterior fontanelle was open and her skull thickness at the trajectory entry points was one to two millimeters. Ten PMT SEEG electrodes (PMT Corporation, Chanhassen, Minnesota) were placed in the left frontal and temporal lobes. Six distinct candidate tubers were monitored. As in other SEEG cases, a strategy was employed to minimize the number of electrodes while monitoring as many areas of interest as possible. This included monitoring the edges of more than one tuber with the same electrode in some cases. PMT bolts were secured into the skull, approximately 1–2 mm deeper than the inner table of the skull. Xeroform gauze was wrapped around each bolt, and gauze padding was placed around them under a headwrap (Fig. 3b). Rescue bolts were available but did not prove necessary, as the standard bolts were holding, especially with the Xeroform wrap and padded headwrap.

Postoperative CT for quality assurance confirmed accurate placement with a mean target point error of 0.81 mm and a maximum error of 1.68 mm. These error measurements are made by using a cross-sectional view on the planning software of the merged post-operative CT with the pre-operative plan. The

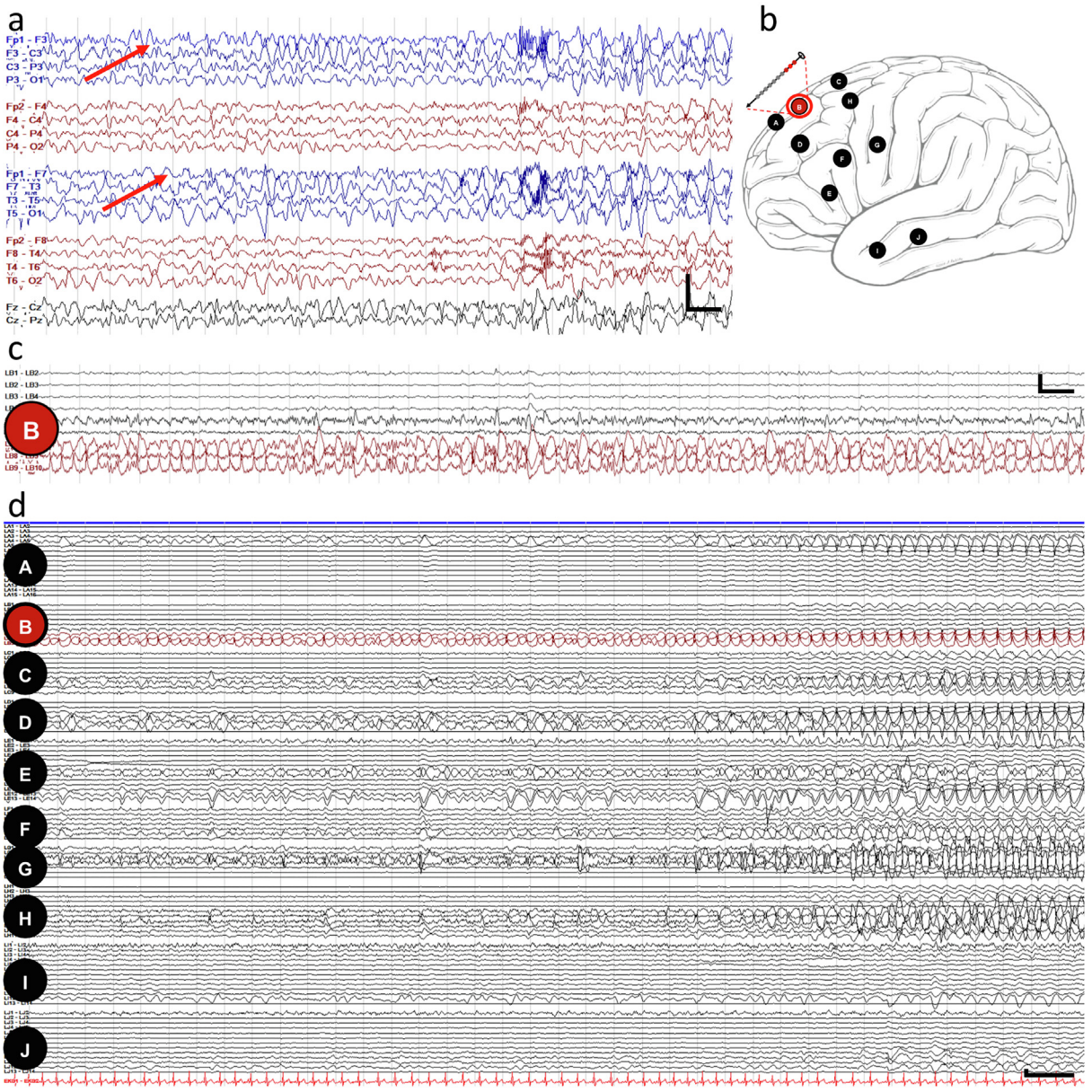

Fig. 2. An example of left frontal (F3/F7 maximal) seizure onset on scalp EEG captured during phase 1 presurgical evaluation (a). Electrode placement plan diagram for intracranial phase 2 SEEG with the superficial contacts (contacts 8–10) of the electrode in the middle superior frontal gyrus (labeled B) highlighted in red and additional electrodes labeled A and C-J in the approximate locations indicated (b). Near-continuous interictal epileptiform discharges were seen in the superficial contacts (8–10, highlighted in red) of the middle superior frontal gyrus (B) electrodes (c). An example of seizure onset captured during the intracranial phase 2 SEEG arising from the superficial middle superior frontal gyrus (B8-10– highlighted in red) with spread to other electrodes and evolution in amplitude and frequency (d). Scale bars for all panels: horizontal: 1 s; vertical: 200uV. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

distance between the planned target and the center of the electrode is recorded (Fig. 3c).

SEEG was very well tolerated, and the patient demonstrated minimal discomfort. Digital 128-channel XLTEK video-EEG system (Natus Biomedical, San Carlos, CA) was used for recording. Over the next three and a half days, SEEG captured 80 of her typical seizures, all localized to an EZ around a tuber in the left dorsolateral frontal region. The first change occurred in B9 on the posterior edge of a left frontal tuber, and this was followed by the superficial A electrode through the anterior edge of the same tuber. Further, she exhibited interictal discharges which were at times nearly continuous, maximal at the same electrode contact as the ictal onset, typical of TS patients (Fig. 2c). On the fourth post-operative day, she underwent removal of electrodes and a stereotactic craniotomy to remove the tuber identified by SEEG with a minimal rim of perituberal cortex (Fig. 4). Seizures stopped immediately, and she was discharged from the hospital four days after resection.

Follow-up

Postoperatively, the patient experienced complete remission from her seizures. Serial EEGs during the postoperative period showed fewer left frontal sharp waves. At her six-month postoperative visit, she remained seizure-free and had made significant developmental progress including using her right hand again, and for the first time, clapping, crawling, and attempting pull-to-stand. From a language perspective, additional new milestones at

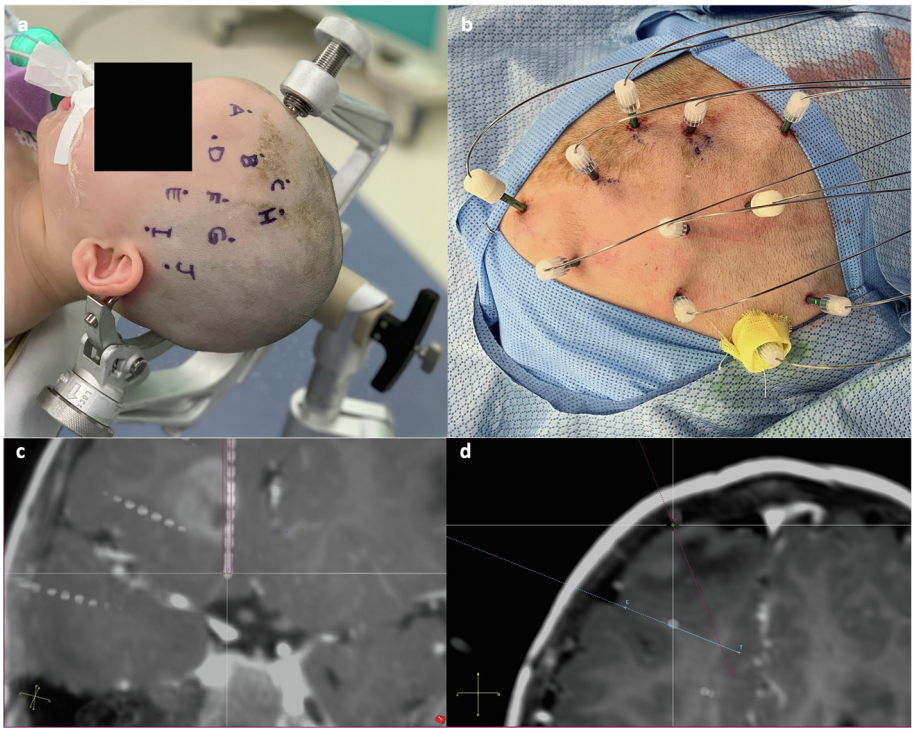

Fig. 3. Patient positioned in the Mayfield frame and attached to the robot (a). SEEG bolts secured to the skull (b). One bolt has been wrapped with the xeroform gauze. One bolt and electrode are placed in the skull to be used for ground and reference, resulting in 11 pictured electrodes. Screenshot from the robotic planning software of T1 post-contrast MRI fused with post-SEEG CT demonstrating the proximity of the longest electrode to its pre-operative plan. Also seen is a nearby electrode monitoring an interface between the enhancing SEGA and cortex and a temporal electrode monitoring an anterior temporal tuber (c). Axial screenshot demonstrating the proximity of the B electrode (blue) and the A electrode (red) and their relationships to the resected tuber (d). For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.

6-month follow-up included babbling more, using three words, and an interest in books.

Discussion

SEEG has generally been avoided in the very young. Among series of SEEG involving pediatric patients, the overall reported age range has been 20 months to 69 years [1,4–8,10–16,18–21]. Five groups have included patients under three years old, and four groups under two years old, with the youngest patient reported being 20 months old, three months older than our patient [8,11,18,19]. In a recent large survey of 61 pediatric epilepsy neurosurgeons in the United States, only 31% of respondents had operated on patients under 3 years of age [17]. This survey also found that higher volume centers were more likely to have performed SEEG on younger patients.

The concern in the application of SEEG to very young patients centers around the immature skull. Skull fracture leading to intracranial bleeding and deformation of the skull leading to inaccurate registration and/or electrode placement are among the most salient of these concerns. As a result, bone thickness and sutural fusion have been identified as the primary variables affecting the feasibility of SEEG in this population [3,6,8,22,23]. Concern has also been raised regarding the security of the electrode bolts in thin skull post-operatively. Pediatric epilepsy neurosurgeons have reported a variety of techniques to avoid use of bolt fixation [17,21].

For this patient, SEEG was specifically recommended due to the existence of medial frontal tubers and the interface between the

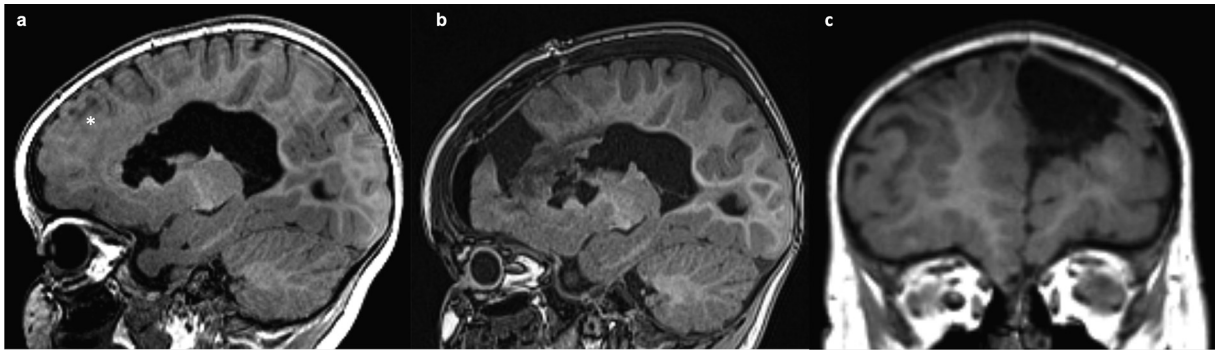

Fig. 4. Preoperative Sagittal T1 MRI demonstrating the left-sided tuber (*) identified as the source of the patient's seizures (a). Postoperative Sagittal T1 MRI demonstrating resection of the left-sided lesion (b). Postoperative coronal T1 MRI demonstrating resection of the left-sided lesion (c).

SEGA and depths of sulci. Alternative invasive monitoring with SDG would have required a large craniotomy, risking the potential morbidities associated with grids, a potential failure to accurately detect deep EZs, patient discomfort, and importantly, in the setting of being at high risk for needing future invasive monitoring or resection, avoiding grids avoids creating subdural scarring that can cause brain injury during repeat grid placement or resection. Her heavy bilateral tuber burden was actually worse on the right side, despite the left-sided seizures, and this made frontal lobectomy or hemispherotomy unreasonable, due to diminished cognitive capacity of the contralateral side, the near certainty of epilepsy recurrence, and the distinct possibility of requiring further epilepsy surgery in the future. For these reasons, SEEG was performed for precise and accurate localization of the active epileptogenic focus prior to resection.

There were several technical factors that contributed to safe and successful registration, as well as accurate electrode placement, despite this patient's age, thin bone, and open fontanelle. Pin locations were chosen to be structurally sturdy, i.e. mastoid, occipital bone, and superior temporal line. Pediatric-style pins were used to prevent plunging of the pin through the thin bone, and to add surface area to the pin to increase pressure without increasing pin depth. Only 40 lbs/sq in were used and slowly applied, with care taken to avoid depressing the skull, and after fixation, to avoid the head migrating in the pins during preparation, draping, and surgery with this relatively low pressure. Further, her bolts were secured in the 1–2 mm skull without incident, intraoperatively or postoperatively, and with excellent accuracy.

Her electrode placement accuracy was excellent, with a mean target point error in line with previous reports [2,7,24,25]. Importantly, the accurate electrode placement in this case demonstrates the feasibility of accurate, safe electrode placement for someone of this age, and with very thin bone and an open fontanelle. She experienced an excellent surgical outcome, with complete resolution of her seizures and significant functional and developmental progression at her six-month postoperative visit. This highlights that the electrodes as placed did indeed accomplish their intended purpose, to accurately identify the offending tuber in a very young girl with a heavy tuber burden and several candidate EZs based on MRI and EEG.

There are limitations to the conclusions that can be reached by this experience. This is a single case report with limited follow-up. All patients are anatomically different, and every patient's epilepsy is unique. There are a variety of stereotactic methods and electrode manufacturers, so generalizability to other patients and other equipment is limited.

Conclusion

Debate continues over the lower age limit for SEEG, with most major centers not operating on children younger than age three due to concerns about safety and accuracy, and no reports of children younger than 20 months of age. This case demonstrates that with minimal modification of technique, robotic SEEG with Mayfield headholder, bolt-based electrode fixation, and facial registration surery can be safely and accurately performed in very young children with thin skulls and open fontanelles with excellent results. Further research with larger patient series is necessary to better delineate patient characteristics and technical nuances that contribute to the lower age limit for safely using SEEG.

Author contributions

Katz – Manuscript and figure preparation and review.

Armstrong – Manuscript review and figure preparation. EEG and SEEG tracing analysis.

Kvint – Manuscript review. Performed procedure on patient.

Kennedy – Manuscript and figure preparation and review. Performed procedure on patient.

Ethical statement

Written informed consent was obtained from the patient's parent/legal guardian for publication of this case report and any accompanying images. No ethics committee review was necessary.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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