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RESEARCH REPORT

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# Feasibility of awake craniotomy in the pediatric population

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## Abstract

**Background:** Awake craniotomy with direct cortical stimulation and mapping is the gold standard for resection of lesions near eloquent brain areas, as it can maximize the extent of resection while minimizing the risk of neurological damage. In contrast to the adult population, only small series of awake craniotomies have been reported in children.

**Aims:** The aim of our study is to establish the feasibility of awake craniotomy in the pediatric population.

**Methods:** We performed a retrospective observational study of children undergoing a supratentorial awake craniotomy between January 2009 and April 2019 in a pediatric tertiary care center. Our primary outcome was feasibility of awake craniotomy, defined as the ability to complete the procedure without conversion to general anesthesia. Our secondary outcomes were the incidence of serious intraoperative complications and the mapping completion rate.

**Results:** Thirty procedures were performed in 28 children: 12 females and 16 males. The median age was 14 years (range 7-17). The primary diagnosis was tumor (83.3%), epilepsy (13.3%), and arterio-venous malformation (3.3%). The anesthetic techniques were asleep-awake-asleep (96.7%) and conscious sedation (3.3%), all cases supplemented with scalp block and pin-site infiltration. Awake craniotomy was feasible in 29 cases (96.7%), one patient converted to general anesthesia due to agitation. Serious complications occurred in six patients: agitation (6.7%), seizures (3.3%), increased intracranial pressure (3.3%), respiratory depression (3.3%), and bradycardia (3.3%). All complications were quickly resolved and without major consequences. Cortical mapping was completed in 96.6% cases. New neurological deficits occurred in six patients (20%)—moderate in one case and mild in 5—being all absent at 6 months of follow-up.

**Conclusion:** Awake craniotomy with intraoperative mapping can be successfully performed in children. Adequate patient selection and close cooperation between neurosurgeons, anesthesiologists, neuropsychologists, and neurophysiologists is paramount. Further studies are needed to determine the best anesthetic technique in this population group.

Presentation: Preliminary data from this study were presented as a poster presentation at the Euroanaesthesia meeting, June 2-4, 2018, Copenhagen.

  

**KEYWORDS**
brain mapping, children, craniotomy, neuroanesthesia, neurosurgery

## 1 | INTRODUCTION

Awake craniotomy is a well-established surgical technique for the resection of pathological lesions located near the eloquent brain cortex, that is, those specific cortical areas that directly control function and that could cause a major focal neurological deficit if damaged or removed. Due to the inter-individual variability in the organization of the cortex and the potential distortion from the tumor mass effect, classic anatomical criteria may be inaccurate for the prediction of brain function.[1] Consequently, cortical mapping via direct stimulation while the patient is awake is the gold standard for delineating boundaries of eloquent cortex,[2] allowing a patient-tailored approach that maximizes the extent of resection while minimizing the risk of neurological damage.[3] In order to map the brain, the patient must be able to communicate, and a great degree of understanding and cooperation is required.[4] Moreover, complications like agitation, restlessness, or somnolence pose a real danger in the context of open brain surgery. Therefore, the role of anesthesiologists is paramount, and a careful anesthetic plan is essential to ensure maximal safety and comfort, with minimal use of drugs or techniques that could alter the functional monitoring.[5]

Beyond the highly specific management of awake craniotomy per se, its performance in children poses an additional challenge due to their differences in cognitive development and maturity. The developing brain presents anatomical and functional peculiarities that influence the sensitivity of the cortical mapping, limiting the practice of awake craniotomy.[6] Moreover, only 30%-40% of brain tumors in childhood are supratentorial, and they are most frequently diagnosed in the first 2 years of life, where awake craniotomy is not viable.[7] Besides, ethical concerns regarding negative psychological experience and possible emotional distress have also been raised.[8] Due to these limitations, only small series of awake craniotomy have been conducted in children,[8-10] in contrast to the larger cohorts within the adult population.[3,11] Similarly, data about the anesthetic technique are very scarce in the literature and frequently limited to case reports.[12-15] Consequently, the anesthetic management of awake craniotomy in children is often inferred from adult practice.[16]

The aim of our study is to establish the feasibility of awake craniotomy in the pediatric population, our main hypothesis being that awake craniotomy is feasible in children.

### What is already known about the topic

- Awake craniotomy with direct cortical stimulation and mapping is the gold standard surgical technique for the resection of pathological lesions located near eloquent cortex. However, its performance in children is heavily limited by their differences in cognitive development and maturity, and in some cases, by ethical concerns. Due to these limitations, only small series of awake craniotomy have been conducted in children and numerous hesitations exist regarding feasibility, safety, and anesthetic management of awake craniotomy in the pediatric population.

### What new information this study adds

- After a retrospective analysis of the cases performed at our institution between 2009 and 2019, we have found that awake craniotomy could be completed without conversion to general anesthesia in 96.7% cases and devoid from serious complications in 80% cases. All complications, however, were quickly solved and without major consequences. Therefore, we conclude that awake craniotomy in children is feasible. Moreover, we provide a comprehensive description of the anesthetic management of awake craniotomy in this population group.

## 2 | MATERIALS AND METHODS

Institutional ethics review board approval was obtained, and the requirement of informed consent was waived before data collection (SickKids REB#1000041548, November 2017). We performed a retrospective single-center observational study evaluating the feasibility, complications, and anesthetic management of awake craniotomy in the pediatric population. Inclusion criteria were patients under 18 years undergoing awake craniotomy for resection of supratentorial brain lesions at our institution from January 2009 to April 2019. Patients with incomplete data were excluded.

In our center, awake craniotomy constitutes the mainstay approach for the resection of lesions near eloquent brain areas. Whenever a child is identified by neurosurgery as amenable to awake craniotomy, the appropriateness of the technique should be determined based upon the child's maturity and cognitive abilities. Therefore, an assessment by a neuropsychologist is performed, including evaluation of intellectual abilities (intellectual quotient), visual-motor, visual-spatial, language and memory skills, manual dexterities, academic capabilities, and executive function. Since the main goal is to preserve the eloquent cortex, a special focus is placed on the language test.

Anesthesiologists play a crucial role in the preoperative work-up for awake craniotomy. A detailed preoperative evaluation is mandatory, focusing on neurological deficits and presenting symptoms. Meticulous airway assessment is vital, since a difficult airway could contraindicate the technique given the suboptimal access to the airway due to the surgical head fixation. In addition, preanesthetic consultation is essential to build rapport and

trust with the child and the family. Detailed information about the stages of the surgery, tasks involved, and potential complications should be provided, and adequate comprehension and acceptance must be ensured. We typically use pictures and videos to provide a more realistic explanation.

At our center, awake craniotomy is performed under an asleep-awake-asleep approach. Initially, surgical access is achieved under general anesthesia. The child is then awoken and brain mapping ensues prior to, and during resection of the lesion. Once resection is complete, general anesthesia is resumed for surgical closure. Anesthetic monitoring is applied according to the ASA standards: 5-lead electrocardiogram, oxygen saturation, capnography, and continuous invasive blood pressure. Depth of anesthesia is monitored using a three-channel electroencephalography. In addition, all patients undergo continuous monitoring of somatosensory and motor evoked potentials.

Induction of general anesthesia is typically intravenous. Placement of an intravenous catheter is usually well tolerated with topical anesthetic cream (Eutectic mixture of local anesthetic, EMLA®), although sevoflurane and/or nitrous oxide are occasionally required for cannulation. Antibiotic prophylaxis and nonsedating anti-emetic prophylaxis are also given at induction. For airway management, a laryngeal mask airway is the preferred choice as it can be easily removed or introduced in the awkward neck flexion positioning required for surgery. Once the patient is under general anesthesia, an additional large-bore catheter, an arterial line, and a urinary catheter lubricated with 2% lidocaine are inserted. The patient is then turned to a semi-lateral position. Meticulous positioning and padding minimize discomfort during the awake stage, and warming devices are useful to avoid shivering that could compromise the microscopical resection of the lesion. Surgical drapes are arranged in an "open-tent fashion," leaving the patient's face uncovered facing the anesthesiologist. This reduces claustrophobia and anxiety, allows direct eye contact and communication, and, most importantly, enables a direct access to the face and airway.

Prior to incision, scalp blocks are performed. We use a 25G needle to infiltrate 0.25% bupivacaine with epinephrine 1:200 000, which can last up to 8-10 hours. The main nerves blocked are supratrochlear, supraorbital, zygomaticotemporal, auriculotemporal, lesser and greater occipital, greater auricular, and third occipital. The block is supplemented with pin-site infiltration for the head frame. Maintenance of anesthesia is conducted with total intravenous technique titrated to depth of anesthesia via electroencephalography.

When the craniotomy is complete and the dura is being opened, the anesthetic drugs are slowly weaned. Subsequently, primary motor cortex and central sulcus mapping are achieved via high-frequency train-of-five, anodal stimulation, and phase reversals, respectively. Once this preliminary mapping is completed, propofol and remifentanil are stopped and a "no-touch" technique is used for extubation, that is, the laryngeal mask is removed only when the patient spontaneously wakes up and effective spontaneous respiration is ensured, and without any kind of stimulation during emergence. Therefore, a calm environment is mandatory to prevent coughing or bucking. Once the laryngeal mask has been removed, supplemental oxygen is provided via face mask or nasal prongs.

At this stage, the awake phase begins, during which the brain is mapped to identify a speech arrest. Mapping is performed by applying direct cortical bipolar stimulation with 100 microsecond pulse width at a frequency of 60 hertz. Stimulation intensity begins at 3 milliAmps and is increased in a stepwise manner by 3 milliAmps up to a maximum of 18 milliAmps. The assistance of a neuropsychologist is of utmost importance for the mapping, which is tailored to the patient's age and language skills. The test consists of varied tasks, such as pictorial cue cards, counting, and memory games. Motor monitoring is accomplished with the patient moving specific limbs as instructed. Any alteration of speech or motor function by stimulation must be immediately communicated to the surgical team, while mapped regions that do not produce speech or motor arrest are safe for resection. Pain scores are frequently obtained using a Numerical Pain Rating Scale to ensure patient's comfort and, in case of residual pain or discomfort, the infusions can be restarted at low doses.

Upon completion of surgical resection, general anesthesia is re-induced and a new laryngeal mask is placed. A long-acting opioid can be added for postoperative pain control. Occasionally, the procedure can continue without general anesthesia, with the patient under sedation and spontaneous ventilation. Once the procedure is finished, patients emerge from anesthesia in the operating room. They are routinely admitted to intensive care unit and discharged to the ward on the following day unless any complication occurs.

## 2.1 | Data collection

All children who underwent a supratentorial awake craniotomy during the study window were identified using the Surgical Information System database. Two anesthesiologists (G.A. and G.E) independently retrieved data from the electronic medical records (SickKids patient records, KidCare®). A senior anesthesiologist (T.D) verified the collected data to ensure accuracy.

Demographic information included date of birth, weight, and sex. Clinical data included presenting symptoms, lesion location, and pathology. Intraoperative data comprised neurophysiological monitoring, type of mapping, mapping completion rate, and complications. Data related to anesthetic management included anesthetic technique, drugs and doses administered, and airway device. For cases under asleep-awake-asleep, we recorded the time to awake, defined as the appearance of low amplitude, irregular alpha (8-12 hertz) and beta (>12 hertz) fast activity on the electroencephalography, as well as time to follow commands after stopping the infusions. Surgical data included extension of resection and postoperative complications.

## 2.2 | Outcome measures

The primary outcome was feasibility of awake craniotomy, defined as the ability to complete the procedure without conversion

to general anesthesia. The secondary outcomes were the incidence of serious or life-threatening intraoperative complications and the success of the cortical mapping, defined as the ability complete it. Complications considered serious were those that could lead to a fatal event or major sequelae without any intervention from the anesthesiologist. These were defined prior to data collection based on previous reports of awake craniotomy both from the pediatric[10,14,15,17] and the adult[11,16] population, and included seizures, increased intracranial pressure (presence of "tight brain" as indicated by the neurosurgeon), respiratory depression (oxygen saturation below 90% and/or respiratory rate below 8 rpm), airway obstruction (blockage in any part of the airway with or without oxygen saturation below 90%), bradycardia (heart rate below 60 lpm), vomiting, or severe agitation. Mild complications included moderate pain (numeric pain scale score ≥ 6) or and systolic hypertension above 20% of baseline. The incidence of new neurological deficits after surgery was also evaluated.

### 2.3 | Statistical analysis

Continuous variables with normal distribution are described with mean and standard deviation values. Non-normally distributed variables are described with median and range. Categorical variables are described as proportions.

## 3 | RESULTS

Thirty procedures were performed in 28 children: 12 females and 16 males. Two children underwent two awake craniotomies. No patients were excluded. Median age was 14 years (range 7-17), and median weight was 54.6 kg (range 20.7-78.7) (Table 1).

### 3.1 | Clinical data

The surgical indication was tumor (83.3%), epilepsy (13.3%), or arterio-venous malformation (3.3%). The main presenting symptoms were seizures (80%), headache (23.3%), neurological deficit (20%), vomiting (3.3%), and papilledema (3.3%). Four patients (13.3%) were asymptomatic.

The lesion was most frequently left-sided (70%). The specific location was frontal (50%), temporal (36.7%), and parietal (13.3%). Preoperative work-up with functional imaging was performed in 23 cases (76.7%).

From the 25 patients undergoing tumor surgery, gross total resection was accomplished in 64% cases and subtotal in 36%. The median procedure time (anesthesia and surgical time) was 288 minutes (range 205-560). The median length of intensive care unit and hospital stay was 1 day (range 1-2) and 3 days (range 2-17), respectively.

### 3.2 | Neurophysiological data

Cortical mapping was attempted in 29 cases (96.7%): Nine patients had speech mapping, 6 had motor mapping, and 14 had both. From these, mapping was successfully completed in 28 cases (96.6%), being incomplete in 1 case because of poor cooperation. During mapping, 8 patients had speech arrest, with consequent subtotal resection in 5 of them so as to preserve language.

### 3.3 | Anesthetic management

The anesthetic approach was asleep-awake-asleep in 29 cases (96.7%), while one patient was managed entirely under conscious sedation. Awake craniotomy was feasible in 29 cases (96.7%), conversion being required in 1 patient due to severe agitation.

For patients under an asleep-awake-asleep approach, induction was intravenous, although 5 patients (17.2%) required sevoflurane and 6 (20.7%) required nitrous oxide for intravenous cannulation. Once the intravenous access was accomplished, propofol was used for induction in all cases, combined with an opioid—fentanyl or remifentanil—in 25 cases. Dosages are shown in Table 2.

For the first asleep phase, a combination of propofol and remifentanil infusions was always used. Additionally, two patients received dexmedetomidine. During the awake phase, 17 patients (58.6%) received a remifentanil infusion, either alone (51.7%) or combined with a propofol infusion (6.9%). Among the rest, 8 patients (27.6%) did not receive any anesthetic agent, 3 (10.3%) were managed with fentanyl boluses, and 1 (3.4%) received a dexmedetomidine infusion.

Upon completion of the awake phase, general anesthesia was re-induced in 21 cases (72.4%), while 8 (27.6%) remained under sedation. General anesthesia was induced with propofol, alone in 17 cases and combined with fentanyl in 4 cases, and maintenance was based on a combination of propofol and remifentanil, with addition of dexmedetomidine in 1 patient. Regarding patients remaining under sedation, 5 received a combination of propofol and remifentanil, 2 received remifentanil alone, and 1 received propofol alone. Drug combinations are shown in Figure 1.

Aside from the asleep-awake-asleep group, one patient was managed under conscious sedation for the entire procedure, with a combination of propofol (75-150 μg/kg/min), remifentanil (0.01-0.04 μg/kg/min), and dexmedetomidine (0.2-0.5 μg/kg/min).

Long-acting opioids were provided in 10 cases (33.3%): morphine in eight patients and hydromorphone in 2, with a mean ± STD dose of 64.9 ± 22.9 μg/kg and 10 ± 0 μg/kg, respectively.

In the asleep-awake-asleep group, the median (IQR) times to awake and to follow commands after stopping the infusions were 13 (10 to 21) and 21 (14 to 30) minutes, respectively. This wake-up time was longer among the two patients receiving additional dexmedetomidine versus the 27 patients who did not: 32 minutes (26 to 38) vs 12 minutes (9-20), respectively.

The mean ± STD duration of the awake phase was 67.9 ± 39.5 minutes.

**TABLE 1** Demographic and clinical data

| Patient ID# | Sex | Age (y) | Weight (kg) | Handedness | Presenting symptoms | Diagnosis | Lesion side | Lesion location | Pathology |
|---|---|---|---|---|---|---|---|---|---|
| 1 | F | 16 | 58.4 | R | Seizures | Tumor | L | Frontal | Anaplastic Astrocytoma |
| 2 | M | 17 | 77.7 | R | Seizures | Tumor | L | Frontal | Low-Grade Glioma |
| 3 | F | 15 | 48.5 | R | Seizures, Headache | Tumor | L | Frontal | Recurrent Glioblastoma |
| 4 | M | 17 | 78.7 | L | Seizures | Tumor | L | Frontal | Ganglioglioma |
| 5 | M | 14 | 52.9 | R | Seizures | Tumor | R | Parietal | Dysembryoplastic Neuroepithelial Tumor |
| 6 | F | 17 | 72.6 | R | Seizures | Tumor | R | Parietal | Pleomorphic Xanthoastrocytoma |
| 7 | M | 13 | 64.2 | L | Seizures | Epilepsy | L | Temporal | Gliosis with Microcalcification |
| 8 | M | 14 | 68.0 | R | Seizures | Epilepsy | L | Temporal | Neocortex |
| 9 | M | 17 | 58.5 | R | Seizures | Tumor | R | Parietal | Low-Grade Glioma |
| 10 | F | 11 | 40.0 | L | Seizures, Dysphasia, Headache | Tumor | R | Temporal | Residual Ganglioglioma |
| 11 | F | 16 | 67.5 | R | Seizures | Epilepsy | L | Frontal | Gliosis |
| 12 | M | 11 | 67.5 | R | Seizures | Tumor | L | Frontal | Anaplastic Astrocytoma |
| 13 | F | 13 | 47.0 | L | Seizures, Dysphasia, Headache | Tumor | R | Temporal | Recurrent Ganglioglioma |
| 14 | M | 11 | 38.8 | R | Headache | Tumor | L | Frontal | Inconclusive |
| 15 | F | 13 | 55.7 | R | Seizures | Tumor | R | Frontal | Residual Ependymoma |
| 16 | M | 12 | 39.0 | R | Aphasia, Seizures | Tumor | L | Frontal | Gangliglioma |
| 17 | M | 7 | 20.7 | R | Seizures, Hand Weakness and Tingling, Headache | Tumor | L | Frontal | Ependymoma |
| 18 | M | 15 | 68.0 | R | Seizures | Epilepsy | L | Frontal | Gliosis |
| 19 | M | 10 | 29.8 | R | Seizures | Tumor | L | Temporal | Diffuse Glioma |
| 17 | M | 8 | 23.4 | R | Asymptomatic (Imaging Recurrence) | Tumor | L | Frontal | Recurrent Ependymoma |
| 20 | M | 15 | 77.2 | R | Seizures | Tumor | L | Temporal | Diffuse Astrocytoma |
| 15 | F | 15 | 58.0 | R | Asymptomatic (Imaging Recurrence) | Tumor | R | Frontal | Recurrent Ependymoma |
| 21 | M | 12 | 65.5 | R | Seizures | Tumor | L | Parietal | Low-Grade Glioma |
| 22 | F | 10 | 45.8 | R | Seizures | Tumor | L | Temporal | Oligodendroglioma |
| 23 | M | 15 | 47.8 | R | Dysphasia, Headache, Vomiting | Arterio-Venous Malformation | L | Temporal | Arterio-Venous Malformation |

(Continues)

TABLE 1 (Continued)

| Patient ID# | Sex | Age (y) | Weight (kg) | Handedness | Presenting symptoms | Diagnosis | Lesion side | Lesion location | Pathology |
|---|---|---|---|---|---|---|---|---|---|
| 24 | F | 16 | 53.5 | L | Incidental Finding (Volunteer for MRI) | Tumor | R | Frontal | Oligodendroglioma |
| 25 | F | 12 | 52.9 | R | Seizures | Tumor | L | Temporal | Low-Grade Glioma |
| 26 | F | 12 | 44.7 | L | Seizures, Headache, Papilledema | Tumor | L | Temporal | Astrocytoma |
| 27 | M | 14 | 44 | L | Incidental Finding (Family History) | Tumor | R | Temporal | Pleomorphic Xanthoastrocytoma |
| 28 | F | 7 | 20.5 | R | Seizures, Aphasia | Tumor | L | Parietal | Dysembryoplastic Neuroepithelial Tumor |

### 3.4 | Airway management

A laryngeal mask was the airway device of choice during the first asleep phase in all patients under an asleep-awake-asleep approach. Once awake, supplementary oxygen was provided via nasal prongs (86.2%) or face mask (13.8%). For the second asleep phase, all patients under general anesthesia had a new laryngeal mask inserted, while those remaining under sedation were oxygenated with nasal prongs. Emergent endotracheal intubation was not required for any of the patients remaining under sedation.

### 3.5 | Complications

Awake craniotomy was devoid of serious complications in 24 cases (80%). Serious complications included agitation (6.7%), seizures (3.3%), increased intracranial pressure (3.3%), respiratory depression requiring naloxone (3.3%), and bradycardia (3.3%) (Figure 2). Each of these occurred in a different patient, and none of them experienced more than one serious complication. No association was detected between the age or diagnosis and the development of serious complications. All complications were solved quickly and without major consequences. For agitation, a 1 mg/kg propofol bolus was administered in one of the patients, while the other required conversion to general anesthesia. This was accomplished with administration of sevoflurane up to 2 MAC and a 2 mg/kg propofol bolus, followed by insertion of a laryngeal mask; no further attempts of awaking the patient were made until the procedure was completely finished. On the other hand, seizures ceased after irrigation of the cortex with cold saline and high intracranial pressure was treated with intravenous mannitol at a dose of 0.5 g/kg. Mild complications happened in 6 patients (20%). Moderate pain was the main issue, occurring in all these 6 patients (20%), and accompanied by systolic hypertension in 4 of them (13.3%). There were no cases of isolated systolic hypertension. Pain was treated with fentanyl boluses or an increase in the remifentanil infusion, while systolic hypertension was managed with boluses of hydralazine. No other mild complications were detected.

New neurological deficits occurred in 6 patients (20%): Two patients experienced mild aphasia, 2 had mild peripheral sensory deficits, 1 had hemiparesis, and 1 had ataxia. Deficits were detected postoperatively and were all transient, with complete resolution at 6 months of follow-up. Surgical complications included wound dehiscence in 1 patient and extradural collection in 1 patient.

## 4 | DISCUSSION

This study presents a detailed description of the anesthetic management of pediatric patients undergoing awake craniotomy. Our main findings are that awake craniotomy was feasible in 96.7% cases and devoid of serious complications in 80% cases. Cortical mapping was

**TABLE 2** Percentage of patients and mean drug dosages in the different anesthetic stages

| Anesthetic stage | N (%)[a] | Dose (Mean ± STD) |
|---|---|---|
| Asleep 1 | | |
| Induction 1 | | |
| Propofol Bolus | 29 (100) | 3.4 ± 1.8 mg/kg |
| Fentanyl Bolus | 23 (79.3) | 1.3 ± 0.8 μg/kg |
| Remifentanil Bolus | 2 (6.9) | 1.1 ± 0.6 μg/kg |
| Maintenance 1 | | |
| Propofol Infusion | 29 (100) | Mean 126.2 ± 25.6 μg/kg/min<br>Min 96.2 ± 24.8 μg/kg/min<br>Max 156.2 ± 37.6 μg/kg/min |
| Remifentanil Infusion | 29 (100) | Mean 0.16 ± 0.08 μg/kg/min<br>Min 0.09 ± 0.06 μg/kg/min<br>Max 0.2 ± 0.1 μg/kg/min |
| Dexmedetomidine Infusion | 2 (6.9) | 1.7 ± 0.4 μg/kg/h |
| Awake | | |
| Remifentanil Infusion | 15 (51.7) | Mean 0.06 ± 0.03 μg/kg/min<br>Min 0.04 ± 0.02 μg/kg/min<br>Max 0.07 ± 0.04 μg/kg/min |
| Remifentanil + Propofol Infusion | 2 (6.9) | Remifentanil<br>Mean 0.04 ± 0.004 μg/kg/min<br>Min 0.02 ± 0.01 μg/kg/min<br>Max 0.06 ± 0.007 μg/kg/min<br>Propofol<br>Mean 21.3 ± 5.3 μg/kg/min<br>Min 17.5 ± 10.6 μg/kg/min<br>Max 25 μg/kg/min |
| Fentanyl Bolus | 3 (10.3) | 2 ± 1.7 μg/kg |
| Dexmedetomidine infusion | 1 (3.4) | 0.5 μg/kg/h |
| No Drugs | 8 (27.6) | |
| Asleep 2 | | |
| (a) General anesthesia | 21 (72.4) | |
| Induction 2 | | |
| Propofol Bolus | 21 (72.4) | 3.3 ± 1.1 mg/kg |
| Fentanyl Bolus | 4 (13.8) | 0.6 ± 0.4 μg/kg |
| Maintenance 2 | | |
| Remifentanil Infusion | 21 (72.4) | Mean 0.15 ± 0.07 μg/kg/min<br>Min 0.12 ± 0.06 μg/kg/min<br>Max 0.19 ± 0.09 μg/kg/min |
| Propofol Infusion | 21 (72.4) | Mean 107.5 ± 21.1 μg/kg/min<br>Min 95.2 ± 29.2 μg/kg/min<br>Max 119.8 ± 27.7 μg/kg/min |
| Dexmedetomidine Infusion | 1 (3.4) | 0.5 μg/kg/h |
| (b) Sedation | 8 (27.6) | |
| Remifentanil + Propofol Infusion | 5 (17.2) | Remifentanil<br>Mean 0.04 ± 0.01 μg/kg/min<br>Min 0.04 ± 0.01 μg/kg/min<br>Max 0.05 ± 0.01 μg/kg/min<br>Propofol<br>Mean 77 ± 52.5 μg/kg/min<br>Min 64 ± 49.8 μg/kg/min<br>Max 90 ± 67.5 μg/kg/min |
| Remifentanil infusion | 2 (6.9) | Mean 0.06 ± 0.05 μg/kg/min<br>Min 0.04 ± 0.02 μg/kg/min<br>Max 0.09 ± 0.07 μg/kg/min |
| Propofol infusion | 1 (3.4) | Mean 75 μg/kg/min<br>Min 50 μg/kg/min<br>Max 100 μg/kg/min |
| **Postoperative pain** | **N (%)[b]** | **Dose (Mean ± STD)** |
| Morphine | 8 (26.7) | 64.9 ± 22.9 μg/kg |
| Hydromorphone | 2 (6.7) | 10 μg/kg |
| Tylenol | 12 (40) | 15 mg/kg |
| **Adjuncts** | **N (%)[b]** | **Dose (Mean ± STD)** |
| Glycopyrrolate | 9 (30) | 3.3 ± 2.7 μg/kg |
| Ondansetron | 30 (100) | 0.1 mg/kg |
| Dexamethasone | 27 (90) | 0.1 mg/kg |

[a]Percentages are calculated with respect to the asleep-awake-asleep group (29 patients).

[b]Percentages are calculated with respect to the whole cohort (30 patients).

successfully completed in 96.6% cases. New postoperative neurological deficits occurred in 6 patients (20%), the majority being mild (80%), and all resolved by 6-month follow-up.

To our knowledge, this is the largest cohort of pediatric awake craniotomy. While awake craniotomy has been previously considered unfeasible in children under 10 years,[18] in our series awake craniotomy and mapping were successfully performed in two patients as young as 7 years old. Moreover, our rates of failure (3.3%) and unsuccessful mapping (3.4%) are comparable to those reported in the adult population: 2%[16] and 4.3%,[11] respectively. Serious complications occurred in 20% of the patients, yet they were all quickly resolved and without major consequences. In contrast to the adult population, where seizures are the most frequent complication,[16] agitation was the main issue in our cohort (6.7%). This probably reflects a lower degree of maturity inherent to childhood, highlighting the importance of an adequate patient selection and preparation among this population group.

With regard to the anesthetic management, asleep-awake-asleep was the approach of choice in our cohort. Both asleep-awake-asleep[8,10] and conscious sedation are present in the literature,[9,12,14] while none has demonstrated any superiority in children.

With respect to conscious sedation, many different drug combinations have been reported, including a neuroleptanalgesic technique, combining fentanyl or sufentanil with droperidol,[19] a propofol infusion, either alone[13] or combined with fentanyl,[14] and an infusion of dexmedetomidine.[12]

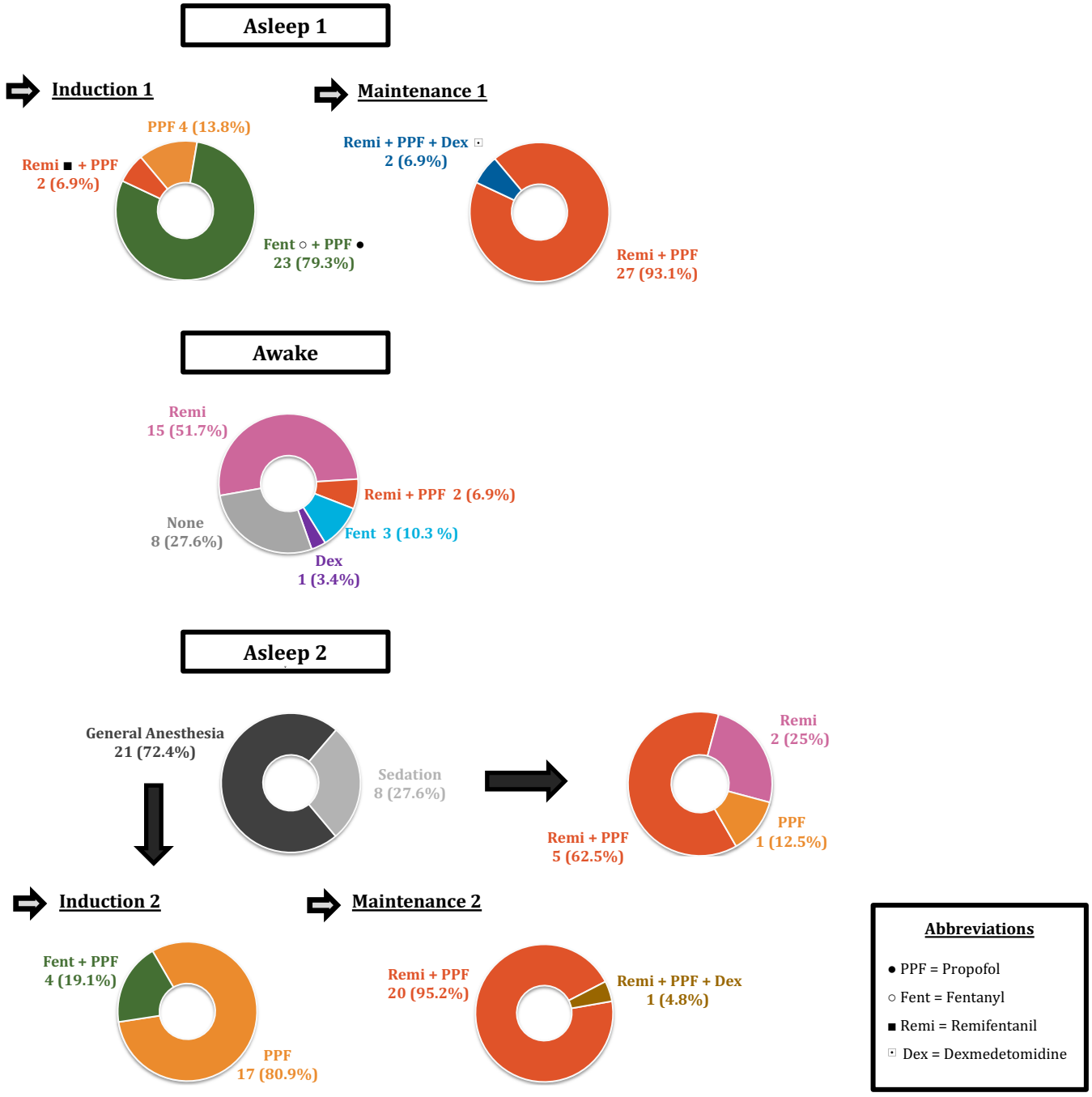


**FIGURE 1** Drug combinations within the asleep-awake-asleep group (29 patients). The number of patients on each group is expressed in n (%). Percentages are calculated with respect to the number of patients in each subgroup

From our experience, asleep-awake-asleep offers a stress-free procedure up to the point of functional testing and mapping, and controlled ventilation remains helpful should brain swelling became an issue. Focusing on the anesthetic drugs, premedication with benzodiazepines was avoided because of their potential lingering effect during cortical mapping. While some authors have opted for intraoperative reversal with flumazenil,[9] in our experience pharmacological anxiolysis was not required thanks to the high confidence and motivation of the patients. Muscle relaxants were also avoided to prevent residual weakness and interference with motor mapping.[20] Once general anesthesia was induced, sevoflurane was avoided for maintenance to decrease the likelihood of emergence delirium during the awake phase.[21] Instead, a combination of propofol and remifentanil was the regimen of choice. Propofol has a rapid onset and offset that allow a quick change on the depth of anesthesia, which is essential for awake craniotomies. Similarly, remifentanil is an ultra-short-acting opioid that can be easily titrated to effect and has a very short context-sensitive half-life (2-5 minutes) unaffected by the duration of the infusion. This makes it an ideal adjunct for rapid awakening and neuromonitoring, with little chance of respiratory depression after discontinuation.[15,22]

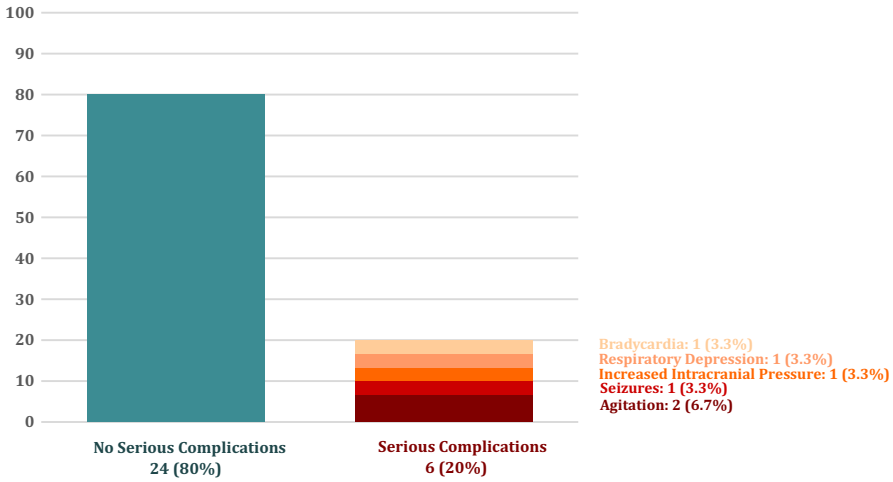


**FIGURE 2** Incidence of serious complications during awake craniotomy. Results are expressed in n (%)

The absence of pain is of utmost importance to ensure good cooperation during the awake phase, and therefore, regional anesthesia is the key for success.[23] However, despite an adequate block, patients often require opioids to alleviate residual discomfort, the safest alternative being small doses of a rapid-acting agent like fentanyl or remifentanil.[24] In our series, remifentanil was the opioid of choice, alone or combined with propofol. Many studies have demonstrated that remifentanil has no impact on electrocorticography recordings at doses up to 0.1 μg/kg/min,[25] which is consistent with our maximum doses during the awake phase (0.07 ± 0.04 μg/kg/min). Propofol has also shown not to influence mapping if it is suspended at least 15 minutes in advance.[14] In our series, electrophysiological studies were not started until patients were able to follow commands, which took a median of 21 minutes after stopping the infusions. This interval was wide enough to allow an adequate clearance of propofol. Dexmedetomidine has gained popularity for awake craniotomy due to its unique pharmacologic characteristics. It is a selective α-2 adrenoceptor agonist with central sympatholytic effects and without respiratory depression. As a result, patients are sedated but remain rousable and cooperative when stimulated.[26] In our center, the experience with dexmedetomidine in neuroanesthesia during the time of the study was very limited, and therefore, it was seldom used for awake craniotomy. Nevertheless, some authors have reported the successful use of dexmedetomidine for pediatric awake craniotomies with an asleep-awake-asleep approach.[15,17]

We did not specifically assess the psychological impact of the technique. However, there were no explicit complaints of emotional distress or posttraumatic disorder during postoperative follow-up. Moreover, the fact that two patients agreed to undergo to two procedures is quite reassuring in this regard.

Despite the paucity of reports on pediatric awake craniotomy, we believe this is a feasible and useful approach in select children, facilitating maximal resections with minimal morbidity. Moreover, it eliminates the need for an additional operation for extra-operative mapping. In our experience, adequate patient recruitment and extensive preoperative preparation is paramount, ensuring a high level of motivation and compliance with the technique. In addition, close cooperation and communication between team members is essential for a successful outcome.

### 4.1 | Limitations

This retrospective study is inherently subjected to information bias, despite our data coming from prospectively collected databases and standard anesthetic records. Besides, in the absence of a control group, the net impact of the specific anesthetic approach (asleep-awake-asleep versus conscious sedation) and drugs used remains difficult to ascertain.

## 5 | CONCLUSION

Awake craniotomy with intraoperative mapping can be successfully performed in children. Adequate patient selection and preparation, combined with close cooperation between neurosurgeons, neuropsychologists, neurophysiologists, and anesthesiologists, is the cornerstone of success. Further studies are needed to determine the best anesthetic approach and drug combinations for awake craniotomy in the pediatric population.

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### CONFLICTS OF INTEREST

The authors report no conflict of interest.

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