RESEARCH PAPER

Neurologia i Neurochirurgia Polska
Polish Journal of Neurology and Neurosurgery
2024, Volume 58, no. 3, pages: 292–299
DOI: 10.5603/pjnns.96409

ISSN: 0028-3843, e-ISSN: 1897-4260

This Research Paper is accompanied by Invited Editorial, see page 215

Middle temporal gyrus approach to mesial temporal lobe tumours in children

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ABSTRACT

Aim of the study. To assess whether the middle temporal gyrus (MTG) approach to mesial temporal lobe (MTL) tumours is an effective procedure for the treatment of epilepsy in children.

Clinical rationale for the study. MTL tumours are a common cause of drug-resistant epilepsy in children. There is as yet no consensus regarding their treatment. One possibility is resection via a MTG approach.

Material and methods. We assessed the medical records of patients treated at the Department of Neurosurgery, Children's Memorial Health Institute,Warsaw, Poland between 2002 and 2020. A prospectively maintained database including clinical, laboratory, and radiographic presentation, as well as pre- and post-operative course, was analysed. Patients with at least a one--year follow-up were included.

Results. There were 14 patients aged 4–18 years who underwent a MTG approach for a MTL tumour. All presented with epileptic seizure, and none had neurological deficit on admission to hospital. Median follow-up was 2.5 years. Neuronavigation was used to adjust the approach, localise the temporal horn, and achieve radical resection of the tumour and the hippocampus. Gross total resection was performed in all cases. In most patients, histopathological examination revealed ganglioglioma. One patient had transient aphasia. Two patients developed hemiparesis after surgery, which later improved. One of them also experienced visual disturbances. Acute complications were more frequent in younger patients ($p = 0.024$). In all cases, MRI confirmed complete resection and there was no tumour recurrence during the follow-up period. 13/14 patients remained seizure-free (Engel class I).

Conclusions and clinical implications. The MTG approach to MTL tumours is an effective procedure for the treatment of epilepsy in children. It avoids removal of the lateral temporal lobe and poses only a minor risk of permanent neurological complications.

Keywords: middle temporal gyrus, mesial temporal lobe, epilepsy surgery, seizure-free outcome, children

(*Neurol Neurochir Pol 2024; 58 (3): 292–299*)

Introduction

Mesial temporal lobe (MTL) tumours and developmental disorders of the cerebral cortex are the most common cause of drug-resistant epilepsy in children. They are usually benign in nature and slow growing, and can remain stable on neuroimaging studies over many years [1–3]. Histopathology often reveals ganglioglioma, pilocytic astrocytoma, or dysembryoplastic neuroepithelial tumour (DNT), which may be accompanied by abnormal cytoarchitectonics of the cerebral cortex. Most of them can be removed completely.

Temporal lobe epilepsy (TLE) is characterised by its typical clinical course. It is progressive in nature, and at some point

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Received: 27.07.2023 Accepted: 15.01.2024 Early publication date: 23.02.2024

becomes refractory to pharmacological treatment. Frequent seizures and the administration of antiepileptic drugs (AED) result in significant cognitive impairment including decreased intelligence quotient and impaired learning ability. In some patients, TLE can be controlled pharmacologically, but long-term seizure outcomes are better after surgery [4, 5].

Wilder Penfield is considered to be the pioneer in the surgical treatment of TLE. He proposed temporal lobectomy for patients with drug-resistant seizures [6]. The development of operative techniques has allowed the extent of resection to be limited. Selective procedures have therefore included a middle temporal gyrus (MTG) approach for resection of the hippocampus, and amygdalohippocampectomy via a transsylvian approach [7]. The MTG approach was introduced by Paulo Niemeyer in 1958 [8]. It provides a surgical corridor for removal of lesions located in the amygdala and posterior part of the hippocampus. The difficulty of this approach lies in removing the tumour *en masse*. It is rarely used due to the low incidence of tumours in the posterior hippocampus, and to the anatomical complexity of the mesiobasal region, notably the vicinity of the optic pathway [9, 10].

The goal of surgery for low grade tumours associated with TLE in adults is gross total resection (GTR), as this offers the possibility of a cure. In children, c.80–90% remain seizure-free, but there is no consensus regarding the extent and type of surgery, as the results of different approaches are comparable [11, 12]. Clinical decision-making is individualised and depends on the surgeon's experience and the location of the tumour.

The aim of this study was to present our experience in the surgical treatment of MTL tumours using the MTG approach in children.

Material and methods

This study was approved by the Institutional Review Board and adheres to ethical guidelines concerning human subjects. We performed a retrospective analysis of patients treated at the Children's Memorial Health Institute between 2002 and 2020. 116 consecutive patients with a tumour located in the hippocampus or the parahippocampal gyrus were screened for eligibility. Transsylvian approaches and temporal lobe resections were excluded.

Seizure reduction after treatment was assessed according to the Engel Epilepsy Surgery Outcome Scale [13]. Treatment outcomes were compared between patients whose first seizure occurred in early childhood, defined as up to the age of eight, and late childhood. This threshold was chosen because it corresponds to the reading learning age which allows for further education, and it is important for the patient's future independence and quality of life. A satisfactory outcome was defined as the presence of minor complications or rare disabling seizures (Engel class II). The best outcome was defined as seizure free-survival (Engel class I) with no complications.

The surgical approach to MTL tumours depends on their location (Fig. 1). A transsylvian approach is performed for tumours classified as Schramm type A, which are confined to the most medial aspect of the temporal lobe without involvement of the lateral occipitotemporal gyrus, and are usually seen in patients with a short duration of epilepsy. In Schramm type A tumours located in the posterior part of the hippocampus, the MTG approach is an option. When using this approach, it is highly beneficial to use neuronavigation to guide the trajectory to the temporal horn of the lateral ventricle, and to assess the extent of resection. Temporal lobe resection is useful for the treatment of tumours accompanied by cortical dysplasia in patients with a long duration of epilepsy. This approach is usually chosen for Schramm type C and D tumours.

Our strategy was to perform GTR of a benign MTL lesion with a limited growth pattern, as this is considered the optimal treatment. It increases the chances of seizure-free survival, and reduces seizure frequency over the long-term follow-up. If the risk of complications associated with GTR is too high, subtotal resection (STR) is considered. This usually applies to tumours that involve the temporal stem, the insula, and the basal ganglia i.e. Schramm type D tumours [10].

Patient positioning for a MTG approach is typical of temporal opening. No lumbar drainage is inserted. Craniotomy is performed after determining its size using neuronavigation. Medtronic optical navigation has always been used for MTL tumour resection. Hyperventilation is applied and mannitol is administered to improve intraoperative conditions. The approach and transcortical trajectory are adjusted using neuronavigation. The tumour is removed using microsurgical techniques, and the extent of resection is confirmed by neuronavigation.

Statistical analyses were performed using Statistica software (Version 13, StatSoft, Inc., Tulsa, OK, USA) and R programming. Quantitative data was reported as median with interquartile range (IQR) due to the small number of patients. Categorical data was presented as counts and frequencies. We compared continuous variables between two groups using a Mann-Whitney U test. The frequencies of categorical variables were compared using a two-sided Fisher's exact test. For all tests, $p < 0.05$ was deemed to be significant. The clustering analysis was performed in R studio (version 2022.07.1 + 554) using the *pheatmap* package.

Results

The study group consisted of 14 child patients (eight females, six males) with a median age of 11 years (IQR: 9–16) who underwent a MTG approach for MTL tumour resection. Five patients were older than 16 years at the time of surgery. Median follow-up after surgery was three years (IQR: 1–5). Results are depicted in a swimmer's plot (Fig. 2).

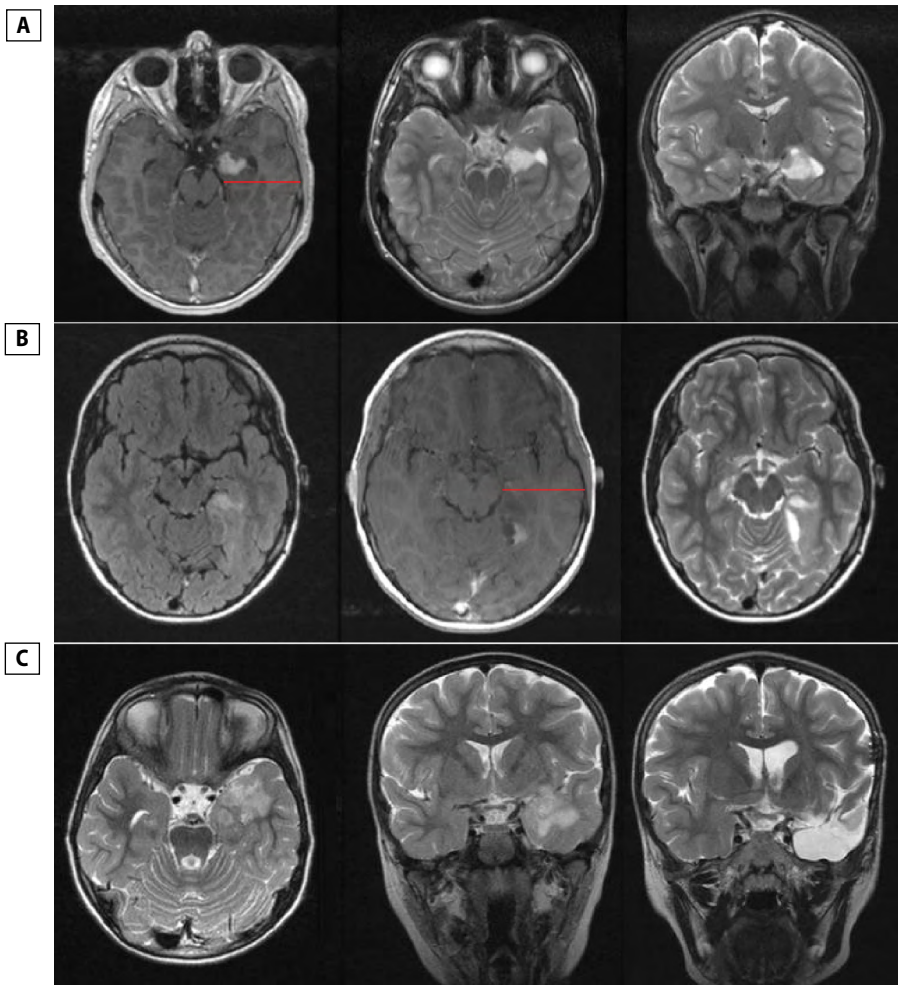

Figure 1. MRI images of different types of MTL lesion in children, along with suggested approaches for their treatment. Figure is divided into three parts: (**A**) Type A tumours located in anterior portions of MTL — transsylvian approach (Yasargil approach); (**B**) Type A tumours located in posterior portions of MTL– transcortical MTG approach (Niemeyer approach); (**C**) Type C, D and large Type A tumours — anterior temporal lobectomy with removal of MTL (Spencer approach). In depicted cases, histopathology revealed ganglioglioma (**A**), oligodendroglioma (**B**), and astrocytoma pilocyticum (**C**). MTG — medial temporal gyrus; MLS — mesial temporal lobe

Given the symptoms prompting diagnosis, all patients had MRI for epileptic seizures. 11/14 patients had generalised seizures, specifically: absence (nine patients) and tonic-clonic (four patients). Two patients had both generalised and partial seizures, and three patients had only partial seizures. The only type of partial seizures were partial complex seizures. In girls, the first seizure tended to occur at a later age ($p = 0.059$). The median duration of epilepsy before surgery was 30 months (IQR: 4–56). None of the patients were found to have neurological deficits or impaired consciousness on hospital admission. Four patients were operated on during the first year after the onset of symptoms. Half of the patients had early childhood onset of epileptic seizures, defined as age up to 8, and had more complications (4/7 *vs.* 0/7, $p < 0.07$). On the other hand, late onset of seizures was associated with the best outcome (7/7 *vs.* 2/7, $p = 0.021$).

Gross total resection was done in all patients and no residual tumour was found in the postoperative MRI. There were no perioperative mortalities. Acute complications were more frequent in younger patients ($p = 0.024$). One five-year-old girl had an epidural haematoma, while neurological deterioration immediately after surgery tended to occur in boys (3/6 *vs.* 0/8, $p = 0.055$). Two of them developed hemiparesis that improved in the long-term follow-up to a Lovett score of 4/5, and one had aphasia, which later resolved.

Histopathological examination revealed nine cases of ganglioglioma, two cases of pilocytic astrocytoma, one oligodendroglioma, and one dysembryoplastic neuroepithelial tumour (DNT). The first seizure occurred at a later age in the patients with pilocytic astrocytoma ($p = 0.005$). There was no tumour recurrence during the follow-up period. Seizure recurrence (Engel class II) was observed in one girl over a one-year period, who had

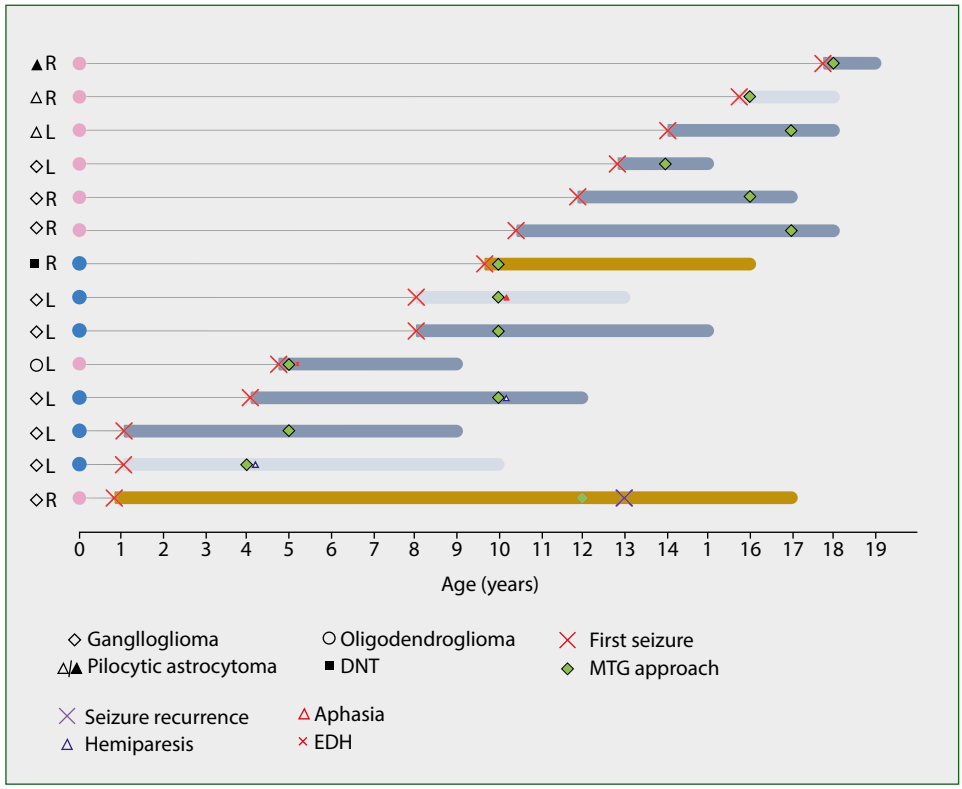

Figure 2. Swimmer's plot showing first seizure and time to surgery in 14 consecutive paediatric patients after MTG approach for MLS tumour resection. Time 0 is defined as birth of a girl (rose circle) or a boy (blue circle). Colour bars on plot show follow-up period from first seizure, and colour shows type of seizure: only generalised seizures (steel blue), generalised or partial seizures (brown), and only partial seizures (light blue). Regarding signs on left of plot that show histopathological diagnosis: gangliogliomas are marked with a diamond, pilocytic astrocytomas are marked with a triangle, oligodendroglioma is marked with a circle, and DNT is marked with a square. Those with a solid filling indicate tumours accompanied by a hippocampal lesion. Letters R and L indicate right and left side of tumour. DNT — dysembryoplastic neuroepithelial tumour; MTG — medial temporal gyrus; MLS — mesial temporal lobe

had epilepsy for 11 years before surgery; the others remained seizure-free (Engel class I). The best outcome was obtained in nine patients (64%), and the rest had satisfactory outcomes (Table 1).

A heatmap representation of hierarchical clustering analysis of the selected data, as depicted in Figure 3, shows two clusters of patients. Cluster A contains only patients with early onset of epileptic seizures; these are boys who were diagnosed with left MTL ganglioglioma and who developed neurological complications — two had hemiparesis and one had aphasia. Cluster B contains the remaining patients, the majority of whom were girls and most were diagnosed with ganglioglioma. Only in this cluster did patients have absence seizures, hippocampal lesions, a history of seizures of less than one year, and the best outcome.

Discussion

The primary goal of treatment of MLS tumours is GTR confirmed on postoperative MRI. Even a small part of the neoplasm left behind can progress and cause seizure recurrence. To date, there has been no oncological treatment for low grade MLS tumours.

The elimination of epileptic seizures should be considered as a secondary goal of treatment. TLE is a progressive disease and longstanding seizures affect quality of life. Due to the risk of psychological complications, some authors suggest adopting the motto 'the sooner the better' [14]. However, the benefits of surgical treatment must be carefully weighed against the risk of complications. Assessing the risk of surgery should be based on the surgeon's experience and any patient burdens that could affect the outcome.

In 2001, Wiebe et al. [15] confirmed the superiority of surgical treatment for TLE over conservative management in a prospective, randomised trial. In 2003, the American Academy of Neurology recommended surgery as the treatment of choice for drug-resistant TLE [16]. In children, surgical outcomes are better compared to adults, who have a higher incidence of seizure recurrence [2, 3, 17].

GTR offers seizure-free survival in most patients, which is clearly an argument for surgical treatment. An important benefit is the preservation of normal intellectual and

Figure 3. Heatmap representation of hierarchical clustering analysis of selected clinical and radiographic characteristics as well as intra- and post-operative findings (Y axis) in 14 consecutive paediatric patients (X axis) after MTG approach for MTL tumour resection. In all cases, red indicates 'yes' and blue indicates 'no'. MTG — middle temporal gyrus; MTL — mesial temporal lobe

psychological development during long-term follow-up [3, 17–20]. Microsurgical resection of the tumour is considered a definitive, time-sustainable treatment that offers a good chance of a cure for epilepsy.

Surgical management

A literature review shows there is no consensus regarding the surgical treatment of TLE. Studies have looked for the best extent of resection and type of surgery. Even so, at present it is only an estimation that satisfactory results (Engel I) of surgical treatment of tumour-related TLE may be achieved in up to 90% of patients [12, 21, 22]. Decision-making should be individualised, depending on the surgeon's experience, and treatment should be carried out in a centre with a high volume of cases.

There have been a few studies comparing the efficacy of GTR versus STR in the treatment of tumour-related TLE [23]. Some authors have advocated GTR because they have observed a higher chance of seizure-free survival compared to STR [17, 24, 25]. A good outcome has been observed in up to 90% of patients after GTR, as opposed to 25–36% after STR [2, 3, 12, 16].

On the other hand, there have been studies in which no difference in seizure outcome has been observed depending on the extent of resection [17, 26]. The differences in conclusions are due to the lack of uniform, and large, groups of patients studied. Moreover, adults and children with different histopathological diagnoses have often been included in the same group [27, 28]. One meta-analysis compared outcomes of 1,181 patients from 41 publications who underwent surgery for a benign temporal lobe tumour [27]. A good outcome was defined as the cessation of seizures (Engel I), and more often good results were observed after GTR (79% *vs.* 43%).

When deciding on surgical treatment, there are three types of lesionectomy that can be distinguished for MLS tumours [29]. The first involves removing the tumour within its confines without resecting surrounding tissues, which is referred to as a lesionectomy alone. In most cases, this procedure offers a good outcome, although sometimes this type of surgery may not be enough to stop the seizures. The second type of surgery involves resecting the tumour along with a part of the surrounding brain, the epileptogenic cortex, and this is known as an extended lesionectomy. The least frequently

Table 1. Comparative analysis of clinical characteristics found in 14 paediatric patients after MTG approach for MTL tumour, with either satisfactory or best outcome, defined as seizure-free outcome with no medical complication

	Satisfactory outcome n = 5	Best outcome n = 9	P-value
Median age at time of surgery (years)	10 (5–11)	16 (10–17)	0.042
Median age at first seizure (years)	4 (1–6)	12 (9–15)	0.007
Number of patients with early childhood onset of seizures	5 (100%)	2 (22%)	0.021
Girls	2 (40%)	6 (67%)	NS
Generalised seizures only	2 (40%)	7 (78%)	NS
Generalised and focal seizures	1 (20%)	1 (11%)	NS
Focal seizures only	2 (40%)	1 (11%)	NS
Complex partial seizures	3 (60%)	2 (22%)	NS
Absence seizures	2 (40%)	7 (78%)	NS
Tonic-clonic seizures	1 (20%)	3 (33%)	NS
Duration of seizures (months)	36 (14–104)	24 (4–49)	NS
Duration of seizures < 1 year	1 (20%)	3 (33%)	NS
Left MLS tumour	4 (80%)	4 (44%)	NS
Oligodendroglioma	1 (20%)	0	NS
Ganglioglioma	4 (80%)	5 (56%)	NS
Pilocytic astrocytoma	0	3 (33%)	NS
Dysembryoplastic neuroepithelial tumour	0	1 (11%)	NS
Hippocampal lesion	0	2 (22%)	NS
Follow-up MRI (years)	4 (3–6)	1 (1–5)	NS
Engel class I after surgery	4 (80%)	9 (100%)	NS

MLS — mesial temporal lobe; MTG — middle temporal gyrus; NS — not significant

performed type of surgery is the removal of the lesion and independent epileptogenic focus. Amygdalohippocampectomy is a selective procedure used to treat MLS tumours, with the goal of removing the tumour and structures responsible for the development of epileptic seizures. The extent of their removal is important for the control of epileptic seizures [7]. Khajavi et al. [26] reported that outcomes after extended lesionectomy did not differ from those after lesionectomy alone. Some authors have suggested that tumour resection removes the epileptogenic focus responsible for seizure formation and is sufficient for a good outcome [29]. Others have seen slightly better results after the addition of a hippocampectomy [27]. In MLS tumours, the most performed procedure is an extended lesionectomy [7, 30].

There are no recommendations as to what type of surgical approach most improves the extent of resection and the long-term seizure outcome. Transcortical approaches are used less often, which may be due to the lower incidence of tumours in the posterior hippocampus, as well as to difficulties in anatomical orientation during surgery [9, 12]. Yasargil and Reeves [31], in a paper involving 120 patients, proposed an exclusively transsylvian approach for MLS tumour removal. Some authors have reported that it is more difficult to achieve GTR of an MLS tumour via the transsylvian approach due to the smaller surgical field [32]. Schramm and Aliashkevich [10] suggested adjusting the approach to the location of the tumour. They divided MLS tumours into four types.

Type A tumours are found in the medial structures, i.e. the hippocampus, the uncus, the parahippocampal gyrus, the amygdala, and the lingual gyrus, and are removed via a transsylvian approach. Type B involves tumours found in the lateral occipitotemporal gyrus that are usually resected via a subtemporal approach. Type C lesions occupy the area of both type A and type B tumours, and for them, temporal lobe resection is usually performed. A similar approach is used for type D tumours, which involve deep structures [10].

In one study, the decision as to the type of surgery depended on the location of the tumour in the dominant or non-dominant hemisphere [24]. Extended lesionectomy with resection of medial structures was used for the non-dominant hemisphere. The surgery included a full hippocampectomy, even though no hippocampal lesions were visible on MRI. In lesions found in the dominant hemisphere, selective treatments without removal of the hippocampus were more common.

Recently, there has been a marked change in the tactics of surgical treatment of epilepsy i.e. more selective procedures are being performed, with fewer resections of the temporal lobe. Minimising the scope of surgery aims to reduce neurological damage [33]. Yet still there remains conflicting data on the type of surgery i.e. resection *vs*. selective surgery. Few papers have

compared these types of operations in children. Some authors have recommended extensive temporal lobe resection along with the tumour and hippocampus, as they see better seizure outcome compared to tumour removal only [25, 34, 35].

Lee et al. [33] compared the results of anterior temporal lobe resection versus transsylvian lesionectomy alone in children. The percentage of GTR in selective procedures was 70%, while after anterior temporal lobe resection, GTR was achieved in more than 95% of cases. Satisfactory results (Engel I) were reported in more than 90% of cases in both groups. Poor seizure outcome was seen after STR, and this was true for both groups. Similar observations have been found in other studies [30, 36].

Clusmann et al. [2], over a mean follow-up period of 38 months, compared outcomes after temporal lobe resection versus transsylvian approach for selective amygdalohippocampectomy. The first method was chosen more often for cortical dysplasia. The authors saw satisfactory results (Engel I and II) in both groups (79% *vs.* 83.4%). However, not all authors express a similar opinion. Joma et al. [37] reported that lesionectomy-only resulted in a worse seizure outcome compared to extended lesionectomy. Uliel-Sibony et al. [17] compared the results of surgical treatment of TLE with lesionectomy--only versus lesionectomy with hippocampectomy. Interestingly, satisfactory results (Engel class I) were more often achieved after selective procedures (93% *vs.* 58%). However, no explanation was given, and perhaps the difference could be due to the duration of the epilepsy, the location of the tumour, or the coexistence of different pathologies. In another study, a good outcome was achieved in 74% of patients after selective procedures *vs.* 94% after temporal lobe resection [38]. None of above studies were prospective.

Conclusions

The MTG approach to MTL tumours is an effective procedure for treating epilepsy in children, with very good outcomes. It offers the possibility of GTR without removing the lateral structures of the temporal lobe, and while having a minimal risk of permanent neurological deficit. GTR is associated with seizure-free survival in most patients. Treatment results of tumour-related epilepsy via the MTG approach are comparable to data from the literature on the transsylvian approach and temporal lobe resection. Thus the MTG approach should be considered in selected MTL tumours.

Article information

Disclosure: *To the best of our knowledge, no conflict of interest, financial or other, exists. There was no funding source for this work. All authors listed have contributed sufficiently to the project to be included as authors, and all those who are qualified to be authors are listed in the author byline.*

Data availability statement: *The data that supports the findings of this study is not publicly available. However, it may be available upon request and with appropriate permissions.*

Ethics statement: *The study was approved by the Institutional Review Board and adheres to ethical guidelines concerning human subjects.*

Authors' contributions: *PK — study design, data collection, drafting article, project administration; EJB — data analysis, writing review and editing; WN — data collection, drafting article; MKC — literature review; MR — study conception, design and supervision.*

Funding: *None.*

Conflicts of interest: *The authors state that they have no conflict of interest.*

Supplementary material: *None.*

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