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Preservation of frontal white matter tracts in ventricular surgery: favoring an anterior interhemispheric transcallosal approach vs a transcortical transfrontal transventricular approach

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Abstract

Objective: Secondary to the creation of a surgical corridor and retraction, white matter tracts degenerate, causing long-term scarring with potential neurological consequences. Third and lateral ventricle tumors require surgery that may lead to cognitive impairment. Our objective is to compare the long-term consequences of a transcortical transfrontal approach and an interhemispheric transcallosal approach on corpus callosum and frontal white matter tracts degeneration.

Methods: Surgical patients with ventricular tumor accessible through both approaches were included and clinico-radiological data were retrospectively analyzed. The primary endpoint was the callosotomy length at three-month post-operative T1 MRI, corrected by the extension of the tumour and the use of neuronavigation. Secondary outcomes included perioperative criteria such as: bleeding, use of retractors and duration, FLAIR hypersignal on three-month MRI, re-do surgeries. To assess white matter tract interruption, three-month FLAIR hypersignal was superposed to a tractography atlas.

Results: 70 patients were included, 57 (81%) in the transfrontal group and 13 (19%) in the interhemispheric group. There was no difference in the mean callosotomy length on three-month MRI (12.3mm±5.60 transfrontal vs 11.7mm±3.92 interhemispheric, $p=0.79$) on univariate and multivariate analyses. The callosotomy length was inferior by -3.13mm for tumours located exclusively in the third ventricle ($p=0.016$), independent of the approach. Retractors were used more often in transfrontal approaches (60% vs 33%, $p<0.001$). The extent of frontal FLAIR hypersignal was higher after transfrontal approach (14.1mm vs 0.525mm, $p<0.001$), correlated to the use of retractors ($p<0.05$). After the interhemispheric approach, no tract other than corpus callosum was interrupted, whereas, after the transfrontal approach, frontal arcuate fibers and projections from the thamalus were interrupted in all patients, the cingulum in 19 (33%), the superior fronto-occipital fasciculus in 15 (26%), and the superior longitudinal fasciculus in 2 (3%).

Conclusions: Transfrontal and interhemispheric approaches to the third and lateral ventricles both lead to the same long-term damage to the corpus callosum, but the transfrontal approach interrupts several white matter tracts essential to cognitive tasks such as attention and planning, even in the non-dominant hemisphere. These results encourage all neurosurgeons to be familiar with both approaches and favor the interhemispheric approach when both can give access to the tumor with a comparable risk. Neuropsychological studies are necessary to correlate these anatomical findings to cognitive outcomes.

Introduction

Tumors that develop in the third ventricle, sometimes invading the lateral ventricles, are mainly colloid cysts (25%) in adults but can also include gliomas, ependymomas, central neurocytomas, and meningiomas[10]. Most of these tumors require complete surgical resection whenever possible (ref kazowski). The most common symptoms are secondary to hydrocephalus, including headache (69%), nausea/vomiting (38%), visual deficits (24%), seizures (17%), and changes in behavior (14%)[10]. These tumors may require an emergency surgery, and a salvage obstructive hydrocephalus treatment, such as ventriculocisternostomy or external ventricular drainage (EVD), may be performed before surgical resection. In this study, we will focus on surgical approaches to tumors located in the third ventricle with minimal extensions to the lateral ventricles that can be reached through two main approaches: anterior interhemispheric transcallosal approach (referred as interhemispheric in this study) or transcortical transfrontal transventricular (transfrontal) approach.

The interhemispheric approach is based on the microscopic pre-coronal anatomic dissection of a hemisphere, usually the right, ornon-dominant one for language processing, along the falx, down to the corpus callosum, which is then slightly opened rostro-caudally to give access to the ventricular space[1, 2, 15, 21]). The transfrontal approach creates a small cortex incision in the frontal middle gyrus to access the frontal horn of the lateral ventricle, usually the right one, through an intracerebral corridor[13]. A dominant side approach may be preferred for anatomical reasons based on each case. Both approaches give direct access to the frontal part of the third ventricle and may be extended to the more posterior parts through the choroidal fissure into the velum interpositum, and require to be particularly careful of the fornices. It is generally accepted that interforniceal dissection should be avoided because of severe memory deficits induced unless the tumor has already “prepared” the corridor. Lateral ventricles are also accessible through both approaches, except for the posterior lateral ventricle and the apex of the frontal horn, which can only be reached through a transfrontal approach (Figure 1). The main technical down-sides are the more extensive need for brain retraction in the transfrontal approach, and the narrowest surgical corridor with the need for more surgical expertise in terms of anatomical and vascular dissection in the interhemispheric approach[2, 13, 15].

In cases when both approaches give access to the whole tumor, choosing one approach rather than the other is debatable and based on the surgeon’s experience. They may consider the presence of hydrocephalus, the size of the tumor, or the presence of massive cortical veins[10, 15]. Endoscopic approaches can be considered for some types of small tumors, such as colloid cysts, but this will not be discussed in this study[5]. Previous clinical studies suggest that the interhemispheric approach may decrease the risk of white matter tract damage, postoperative seizures, porencephalic cyst formation, or subdural hygroma when compared to transfrontal surgery[15], although the decreased risk of seizures has not been confirmed in all series[17]. In return, it may be associated with a higher risk of vascular damage to the anterior cerebral arteries, and for most authors[2, 10, 12, 15, 21], venous infarction is the main concern of this approach, but we show that the risk of venous damage theoretically associated with this approach is extremely low if the bone flap is anterior to the coronal suture, with 91% of patients not presenting a single cortical vein in this area[1].

A major concern of both strategies is the cognitive consequence of the surgical approach, especially in case of fornices damage. There is also growing evidence that the so-called non-eloquent parts of the right frontal lobe play an important part in cognitive functions[6, 9, 13]. Although we lack systematic data in daily practice, full neuropsychological assessment of five post-operative adults did not prove that the interhemispheric approach had any negative impact on cognitive performance. In contrast, systematic neurospsychological testing of 30 children post-operative for lateral ventricular tumors showed that both interhemispheric and transfrontal approaches had a negative impact on their intellectual quotient six months after surgery, making no approach ideal. The interhemispheric approach was shown to impact the working memory, whereas the transfrontal approach impacted attention and reasoning networks[13]. The consequences of each approach are not only due to the direct destruction of part of the brain, either frontal surgical corridor or corpus callosum incision, but to the interruption of white matter tracts. Indeed, when part of a network is damaged, Diffusion Tensor Imaging (DTI) shows that secondary white matter degeneration chronically spreads along the entire length of the damaged tract[14]. The tract interrupted in the interhemispheric approach is the anterior corpus callosum, which connects both frontal lobes. A transfrontal approach through the middle frontal gyrus will interrupt U fibers, the cingulum, frontal projections from the thalamus, branches of the superior longitudinal fasciculus, the corpus callosum, and the more hypothetic superior fronto-occipital fasciculus (SFOF), all of which make the middle frontal gyrus a key anatomical support for attention and working memory[7, 24]. Unilateral brain damage leads to chronic deafferentation and wallerian degeneration of the corpus callosum in different types of pathologies, including after surgery, which is visible on DTI and MRI[8], meaning that a transfrontal approach also leads to corpus callosum degeneration. Complementarily, corpus callosum section may impede frontal lobes functions.

There is controversy about which approach is optimal, and, although many clinical series give elements about how to choose the best option, there is no definitive answer. Our knowledge gap is due partly to the rarity of these tumors, which, at fewer than 3% of intracranial tumors, makes series heterogeneous and dependent on the surgeon's experience. We also must contend with the fact that these tumors may present late in already neurologically compromised patients. The largest recent series of 127 patients found no difference in neurological outcome between the two approaches, except, controversially, that the interhemispheric approach was a risk factor for epilepsy[17].

To give more anatomical ground to clinical findings about both approaches, we analyzed the functional anatomical corridor based on long-term imaging. As a proxy for the approach invasiveness, we chose to compare the size of the callosotomy on a three-month postoperative MRI as a primary outcome, whether it be the direct corridor of the surgeon or the degenerative consequence of a frontal white matter interruption, and interruption of frontal white matter tracts as a secondary outcome. Other secondary outcomes were perioperative events, immediate postoperative imaging findings, complications, and the need for re-do surgery.

Methods

Data acquisition

All patients (5 to 63 years, median 22) who have been surgically treated for an intraventricular tumour in our institution from 2010 to 2020 were screened. Only those having a tumour of the third ventricle or having an extension in the lateral ventricle accessible, in terms of surgical exposure, to both an interhemispheric and a transfrontal approaches were included in the study (Figure 1). In our department, the choice between the two approaches is made by each surgeon, based on experience and personal reasoning. Some surgeons systematically use a neuronavigation system (Stealth S7 Medtronic or BrainLab), while others never use it in those cases, because intraventricular surgery is anatomically well defined. All patients had a post-operative MRI. All the data were collected retrospectively to construct an anonymous database, based on the medical records and a double blinded analysis of MRI (YE and PB). Patients were divided in two groups according to the surgical approach they received: interhemispheric or transfrontal. No patient objected to the anonymous use of health data in accordance with the French law (n° 2012-300).

Primary outcome

The primary outcome was the callosotomy length measured on the three-month post-operative T1 MRI. The position of the callosotomy was both anatomically classified according to the canonical subdivisions[20, 22, 23] and measured (Figures 1 & 2):

$$\frac{\text{Anterior limit of the callosotomy} + \dfrac{\text{Length of callosotomy}}{2}}{\text{Total length of the corpus callosum}}$$

The tumour localisation (exclusively in the third ventricle or in/with a lateral ventricle extension) and the use of a neuronavigation system were included in the multivariate analysis as possible confounding factors, along the tumour histology.

Secondary outcomes

Secondary outcomes were the occurrence of an intra-operative haemorrhage; the duration of the surgical procedure; the use of conventional (rigid and metallic, such as Vincent, Yaşargil or Sugita retractors) or soft brain retractors (as soft inflated glove digit or material such as cotton pad); the occurrence of a post-operative haemorrhage on immediate post-operative CT-scan; the total length of corpus callosum on MRI; the localisation of the callosotomy measured on the immediate post-operative MRI; the extent of the FLAIR hypersignal on the tree month post-operative MRI; the number of re-do surgery after the initial procedure.

Analysis of three-month white matter tracts degeneration

In order to assess the white matter tracts damaged in each approach, the three-month FLAIR signal on MRI was superposed to the theoretical position of the white matter tracts determined according to the Mori's tractography atlas [18]. In transfrontal approaches, the coordinate cortical entry point was determined based on the distance from the midline and from the coronal suture (0 being on the coronal suture, negative values posteriorly and positive values anteriorly).

Data analysis and statistics

The comparisons between the groups for continuous numeric quantitative variable were performed by using a Mann–Whitney Wilcoxon non parametric test. The quantitative nominal variables were analyzed through a chi square test with a Yates correction. When the conditions for applying chi square test were not met, a Fischer exact test was performed.

For the primary outcome, we performed a linear regression, the explanatory variables being surgical approach, neuronavigation, and tumor localization. The covariates were included in a Least Absolute Shrinkage and Selection Operation (LASSO) penalized regression model. The penalty coefficient λ was chosen to compute an estimation error lower than 1 standard deviation (std) of the minimum error obtained by 10-fold cross-validation, while being as parsimonious as possible. With this λ coefficient, no variable had a coefficient different from 0. No variable had more than 20% missing data. For variables having less than 5% missing data, a median imputation for quantitative variables and mode imputation for qualitative variables was performed. If a variable had between 5% and 20% missing data, a multiple imputation by chain equations (MICE) was performed.

All statistical analyses were performed with Matlab© R2021a v9.2.0.556344 (Copyright © 1984-2017, The MathWorks©, Natick, Massachusetts, USA) and Medistica. pvalue.io, a Graphic User Interface to the R statistical analysis software for scientific medical publications. 2019. Figures and artworks were performed with Glimpse Image Editor © 0.1.2.

Results

Description of the population and primary outcome

Of the 72 patients who were screened, 70 were included. A transfrontal approach was performed for 57 patients (81%) and an interhemispheric approach for 13 (19%). The two groups did not differ in terms of age (25.6 years ±15.8), sex (32 females (46%) and 38 males (54%)), corpus callosum length, localization of the lesion nor preoperative hydrocephalus (Table 1). Histology is detailed in table 2.

Univariate analysis of the primary outcome did not show any statistically significant difference between the two groups (mean callosotomy on three-month MRI length 12.3mm (±5.60) in the transfrontal group vs 11.7mm (±3.92) in the interhemispheric group, $p=0.79$). With a 5% risk, by adjusting for use of neuronavigation and the tumour localisation, we have not been able to show any statistically significant relationship between callosotomy length and the surgical approach. Callosotomy length was significantly ($p = 0.016$) related to tumour localization independently of the surgical approach chosen: in patients having a tumour in the third ventricle exclusively, the callosotomy length was on average inferior by -3.13mm to the patients with a tumour located or having an extension in a lateral ventricle (Table 3).

Secondary outcomes

Retractors were used significantly more often in transfrontal approaches than in interhemispheric approaches (rigid retractors in 26 (60%) vs 4 (33%), soft retractors in 14 (33%) vs 1 (8%), and no retractor in 3 (7%) vs 7 (58%), $p<0.001$). Patients needed more redo surgeries after transfrontal compared to interhemispheric approaches (1.33 (±0.577) vs 1.00 (±0), $p=0.033$).

Contrary to the length of the callosotomy after three months, the extent of FLAIR hypersignal in the mesial part of the ipsilateral frontal lobe was significantly higher after the transfrontal approach (14.1 (±8.18) mm) than after interhemispheric approach (0.525 (±1.48) mm) ($p<0.001$), with a correlation to the use of rigid retractors ($p<0.05$).

Finally, the position of the callosotomy was significantly ($p=0.016$) more posterior (0.384 (±0.0837)) in the group having had transfrontal surgery than in the interhemispheric group (0.310 (±0.0885)). However, this difference did not translate to the segmented anatomical region of the corpus callosum where the callosotomy was performed (Figure 3).

No other endpoint showed a significant difference between the two groups (Table 1).

Analysis of three-month white matter tracts degeneration

Analysis of FLAIR hypersignal in the group of patients who underwent surgery via the interhemispheric approach showed no patient with damage to the cingulum, the main white matter structure that could be threatened by this approach (Figure 4). Therefore, the study of involvement of the white matter tracts was limited to the transfrontal group.

As expected, frontal arcuate fibers, and frontal projections of the anterior ventral nucleus and of the posterior part of the frontal projection of the dorsomedial nuclei of the thamalus were interrupted in all patients. In 19 patients (33%), the cingulum was at least partly in the trajectory of the surgical approach or of the post-operative FLAIR hypersignal, the superior fronto-occipital fasciculus in 15 (26%), the superior longitudinal fasciculus I in 21 (36%) and the superior longitudinal fasciculus II in 2 (3%). The internal capsule was never involved in the approach for its motor component.

Discussion

Our study shows that a transfrontal approach to the third or lateral ventricle creates the same damage to the corpus callosum as an interhemispheric approach, interrupting in addition most frontal white matters tracts, namely arcuate fibers, projections from the ventral nucleus and dorsomedial nuclei of the thalamus in all cases, the cingulum in 33%, the superior fronto-occipital fasciculus in 26%, and the superior longitudinal fasciculus in 3% of cases, even in the absence of any complication. These findings may account for the cognitive impairment observed in those patients, concerning attention and planning tasks[13], although we tend to underestimate the cognitive consequences of both approaches, especially when focusing on the risk of damaging the fornices, at the expense of frontal white matter tracts damage. The main result of our study is that the transfrontal approach creates the same long-term corpus callosum damage as the interhemispheric approach, in addition to extensive frontal damage. One of the main limitations of this study is that the primary endpoint is purely anatomical and not based on a clinical assessment. The difficulty in collecting retrospectively good quality clinical information regarding the cognitive evaluation of patients before and after surgery illustrates the heterogeneity of clinical practices. However, solid data exist on the white matter tracts that can be damaged in the surgical approaches to the ventricles and the cognitive functions that can be altered by their interruption [4, 11]. We therefore encourage a systematic evaluation of all the cognitive fields that could be impacted by such a surgical approach (Table 4). Concerning the superior occipito-frontal fasciculus, the existence of which as a distinct structure is now controversial and it has been kept in this study in order to be systematic, the associated functions being close to the arcuate fasciculus[3, 16].

In terms of surgical performance, our results are comparable to already published data, making our results transferable to other surgical teams: the callosotomy size in the interhemispheric approach 11.7mm (±3.92) is similar to that advocated in this approach description (15-20mm)[21] and in series (up to 24mm)[19]. Unsurprisingly, the callosotomy was 3.13mm larger in patients with lateral ventricle extension compared to exclusively third ventricle tumors to allow access to the whole lesion. In our series, the surgery duration was similar in the two approaches (188 minutes in transfrontal vs 203 minutes in interhemispheric approaches), though interhemispheric approaches are reported to be longer, a mean 295 minutes for colloid cysts of the third ventricles[5]. Many factors account for this variability, including the surgeon’s experience and habits, and the nature of the tumour. The use of retractors is difficult to study objectively since the duration and strength of retraction may vary. However, there is a correlation between the use of rigid retractors and the extent of frontal FLAIR hypersignal, which discourages retractor usage. Softer alternative retraction methods include using a soft glove digit inflated on the trajectory to the ventricle to part rather than cut the white matter tracts.

Patients with a transfrontal approach were operated on 1.33 (±0.577) times, vs 1.00 (±0), p=0.033, in interhemispheric cases. Previously published data tend to show that the interhemispheric approach gives less access to the tumour and is therefore associated with a higher risk of tumour residue or recurrence. In our series, the histology may account for the results, only benign tumours having been operated on through the interhemispheric approach (table 2), and our study was not designed to answer this specific question.

Our results tend to favour an interhemispheric approach compared to a transfrontal approach whenever possible, to minimize damage to cognitively relevant structures. As such, they encourage surgeons to prepare for this surgery that could be necessary in emergency situations and to practice it to benefit the patients who could also be operated transfrontally, an approach which every neurosurgeon is familiar with, in order to give them expertise and confidence when those rare cases may present. Interhemispheric approach is anatomically demanding and this series does not account for the vascular risk of dissecting anterior cerebral arteries or of venous infarction. We previously showed that a completely precoronal bony flap avoids more than 90% of cortical venous drainage[1]. Some authors also suggest that preoperatively placing an external ventricular drainage in the ipsilateral or contralateral lateral ventricle may ease the interhemispheric approach by decreasing hydrocephalus[15]. In our experience, slow and gentle dissection of the interhemispheric scissure, associated with head elevation, hyperventilation, and osmotic treatments, allows minimal brain retraction at the beginning of the procedure and avoids combining the effects of a direct callosotomy and a minimal transfrontal approach. In case of perioperative hemorrhage, an external drainage can still be left in the ventricle to avoid postoperative acute hydrocephalus. In some cases, endoscopy can also be used to visualize more intraventricular spaces without using extra retraction[15]. The use of neuronavigation, although not associated with a decreased surgical corridor, may help less experienced neurosurgeons to develop their anatomical dissection in interhemispheric approaches or to minimize frontal corridor in transfrontal approach.

The interhemispheric approach is not adapted to every situation, and each case requires a specific discussion based on the tumour characteristics, especially its extension and vascular supply. Globally, surgery for ventricular tumors remains a challenge, with up to 24-37% having complications and 8% mortality in some series[12, 17]. Moreover, in some extremely rare patients, transcallosal approaches are associated with additional risks, that might lead to neurological deficits greater than expected in the general population and contraindicate it: exceptional cases of crossed-dominance, when the hemisphere controlling the dominant hand is contralateral to the hemisphere mediating language and speech, which can occur following cerebral injury during childhood, or if the splenium of the corpus callosum is also sectioned, causing postoperative speech, writing, or reading deficits[15].

In total, this study gives important information about the long-term consequences of the surgical approach performed for third ventricle tumors, but we realize it is limited by the non-randomized decision of the surgical approach, the asymmetry of group size, and the lack of systematic preoperative and postoperative clinical data. No systematic neuropsychological testing was performed, because they are rarely available in practice, especially in emergency cases, and can be hard to interpret depending on the patient background and the damage associated with the tumor itself and associated hydrocephalus. To complement our anatomical analysis, a more systematic cognitive evaluation of all patients would be recommended to optimize our surgical strategies to the patient’s benefit.

Conclusion

Contrary to the general assumption, transfrontal and interhemispheric approaches to the third and lateral ventricles both lead to the same long-term damage to the corpus callosum, but, in addition, transfrontal approach interrupts several white matter tracts essential to cognitive tasks such as attention and planning, even in the non-dominant hemisphere. These results encourage all neurosurgeons to be familiar with both approaches and favor the interhemispheric approach when both can give access to the tumor with a comparable risk. More systematic neuropsychological assessments are needed to confirm the long-term clinical relevance of our anatomical findings.

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Declarations section

Ethical Approval and Consent to participate

No patient objected to the anonymous use of health data in accordance with the French law (n° 2012-300).

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Human and Animal Ethics

No patient objected to the anonymous use of health data in accordance with the French law (n° 2012-300). All the dataset is fully anonymised.

Consent for publication

Not applicable

Availability of supporting data

Fully anonymized numeric data used for the statistics are available on demand

Competing interests

None of the authors has any conflict of interest to disclose
Dr Yehia El Bendary reports no disclosures.
Dr Caroline Apra reports no disclosures.
Dr Sorin Aldea reports no disclosures.
Dr Dorian Chauvet reports no disclosures.
Dr Georg Dorfmüller reports no disclosures.
Dr Sarah Ferrand-Sorbets reports no disclosures.

Dr Caroline Le Guérinel reports no disclosures.
Dr Pierre Bourdillon reports no disclosures.

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Authors' contributions
Dr Yehia El Bendary : data analysis; drafting the manuscript ; figure conception
Dr Caroline Apra : drafting the manuscript; critically revised the manuscript; figure revision
Dr Sorin Aldea : conception and design of the study; data acquisition
Dr Dorian Chauvet : critically revised the manuscript; data acquisition
Dr Georg Dorfmüller : critically revised the manuscript; data acquisition
Dr Sarah Ferrand-Sorbets : critically revised the manuscript; data acquisition
Dr Caroline Le Guérinel : critically revised the manuscript; data acquisition
Dr Pierre Bourdillon : conception and design of the study; data acquisition; data analysis; drafting the manuscript; revision of the statistical analysis; figure revision; supervision of the study

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Authors' information
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Figure 1: a. top of the figure: anatomical segmentation of the corpus callosum; bottom of the figure: diagram showing the measurement used for the calculation of the position of the callosotomy b. surgical exposure of the transcortical transfrontal approach (red) and the interhemispheric transcallosal approach (green). Patients were included if the localization of the tumour could be included in both approaches.

Figure 2: example of a patient operated through a transfrontal approach; a. sagittal immediate post-operative T1 MRI; b. sagittal three months post-operative T1 MRI; c. three-month post-operative FLAIR MRI, the green arrows show the surgical corridor and red arrow shows the extent of the FLAIR hypersignal. Although no callosotomy was directly performed in this approach, secondary degeneration of the corpus callosum is observed after 3 months.

*Figure 3: a. distribution of the position of the callosotomy (all patients) difference of distribution of the position of the callosotomy between the transfrontal and the interhemispheric approaches c. Localisation of the callosotomy in the two groups according to the anatomical segmentation of the corpus callosum (see Figure 1) b. Proportion of the retractors use between the two groups. Significant differences are marked with *.*

Figure 4: a. 64 direction tridimensional tractography representation of the corpus callosum with its F1-F1 projection. The red arrow shows the position of the callosotomy for a transfrontal approach and the green arrow for an interhemispheric approach; b. Schematic representation of a transfrontal (on the top in red) and interhemispheric (on the bottom in green) exposure and their relation with some relevant white matter tracts. The thalamo-frontal projections are not represented (part of the projections of the anterior ventral nucleus and of the dorsomedial nuclei are crossing the surgical corridor).