Clinical and imaging evaluation of transuncus selective amygdalohippocampectomy

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BACKGROUND: Various reports have described the transuncus (TU) approach as a selective route to the amygdala and hippocampus, but this approach has not yet been submitted to solid postoperative imaging analysis. The objective of this study was to evaluate the anatomy, surgical technique, postoperative imaging analysis, and outcome in a series of patients with temporal lobe epilepsy who underwent selective amygdalohippocampectomy via a TU approach.

METHODS: This was a prospective study of 25 consecutive patients who underwent selective amygdalohippocampectomy through a TU approach. The temporal stem and temporal pole were evaluated through different modalities of 3-Tesla magnetic resonance imaging, including tractography of optic radiation (OR), uncinate fascicle, and inferior fronto-occipital fascicle. Visual field analysis was performed with automated perimetry.

RESULTS: The mean age was 40 ± 8.21 years, and mean follow-up was 26.44 ± 12.58 months. Postoperatively, 21 patients (84%) were classified as Engel I (good seizure control). Diffusion tensor imaging (DTI) data showed that 78.2% of patients had some structural damage to the temporal stem and fibers of the uncinate fascicle were identified postoperatively in only 3 patients (13.04%). The inferior fronto-occipital fascicle was identified in 18 patients (78.3%); however, subsequent DTI analysis of the remaining fibers showed them to be damaged. Integrity of the OR did not differ between these 2 groups.

CONCLUSIONS: A TU approach is a feasible and efficient approach to selective amygdalohippocampectomy for surgical treatment of temporal lobe epilepsy. Postoperative DTI analysis suggests that a TU approach results in more injury to the temporal stem and its associated white matter fiber tracts than expected by previous anatomic studies; however, it was efficient in preserving OR.

INTRODUCTION

Temporal lobe epilepsy (TLE) is the most common form of focal epilepsy in adults, in up to 40% of all cases of epilepsy, and also the most common epileptic syndrome refractory to clinical treatment.⁵,⁶ Surgical resection of the mesial structures of the temporal lobe remains the treatment of choice for refractory cases.⁵,⁶ Many selective approaches have been proposed for the resection of the hippocampus and amygdala in an attempt to avoid injuries to both temporal neocortex and optic radiations.⁵,⁶ However, there is no consensus about which procedure is more selective and efficient for refractory TLE.⁷ Advances in anatomic white matter

Key words
- Fiber tracking
- Hippocampus
- Magnetic resonance
- Temporal lobe epilepsy
- Temporal stem
- Uncus

Abbreviations and Acronyms
- DTI: Diffusion tensor imaging
- FGF: Inferior fronto-occipital fasciculus
- MRI: Magnetic resonance imaging
- OR: Optic radiation
- PSD: Pattern standard deviation
- TLE: Temporal lobe epilepsy
- TS: Temporal stem

TU: Transuncus
UF: Uncinate fascicle

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fiber tract studies along with evolution of neuroimaging techniques, especially the introduction of diffusion tensor imaging (DTI) magnetic resonance tractography, allowed the assessment of preservation of most important fiber tracts related to temporal lobe surgery, namely the uncinate fasciculus (UF), inferior fronto-occipital fasciculus (IFOF), and optic radiations (ORs).  

Some investigators have proposed an anteromedial approach, directly through the uncus and mesial structures of the temporal lobe to minimize injury to the temporal stem (TS) and neocortex. This approach is based on the topographic relationship of the uncus and the temporal horn of the lateral ventricle (Figures 1 and 2).  

However, this anatomic proposal has not been submitted to neuroimaging evaluation of the structural impact on both the TS and neocortex. Therefore, we studied a case series with patients submitted to an anteromedial approach through the uncus (a transuncus [TU] approach) for resection of the amygdala and hippocampus and evaluated its consequences for the TS and temporal neocortex.  

The objective of this study was to investigate if this approach is feasible, safe, and selective for the mesial structures.

METHODS

Ethics Approval
The study was approved by the local ethics committee of our university (CEP 776/2009) and all patients and healthy volunteers provided written informed consent.

Study Design
This was a prospective and nonrandomized study of 25 consecutive patients with refractory mesial TLE treated surgically at the Epilepsy Service of the University of Campinas, Brazil.

Patient Population
All patients had the diagnosis of unilateral mesial TLE with magnetic resonance imaging (MRI) evidence of hippocampal sclerosis seen at the outpatient clinic for refractory epilepsy at our institution and fulfilled the following criteria: older than 18 years, clinical and electroencephalographic features of unilateral mesial TLE, failure of seizure control with at least 2 antiepileptic drugs regimens, and minimal follow-up of 12 months. We excluded patients with any additional progressive disease (e.g., neoplasms) and those who had undergone previous epilepsy surgery. All patients completed the preoperative investigation protocol at our institution, which includes electroencephalographic monitoring, MRI, and neuropsychological evaluation.

Clinical data evaluated were 1) age at epilepsy onset; 2) duration of epilepsy; 3) age at surgery; 4) neurologic status; and 5) seizure frequency.

Surgical Technique
The patient was positioned in a neutral dorsal decubitus position with the head extended and with a slight torsion to place the temporal fossa perpendicular to the floor and the choroidal fissure in the surgeon’s view. A petrosal incision and craniotomy were performed with good exposure of the temporal pole (TP).

The sylvian fissure was carefully dissected and inspected to identify the M1 and M2 segments of the middle cerebral artery, limen insulare, uncus, uncal arteries, internal carotid artery, anterior choroidal artery, cuneal cistern, oculomotor nerve, posterior communicating artery, thalamus sulcus, and uncal apex.

Once the anatomic landmarks were identified, a surgical incision was started slightly above the thalamic sulcus on the pyriform cortex (anterior segment of the uncus) and a subpial corticectomy was performed, always preserving the integrity of the arachnoid membrane (Figure 3). The corticectomy was extended posteriorly and gradual resection of the anterior segment of the uncus was performed, trying to preserve the limen insulare and TS, thereby minimizing the risk of injury to the uncinate fascicle and the anterior portions of the ORs (Meyer loop) (Figure 2). Consequently, the temporal amygdala was partially removed, followed by the anterior wall and anterior part of the roof of the temporal horn, and thus, the ventricle was reached through this anteromedial trajectory. Using a self-retaining retractor, the ventricle was then inspected to identify the hippocampal head and body, choroidal fissure, collateral eminence, and anterior choroidal point. Once the anatomy had been carefully examined, the anterior segment of the uncus was resected to create some working space. After that, the choroidal fissure was opened and the cuneal cistern identified, allowing en bloc resection of part of the hippocampus body for further study; then, a subpial resection of the remaining hippocampus and parahippocampus was performed. The posterior limit of resection was the lateral geniculate body, and the collateral eminence served as the lateral limit. After resection of the hippocampus and parahippocampus, the temporal amygdala was inspected again and the resection completed; the optic tract was used as a landmark for the superior limit.

Postoperative Image Evaluation
TP integrity was evaluated by an experienced independent neuroradiologist, according to the presence or absence of TP atrophy. We defined the TP as the portion of temporal lobe anterior to the limen insulare.

The integrity of the TS was determined through 3-T MRI structural and DTI analysis.

Structural Analysis
An experienced independent neuroradiologist used 3-T MRI volumetric T1 acquisitions and divided the TS in 3 similar portions of 10 mm based on the average TS length. For a semi-quantitative analysis of TS, limits were defined as the amygdala anteriorly and lateral geniculate body posteriorly (Figure 4). The findings were classified as damage or no damage and the extension of damage as the anterior, middle, and posterior thirds of TS.

DTI Analysis
The chosen tracts were the UF, IFOF, and OR. An age-matched and gender-matched control group of healthy volunteers was used for comparative purposes. The cutoff limit to establish the presence of the tract was the identification of 5 streamlines or more. In addition, UF streamlines shorter than 10 mm were not considered. The integrity of the remaining tracts was evaluated.
through fractional anisotropy, axial diffusivity, and radial diffusivity.

Outcome Data
All patients who underwent the TU selective amygdalohippocampectomy were seen monthly during the first 3 months after surgery, then bimonthly during the following 6 months and then twice a year or sooner if needed.

Data for neurologic deficits, seizure control, complications (e.g., infection), and mortality were collected. Seizure outcome was classified according to the Engel scale and surgical complications were classified as minor (resolved within 3 months) and major (persisting for longer than 3 months with adverse effects on daily living). Complication data were compared with results from 26 patients who underwent selective transsylvian amygdalohippocampectomy, reported by our group previously.

Postoperative Neuropsychological Evaluation
To evaluate verbal and nonverbal memory, we used the Wechsler Memory Scale—Revised and Rey Auditory Verbal Learning Test. The results of these tests (available for 22 of the 25 patients who underwent the TU approach) were transformed into 2 scores based on normative data and then compared with scores of 24 patients who underwent selective transsylvian amygdalohippocampectomy and 22 patients who underwent anterior temporal lobe resection, as reported by our group recently.
Figure 2. White matter dissections showing the fiber tracts that can be involved during the transuncus approach. (A) The inferior fronto-occipital fasciculus connects the prefrontal region with the occipital and parietal regions. The fibers course through the temporal stem slightly posterior and superior to the fibers of the uncinate fasciculus. The uncinate fasciculus connects the basal frontal region with the temporal pole, its fibers run through the temporal stem deep to the lumen insulae. (B) After removal of the inferior fronto-occipital fasciculus and uncinate fasciculus, the lower division of the optic radiation is exposed. The projection starts at the lateral geniculate body of the thalamus, assumes an anterosuperior direction, forming part of the roof of the temporal horn and continues superomedially to the amygdala (Meyer loop). Then, the fibers course posteriorly and form the lateral wall of the temporal horn on their way to the visual cortex. Clau, claustrum; ext, Cap, external capsule; IFOF, inferior fronto occipital fasciculus; SLF, superior longitudinal fasciculus; UF, uncinate fasciculus; th, Cap, internal capsule; CP, globus pallidus; OR, optic radiation; OT, optic tract; ACoA, anterior communicating artery; Amg, amygdala.

Figure 3. Microsurgical anatomic landmarks in a formalin-fixed, cadaveric human specimen. A posterior to anterior view has been chosen to simulate the intrasurgical view along the sylvian fissure (right side). (A) The sylvian fissure has been opened, allowing for a view onto the insular cortex, the orbital gyrus, and the relevant vasculature. Inferomedially to the lumen insulae, the uncus can be identified. (B) Schematic representation correlates with A) of the sylvian fissure and the main white matter fiber tracts coursing through the temporal stem, from superficial to deep: uncinate fasciculus, inferior fronto-occipital fasciculus, and optic radiation. The dashed line shows the direction of the initial uncal incision, extending from the thalamic sulcus back to the lumen insulae. III, third nerve; ICA, internal carotid artery; M1, M1 segment of middle cerebral artery; M2, M2 segment of middle cerebral artery; ON, optic nerve; SSt, pituitary stalk; IFOF, inferior fronto occipital fasciculus; 1, uncus; 2, lumen insulae; 3, temporal lobe; 4, frontal lobe.
Visual Field Analysis

Visual field analysis was performed with postoperative standard automated perimetry and the variable studied was the pattern standard deviation (PSD) indicator of localized defects. The higher the PSD, the greater the possibility of a localized deep visual field defect.

Statistical Analysis

Statistical analysis was performed with Systat 9 software, using the following methods; analysis of variance (with Turkey as post-hoc) t test, Fisher exact test, and Kruskal-Wallis test.

RESULTS

Demographic Data

We studied the first 25 consecutive patients from our epilepsy clinic who underwent a TU approach to treat refractory mesial TLE, with MRI evidence of unilateral hippocampal sclerosis. The mean age at surgery was 40 ± 8.21 years, and mean seizure frequency was 7.26 ± 4.60 per month. Sixteen patients were female. Clinical and demographic data are summarized in Table 1.

Surgical Outcome at the Last Follow-Up

According to the postoperative Engel scale of seizure control, patients were classified as Engel I A (54), Engel IB (2), Engel IC (1),

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<th>Table 1. Clinical and Demographic Data</th>
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<td><strong>Mean Age (years)</strong></td>
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Engel ID (4), Engel II (0), Engel III (3), and Engel IV (2). Dividing patients in 2 groups of seizure control, 21 (54.8%) were classified as having satisfactory seizure control (Engel I) and 4 (16%) were categorized as having unsatisfactory seizure control. The mean follow-up of patients was 26.44 ± 12.58 months, ranging from 8 to 50 months.

**Neuroimaging Findings**

MRI analysis was performed in 23 patients, once 2 patients were excluded because of the lack of adequate postoperative 3-T MRI results.

TP atrophy was found in 16 patients (69.6%), according to the neuroradiologist’s report (Figure 4).

The semiquantitative analysis of TS was possible in all 23 patients and showed some injury that reached the anterior third in 18 patients (78.3%), middle third in 12 patients (52.1%), and posterior third of the TS in 4 patients (17.3%) (Figure 4).

DTI analysis was performed in 23 patients. The minimum threshold of streamlines was found for UF in 9 patients (39.1%), for IFOF in 18 patients (78.3%), and for OR in all patients. In the control group, a reasonable number of streamlines of UF, IFOF, and OR were identified in all volunteers (Table 2). When comparing the number of voxels of tracts observed in each group, a significant difference was found in the IFOF (P < 0.001) analysis, presenting more voxels in the control group, but it was not found in the OR (P = 0.3232) analysis (Table 2).

The qualitative tract analysis of IFOF and OR of the patient group and its comparison with the control group is summarized in Table 2 and Figures 5 and 6.

Correlations between the presence of UF, TP atrophy, and TS injury were evaluated with a c² test. No significant correlation was found.

**Surgical Complications**

Two patients had postoperative motor deficits: one patient presented with mild but permanent left-side hemiparesis and the other presented with transient hemiparesis. Transitory third nerve palsy was observed in 4 patients, all of whom recovered fully. Two patients presented with septic meningitis (negative cerebral spinal fluid culture) with no further consequences. There were no deaths in this series.

**Postoperative Neuropsychological Evaluation**

There were no differences in postoperative Wechsler Memory Scale—Revised and Rey Auditory Verbal Learning Test z scores among the TU approach, transylvanian amygdalohippocampectomy, and anterior temporal lobe resection in the multivariate analysis of variance (F = 0.92; P = 0.63) and there was no difference in the univariate analyses for each of the tests.

**Visual Field Analysis**

Visual field analysis was possible in only 5 patients. Two had a normal PSD value and higher values were found in the other 3; only 1 patient presented with quadrantanopia.

**DISCUSSION**

To preserve the TS and Meyer loop, Coppens et al. proposed an anteromedial approach to the temporal horn of the lateral ventricle for resection of the amygdala and hippocampus. This proposition is based on the topographic relationship between the amygdala, uncus, and temporal horn, because the anterior segment of the uncus is mainly composed of the temporal amygdala (forming the anterior wall) and the anterior portion of the roof of the temporal horn of the lateral ventricle (Figure 6). The TS, at the inferior limiting sulcus of the insula, starts at the limen insulae and ends at the level of the lateral geniculate body (Figure 4). Therefore, an approach to the temporal horn through the uncus can prevent injury to the TS, ORs, and neocortex, as shown by Choi et al. and Sincoff et al. Wieser and Yagargil and Yagargil et al. described selective resection of the amygdala and hippocampus through the sylvian route (transylvanian selective...
amphictyonic), with some technical changes since the publication of their original study. These investigators described an incision beginning at the limen insulae and extending anteriorly to the uncus, performing a transventricular resection of the amygdala and hippocampus using an inside-out route. On the other hand, Vajkoczy et al. described a transylvian-transtemporal mesial en bloc resection of the amygdala and hippocampus using an outside-in route through the uncus and amygdala. All the approaches are similar and use the concept of the temporal amygdala as the anterior wall and the anterior portion of the roof of the temporal horn of the lateral ventricle, but none reported any postoperative study analyzing the consequences of the approaches to the TS and temporal neocortex. Therefore, the aim of our study was to analyze the feasibility and potential selectivity of an approach through the uncus, minimizing the risk of injury to the TS by trying to stay anterior to it.

The TS semiquantitative structural analysis showed injury to the anterior third in 78.3% of patients and damage that reached the middle third in 52.1%. Postoperative DTI analysis showed UF streamlines in only 3 patients (13.04%) and IFOF streamlines in 15 patients (78.3%). In addition, the analysis of the remaining IFOF fibers suggests some surgical injury (low number of voxels, low
fractional anisotropy, and high radial diffusivity) and consequently, a potential loss of function when compared with the control group. Martino et al. reported that IFOF occupies the posterior two-thirds of the TS, located 10.9 mm behind the limen insulae; on the other hand, Kier et al. described the IFOF extending from the amygdala to the lateral geniculate body (occupying the complete extension of the TS). Our findings showed more damage to UF fibers than to IFOF, because IFOF interruption occurred exclusively in 5 patients (21.7%); this suggests that the UF is probably located more anteriorly as stated by Martino et al.

However, OR qualitative analysis showed no difference between surgical and control groups, suggesting good preservation of its integrity. These results seem to be in accordance with the study of Choi et al., which showed a safe entry zone to the temporal horn of the lateral ventricle through an incision at the level of the limen insulae or adjacent 7 mm of the inferior circular sulcus. Visual field analysis was possible in only 5 patients and showed high PSD values in 3, but only 1 presented with quadrantanopsia.

Although DTI analysis suggested some preservation of the OR, the low number of patients (5) who underwent postoperative standard automated perimetry precluded any functional correlation.

We believe that the high incidence of injury to the anterior third of the TS can be related to the fact that the TU approach provides a narrow surgical field for resection of deeply seated mesial structures (hippocampus and choroidal fissure), requiring the use of self-retaining retractors, which increase the risk of brain injury and tissue ischemia. In addition, a limited approach precludes an en bloc resection of a portion of the body of the hippocampus and parahippocampal gyrus, preventing an adequate diagnosis and experimental ex vivo analyses. Therefore, the surgeon needs to expand the incision to the inferior circular sulcus of the insula to provide better exposure, increasing the risk of injury of the UF, IFOF, and OR, as suggested by Choi et al.

TP evaluation showed a high incidence of atrophy even with a relative short follow-up (26 months), which probably was secondary to the disconnection of TP because of the high incidence of
UF fibers and the use of self-retaining retractors to obtain appropriate visualization of surgical field. The neuropsychological outcomes were similar to that of patients submitted to other approaches previously used by our group (anterior lobectomy and transsylvanian selective amygdalohippocampectomy).

A TU approach resulted in a good seizure control (84%), similar to alternative established approaches for TLE described in the literature (62%-90%). With regards to safety, some patients had a transient third nerve palsy (3 patients) and hemiparesis (permanent in 1 patient). These occurrences were attributed to the extensive cisternal dissection and anterior choroidal artery coagulation at the inferior choroidal point (plexual portion). The plexual portion of the anterior choroidal artery can emit some capsular thalamic branches (58%), and their damage may cause hemiparesis. After this initial experience, we changed our approach to a subpial dissection, with no further incidences of third nerve palsy or hemiparesis. As reported previously by our group, patients underwent transsylvanian amygdalohippocampectomy and only 2 patients had permanent deficits: 1 patient with unilateral amaurosis secondary to central vein and artery thrombophlebitis and another with mild memory deficits that did not compromise his daily life.

Although most of the deficits were transitory, the TU approach appeared to have more complications than did transsylvanian amygdalohippocampectomy. The incidence of major complications (4%) was similar to results from other series reported in the literature (0%-16%).

Our study is limited by a relatively small number of patients and by the fact that we did not have 3-T MRI data of surgical groups using standard approaches (transsylvanian selective amygdalohippocampectomy and anterior temporal lobectomy) to compare with the results of the TU approach. In addition, the number of patients submitted to a postoperative visual field analysis was small (5).

CONCLUSIONS

Although TU selective amygdalohippocampectomy was effective and safe, our postoperative neuroimaging findings showed a high incidence of TP atrophy and injury of the anterior two thirds of the TS. Therefore, we conclude that this approach is not selective and is more technically demanding compared with standard approaches already in use worldwide, without any advantage to its use.

REFERENCES


Conflict of interest statement: The authors declare that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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