Neuropsychology Outcomes Following Trephine Epilepsy Surgery: The Inferior Temporal Gyrus Approach for Amygdalohippocampectomy in Medically Refractory Mesial Temporal Lobe Epilepsy

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Received, January 6, 2017.
Accepted, May 3, 2017.
Published Online, June 8, 2017.

BACKGROUND: Surgery is indicated in cases of mesial temporal lobe epilepsy(MTLE) that are refractory to medical management. The inferior temporal gyrus (ITG) approach provides access to the mesial temporal lobe (MTL) structures with minimal tissue disruption. Reported neuropsychology outcomes following this approach are limited.

OBJECTIVE: To report neuropsychological outcomes using an ITG approach to amygdalohippocampectomy (AH) in patients with medically refractory MTLE based on a prospective design.

METHODS: Fifty-four participants had Engel class I/II outcome following resection of MTL using the ITG approach. All participants had localization-related epilepsy confirmed by long-term surface video-electroencephalography and completed pre/postsurgical evaluations that included magnetic resonance imaging (MRI), Wada test or functional MRI, and neuropsychology assessment.

RESULTS: Clinical semiology/video-electroencephalography indicated that of the 54 patients, 28 (52%) had left MTLE and 26 (48%) had right MTLE. Dominant hemisphere resections were performed on 23 patients (43%), nondominant on 31(57%). Twenty-nine (29) had pathology-confirmed mesial temporal sclerosis (MTS). Group level analyses found declines in verbal memory for patients with language-dominant resections ($P < .05$). No significant decline in neuropsychological measures occurred for patients with MTS. Participants without MTS who underwent a language-dominant lobe resection exhibited a significant decline in verbal and visual memory ($P < .05$). Nondominant resection participants did not exhibit significant change in neuropsychology scores ($P > .05$).

CONCLUSION: Neuropsychology outcomes of an ITG approach for selective mesial temporal resection are comparable to other selective AH techniques showing minimal adverse cognitive effects. These data lend support to the ITG approach for selective AH as an option for MTLE.

KEY WORDS: Epilepsy, Neuropsychological outcomes, Inferior temporal gyrus, Amygdalohippocampectomy

Neurosurgery 82:833–841, 2018 DOI:10.1093/neuros/nyx302 www.neurosurgery-online.com

Mesial temporal lobe epilepsy (MTLE) is a common cause of pharmacoresistant epilepsy.[1] The impact on neurocognitive function associated with MTLE has highlighted the need for early detection and treatment.[2-6] Decline in neuropsychological

ABBREVIATIONS: AED, Anti-epileptic drug; **AH,** amygdalohippocampectomy; **ANOVA,** analysis of variance; **ATL,** anterior temporal lobectomy; **CI,** confidence interval; **fMRI,** functional magnetic resonance imaging; **ITG,** inferior temporal gyrus; **MRI,** magnetic resonance imaging; **MTL,** mesial temporal lobe; **MTLE,** mesial temporal lobe epilepsy; **MTS,** mesial temporal sclerosis; **NINDS,** National Institute of Neurological Disorders and Stroke; **PFSIQ,** prorated full scale IQ; **PRI,** perceptual reasoning index; **RAVLT,** Rey Auditory Verbal Learning Test; **RCI,** Reliable Change Index; **SD,** standard deviation; **STROBE,** Strengthening the Reporting of Observational Studies in Epidemiology; **VCI,** verbal comprehension index; **v-EEG,** video-electroencephalography; **WAIS-IV,** Wechsler Adult Intelligence Scale-Fourth edition function among patients with MTLE is associated with cortical volume changes and metabolic changes in brain function.[7] Pharmacoresistant MTLE negatively impacts an individual's social and economic status,[8-10] and patients with adequate control of seizures are at less risk for neurocognitive decline over time and have improved quality of life.[10-13]

Temporal lobe surgery has been established as an effective treatment.[14,15] The traditional anterior temporal lobectomy (ATL) encompasses an anatomic en bloc resection of the anterior temporal lobe and mesial structures. This approach is associated with neurocognitive risks especially in dominant temporal lobe surgery.[2-6,16-19] Alternative techniques such as the selective amygdalohippocampectomy (AH) have been proposed to reduce postsurgical neuropsychological deficits.[20-26] Several approaches have been described, including the middle temporal gyrus,[27] transsylvian,[28] subtemporal,[29,30] and more recently, inferior temporal gyrus (ITG) approach.[31,32]

Patients with dominant hemisphere clinical semiology are at higher risk of having deficits in memory and language functions.[18,19,25,26,33,34] Selective anterior temporal surgical procedures can reduce postsurgical verbal memory loss in comparison to anatomic ATL.[20-26] Each surgical technique has its own benefits and disadvantages. The transcortical technique may result in transection of functional white matter tracts. Risks of the transsylvian approach include injury to the anterior circulation vasculature and transection of the temporal stem.[28] The subtemporal approach avoids resection of functional lateral neocortex but the small surgical corridor may cause retraction injury to surrounding cortex and vein of Labbe.[29,30] Comparison of the neuropsychological and seizure outcomes for selective procedures to ATL generally shows similar seizure freedom rates with variable and conflicting neuropsychological comorbidities.[21-26] Neuropsychology outcomes are difficult to compare across studies due to differences in test measures used, extent of surgical resections, limited sample sizes, duration of follow-up, and differences in concurrent neuropathology included in samples. The ITG approach was developed to minimize cortical resection and avoid retraction injury. However, neuropsychological outcome for AH using an ITG approach in patients with MTLE has not been reported. This study reports neuropsychological outcomes in a fairly homogenous patient group undergoing ITG approach for MTLE.

METHODS

Patient Characteristics and Study Design

This work represents a prospective study of patients having selective ITG approach for AH to treat unilateral MTLE between April 2010 and September 2015 obtained from a prospective database after approval form the Institutional Review Board. All patients provided informed consent. All patients with confirmed epilepsy due to other causes such as tumors, vascular lesions, or congenital abnormalities were excluded (n = 20). Surgical candidacy was based on a standard presurgical evaluation including: (1) history/physical to include seizure semiology; (2) prolonged video-electroencephalography (v-EEG) that demonstrated unilateral ictal onset; (3) a high-resolution 3 T magnetic resonance imaging (MRI) study with thin cuts through temporal lobes; (4) Wada test or functional MRI (fMRI) to assess language dominance/lateralized memory deficits; (5) a neuropsychology study; and (6) an Engel class I/II outcome. Patients with poor seizure outcome (Engel class III/IV outcome) were excluded from further analyses as the primary aim was to investigate neuropsychology outcome for patients with seizure freedom or clinically meaningful reduction of seizures (Engel class I/II) after ITG approach for AH. Poor seizure freedom outcome is recognized to adversely affect neuropsychological outcome,[25,35] likely due to adverse impact of the epilepsy.

A total of 54 participants were identified. Inclusion criteria were completing all pre- and postsurgical evaluation steps, and postsurgical neuroimaging confirming satisfactory resection of mesial temporal lobe (MTL) structures. Seizure localization and lateralization was determined by v-EEG. Surface v-EEG LTM (International 10-20 system) was conducted using XLTEK (Oakville, Ontario, Canada). Bilateral basilar-temporal placements such as T1/T2 electrodes were used. Sphenoidal electrodes were not used. v-EEG indicated 28 patients had left MTLE and 26 had right MTLE. Wada testing was performed on all left-sided and frequently for right MTLE. A recognition memory asymmetry of $>$three-eighths was considered lateralized for memory.[36] The procedure was performed according to the protocol of Loring et al,[37] with a methohexital adaptation. Language lateralization and recognition memory score for each hemisphere were recorded.

Surgical Description

Details of the technique have been described.[31] Utilizing a linear skin incision and a small craniotomy flush with the middle fossa floor,[38] access is gained to the MTL by minimal resection of the ITG (access corridor). Subpial dissection is guided by intraoperative anatomic landmarks to allow identification of the collateral sulcus and access to the temporal horn. The mesial structures are identified and resected. The hippocampus was sent to pathology for histological analysis in all cases.

Pathology and Seizure Outcome

Outcome was defined according to a modified Engel classification:[16] class I, seizure-free with/without residual auras; class II, rare disabling seizures ($>$90% seizure reduction); class III, $<$90% seizure reduction; and class IV, no worthwhile improvement. Surgical failures were defined as Engel class III and IV. Because poor seizure control after surgery and the adverse effect pharmacoresistent TLE has been associated with progressive neuropsychology decline,[25,35] patients with class III/IV outcomes were excluded from this study. Surgical specimens from the hippocampus were graded according to the degree and localization of neuronal loss and gliosis using Blumcke's criteria.[39] Histology was completed by a board-certified pathologist as mesial temporal sclerosis (MTS) compared to negative/nonspecific pathology.

Neuropsychological Study

The neuropsychological study incorporated NINDS (National Institute of Neurological Disorders and Stroke) common data elements and included measures of intelligence, attention/executive, memory, language, visuospatial, and mood functions.[40] All scores with the exception of the Wechsler Adult Intelligence Scale-Fourth edition[41] (WAIS-IV) prorated full-scale IQ (PFSIQ) were raw scores. Prorated index scores were obtained from the WAIS-IV manual and include

TABLE 1. Neuropsychological Domain and Testing Method

Domain	Assessment
General intelligence	Wechsler Adult Intelligence Scale—fourth Edition (WAIS-IV)[41] prorated full-scale IQ (PFSIQ)
	WAIS-IV[41] verbal comprehension index (VCI)
	WAIS-IV[41] perceptual reasoning index (PRI)
Verbal fluency	Controlled Oral Word Association Test (COWAT) letter (FAS)[43]
	COWAT semantic fluency (animals)[43]
Confrontation naming	Boston Naming Test (BNT)[44]
Visuospatial functioning	Rey–Osterrieth Complex Figure Test[45,46]
Verbal memory	Wechsler Memory Scale-fourth edition (WMS-IV)47 logical memory tests
	Rey Auditory Verbal Learning Test (RAVLT)[48] trials 1–5, short-delay recall, long-delay recall
Visual memory	ROCFT[45,46] 30-min delay
	WMS-IV[47] visual reproduction tests
Mood	Beck Depression Inventory-II (BDI-II)[49]

8 core subtests.[41] Raw scores are reported to both adhere to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement publication guidelines to more accurately evaluate change scores and avoid problems in generalization of these data to other studies due to idiosyncratic differences in the normative data from which standardized scores can be derived.[42] WAIS-IV PFSIQ, verbal comprehension index (VCI), and perceptual reasoning index (PRI) index scores (mean = 100, standard deviation [SD] = 15) were derived from the test manual (see Table 1). All neuropsychological studies were completed by a board-certified neuropsychologist who was blinded to the patient allotment for the study. Neuropsychological study results were determined prior to epilepsy case conferences with the integrated healthcare team.

Statistical Analysis

Statistical analyses were performed with Statistical Package for Social Science (SPSS) version 23 (SPSS Inc, IBM, Armonk, New York). Chi-square and analysis of variance (ANOVA) were used for demographic variables. Repeated measures ANOVA were used to compare pre- and postoperative neuropsychological functioning at the group level. Statistical analysis compared neuropsychological outcome based on several disease variables, including language-dominant resection, and presence of MTS. An alpha level was set at $P < .05$ for all comparisons.

Individual level analyses of neuropsychological outcome based on Reliable Change Index (RCI) scores were calculated using the Jacobson and Truax formula[50] corrected for practice effect.[51] RCI scores are standardized scores that correct the simple difference between pre- and postoperative scores for the standard error of the difference and the pooled practice effect of a test.[51,52] Although diagnostically relevant, RCI scores are not independently indicative of clinically meaningful change. Determination of reliable change cutoff values was established by published criterion derived for patients with medication-refractory epilepsy.[51,53] Adhering to common neuropsychology practice, reliable change is inferred for any individual that obtains a pre/postsurgery difference score that meets or exceeds established RCI 90% confidence interval (CI) score for each test/measure.[51,53] Scores that exceed a 90% CI indicate that the change in test in pre/postoperative test scores is reliable and not due to measurement error. For the Boston Naming Test, the 90% RCI cutoff was ±5 raw points.[51] For the Rey Auditory Verbal Learning Test (RAVLT) trial 6 short-delay and trial 7 long-delay recall, the 90% CI cutoff is –7 points or +5 and –7 and +6 points, respectively.[50] The Rey–Osterrieth Complex Figure Test 90% CI with practice was –7 or +10 points.[53]

RESULTS

There were 63 patients in total that presented with unilateral ictal semiology that met the inclusion criteria. Fifty-four patients underwent pre- and postoperative neuropsychology evaluation. Nine patients did not undergo postoperative psychology evaluation due to financial limitations, insurance denial, or personal reasons. No patients were lost to follow-up. There were no significant differences between the dominant vs nondominant surgery groups in age, education, ethnicity, gender, or handedness. Seizure disease variables did not differ between groups. There were was no significant differences between groups at pre- or postoperative visits in the Anti-epileptic drug (AED) burden. Postoperative follow-up neurocognitive evaluations were conducted at approximately 18 mo postsurgery (mean = 17.67, SD = 12.6) with a range of 5 to 59 mo. There were no differences between the mean postoperative time to follow-up for the nondominant surgery (mean = 16.6, SD = 11.7 mo) compared to the language-dominant resection group (mean = 18.5, SD = 13.4 mo; $P >$ .05). Patient demographics are provided in Table 2.

Clinical semiology and v-EEG indicated that 28 (52%) patients had left MTLE and 26 (48%) patients had right MTLE. Dominant hemisphere for language was based on Wada testing on 49 patients and fMRI for speech mapping in 5 patients (all right-handed patients with right-sided ictal semiology). Dominant hemisphere resections were performed on 23 (43%) patients (all left-sided surgery), while nondominant hemisphere surgery was done on 31 (57%). Five patients had left-sided surgery but were right hemisphere dominant for language.

Language-Dominant vs Language-Nondominant Resection

ANOVA found that patients having a language-dominant AH significantly declined in verbal memory (RAVLT immediate delay

TABLE 2. Postoperative Demographics by Seizure Group

Demographic	Nondominant AH (n = 31)	Dominant AH (n = 23)	F/X^2	*P*
Age	35.0 (11.6)	36.7 (11.3)	.298	.587
Education (years)	13.6 (2.6)	13.9 (2.4)	.001	.981
Gender			1.305	.284
Female	17 (54.8%)	9 (39.1%)		
Male	14 (45.2%)	14 (6.9%)		
Ethnicity			1.729	.631
Caucasian	23 (74.2%)	20 (87.0%)		
African American	4 (12.9%)	2 (8.7%)		
Hispanic	3 (9.7%)	1 (4.3%)		
Other	1 (3.2%)	0 (.0%)		
Dexterity			1.521	.294
Left	4 (12.9%)	6 (26.1%)		
Right	27 (87.1%)	17 (73.9%)		
Employment			8.969	.255
Semiskilled	2 (6.5%)	5 (21.7%)		
Unemployed	7 (22.6%)	3 (8.7%)		
Student	5 (16.1%)	4 (17.4%)		
Technical	2 (6.5%)	0 (.0%)		
Professional	8 (25.8%)	5 (21.7%)		
Disabled	5 (16.1%)	6 (26.1%)		
Part-time	0 (.0%)	1 (4.3%)		
Unskilled	2 (6.5%)	0 (.0%)		
Age at first seizure	16.5 (12.5)	17.1 (13.4)	.032	.859
Years since first seizure	17.8 (12.9)	19.7 (15.4)	.240	.626
Febrile seizures	9 (29.0)	3 (13.0)	1.593	.200
Number of AEDs (preop)	2.10 (.8)	2.50 (.9)	3.862	.055
Number of AEDs (postop)	1.87 (1.1)	1.83 (1.1)	.021	.886
Follow-up time			.192	.664
Mean (SD)	16.6 (11.7)	18.5 (13.4)		
Median	12.7	12.4		
Range	42.7	41.4		

SD = standard deviation.
Note: means (SD) or frequencies (%) are reported for each variable.

[*P* = .049] and RAVLT 30-min delay [*P* = .016]) scores that were of medium effect size (see Table 3). Alternatively, patients having a language-dominant AH had a significant improvement in prorated nonverbal reasoning scores (*P* = .047). Patients having a nondominant language AH resection did not exhibit significant declines in neuropsychological outcome measures and effect size differences were small (all *P* > .05). Subanalyses based on language-dominant resection and MTS status simultaneously (see Table 4) found the language-dominant resection group with no-MTS exhibited significant decline in verbal memory, while no significant decline occurred in the language dominant with MTS resection group.

MTS Pathology

Of the 54 participants, 25 did not have MTS while 29 had pathology-confirmed MTS (see Table 5). Two patients with normal preoperative MRI were diagnosed with pathology-proven MTS and classified within the latter group. ANOVA found that MTS resection group patients exhibited a significant improvement in semantic (animal) fluency (*P* = .034) and a trend improvement in prorated indices of nonverbal intellectual function (WAIS-IV PRI) scores (*P* = .058) that were of small to medium effect size. Patients with no-MTS significantly declined in verbal immediate memory (RAVLT immediate delay; *P* = .023) as a group; however, subanalyses found that the verbal memory decline of the group was due to significant decline by the group with no-MTS and having a dominant language resection (n = 8; RAVLT immediate delay [*P* = .002] and RAVLT delayed recall [*P* < .001]; see Table 4). This subgroup also exhibited a trend decline in visual memory (RCFT 30-min delayed recall [*P* = .83]). Other subgroup analyses of the MTS groups based on language dominance did not exhibit significant decline in postoperative neuropsychological outcomes.

Reliable Change Analyses for Intraindividual Analyses

Table 6 summarizes the proportion of participants in each group exceeding the 90% CI RCI score for a reliable change in neuropsychological score following surgery. The majority of

TABLE 3. Pre- and Postoperative Neuropsychological Results Comparing Dominant Resection to Nondominant Resection

	Dominant (n = 23)			Nondominant (n = 31)		
Test	**Preoperative**	**Postoperative**	**Effect size (d)**	**Preoperative**	**Postoperative**	**Effect size (d)**
Language						
BNT total (raw score)	43.2 (1.9)	43.5 (12.3)	.03	49.4 (8.2)	5.8 (7.1)	.18
FAS total (raw score)	32.0 (1.9)	34.4 (11.9)	.21	34.9 (11.1)	34.1 (11.0)	−.07
Semantic/animal (raw score)	16.7 (5.2)	17.9 (6.1)	.21	18.0 (5.3)	17.9 (5.6)	−.02
Memory						
RAVLT (raw score)						
Imm. delay	7.7 (3.2)	5.7 (3.6)*	−.59	9.0 (3.6)	9.0 (4.1)	0
Delayed recall	6.3 (4.1)	3.6 (3.8)*	−.68	8.3 (4.0)	8.3 (4.6)	0
WMS-IV (raw score)						
Logical memory I	22.0 (9.3)	19.5 (6.2)	−.32	23.1 (6.6)	23.7 (7.3)	.09
Logical memory II	16.8 (7.8)	14.7 (7.0)	−.28	18.2 (7.5)	19.1 (8.9)	.11
Visual reproduction I	3.5 (7.8)	33.7 (6.2)	.45	32.0 (5.3)	3.0 (9.0)	−.27
Visual reproduction II	2.3 (1.9)	18.7 (9.7)	−.16	16.3 (9.0)	17.1 (1.0)	.08
RCFT 30-min delay (raw score)	11.8 (5.8)	11.3 (4.8)	−.09	12.9 (5.7)	11.1 (6.1)	−.31
General cognitive/IQ						
WAIS-IV prorated FSIQ	87.8 (13.7)	9.9 (13.0)	.23	94.4 (11.2)	91.4 (14.1)	−.24
WAIS-IV prorated VCI	87.8 (13.7)	86.4 (13.1)	−.11	91.0 (13.0)	9.0 (14.3)	−.07
WAIS-IV prorated PRI	89.1 (13.9)	94.9 (14.7)*	.43	9.7 (11.5)	91.7 (11.5)	.09
Affect/mood						
BDI (raw score)	14.3 (8.1)	1.0 (9.4)	−.49	13.0 (12.3)	12.8 (1.6)	−.02

*$P < .05$.
Note: mean and standard deviation (SD) are provided for each variable.

TABLE 4. Average Raw Score Difference From Pre- to Postoperative Visit by Subgroup

	Dominant (n = 23)		Nondominant (n = 31)	
Test	**No-MTS**	**MTS**	**No-MTS**	**MTS**
Language				
BNT total (raw score)	.3 (5.7)	−.1 (9.3)	.3 (6.1)	2.4 (4.9)
FAS total (raw score)	2.3 (11.25)	3.5 (9.3)	2.1 (8.1)	−3.0 (8.0)
Semantic/animal (raw score)	−1.0 (8.1)	2.5 (4.8)	−1.3 (4.6)	.7 (3.6)
Memory				
RAVLT (raw score)				
Imm. delay	−4.5 (2.6)*	−.3 (4.2)	−.4 (3.3)	.3 (3.6)
Delayed recall	−5.3 (2.2)*	−.9 (4.6)	.4 (3.2)	−.6 (3.4)
WMS-IV (raw score)				
Logical memory I	−3.7 (7.5)	−.5 (9.7)	2.2 (8.2)	−.2 (6.6)
Logical memory II	−1.7 (7.0)	.0 (8.2)	2.1 (8.5)	.2 (7.0)
Visual reproduction I	.5 (7.2)	5.4 (9.7)	−2.3 (11.4)	−1.3 (5.9)
Visual reproduction II	−3.3 (8.5)	3.4 (9.6)	1.3 (11.2)	.3 (9.7)
ROCFT 30-min delay (raw score)	−3.3 (6.0)	.6 (7.5)	.0 (4.4)	2.0 (5.9)
General cognitive/IQ				
WAIS-IV prorated FSIQ	.4 (12.7)	5.8 (15.9)	2.3 (7.2)	.1 (6.8)
WAIS-IV prorated VCI	−3.1 (9.4)	.6 (14.8)	.4 (6.5)	−2.5 (8.5)
WAIS-IV prorated PRI	3.7 (1.9)	6.8 (13.6)	−.1 (5.2)	4.2 (14.4)
Affect/mood				
BDI (raw score)	−5.7 (9.6)	−2.9 (9.4)	−.2 (8.5)	−.3 (17.5)

*$P < .05$.
Note: mean and standard deviation (SD) raw score differences subtracting postoperative scores from preoperative values for each measure; scores are age-matched IQ standardized scores (mean = 100, SD = 15).

TABLE 5. Pre- and Postoperative Neuropsychological Results Comparing MTS to No-MTS

Test	MTS (n = 29)			No-MTS (n = 25)		
	Preoperative	Postoperative	Cohen's d	Preoperative	Postoperative	Cohen's d
Language						
BNT total (raw score)	42.4 (1.6)	43.9 (11.6)	.13	52.6 (4.2)	52.9 (4.1)	.07
FAS total (raw score)	33.2 (1.7)	32.8 (1.3)	−.04	34.0 (11.5)	36.2 (12.4)	.18
Semantic/animal (raw score)	15.4 (4.1)	17.2 (5.3)*	.38	2.0 (5.5)	18.8 (6.3)	−.20
Memory						
RAVLT (raw score)						
Imm. delay	7.0 (3.2)	6.9 (4.2)	−.03	1.1 (3.0)	8.5 (4.0)*	−.45
Delayed recall	5.6 (3.8)	4.7 (4.3)	−.22	9.6 (3.5)	8.3 (4.9)	−.31
WMS-IV (raw score)						
Logical memory I	21.7 (8.2)	2.5 (6.5)	−.16	23.7 (7.2)	23.5 (7.6)	−.02
Logical memory II	16.1 (7.9)	15.3 (7.4)	−.10	19.4 (6.9)	19.5 (9.0)	.01
Visual reproduction I	29.7 (6.6)	3.9 (7.1)	.18	33.2 (5.6)	32.7 (9.1)	−.07
Visual reproduction II	16.0 (9.6)	16.1 (1.0)	.01	19.9 (1.0)	2.1 (9.2)	.02
ROCFT 30-min delay (raw score)	8.9 (5.6)	1.4 (5.3)	.28	12.9 (5.7)	12.1 (5.7)	−.14
General cognitive/IQ						
WAIS-IV prorated FSIQ	84.0 (13.7)	86.9 (13.5)	.21	94.4 (11.1)	96.6 (11.7)	.19
WAIS-IV prorated VCI	85.5 (14.4)	84.1 (12.5)	−.10	94.3 (1.3)	94.4 (13.4)	.01
WAIS-IV prorated PRI	85.3 (13.6)	9.0 (15.0)	.33	95.9 (8.3)	97.2 (8.4)	.16
Affect/mood						
BDI (raw score)	12.7 (1.5)	11.0 (1.3)	−.16	14.4 (11.1)	12.4 (1.0)	−.19

*$P < .05$.
Note: mean and standard deviation (SD) are provided for each variable.

TABLE 6. Number and Proportion of Patients Exhibiting Reliable Change in Selected Neuropsychological Tests

Test	MTS (n = 29)		No-MTS (n = 25)		Dominant (n = 23)		Nondominant (n = 31)	
	Decrease	Increase	Decrease	Increase	Decrease	Increase	Decrease	Increase
Language								
BNT (−5/+5)	3 (1.3%)	3 (1.3%)	3 (12.0%)	6 (24.0%)	4 (17.4%)	2 (8.7%)	2 (6.4%)	7 (22.6%)
Memory								
RAVLT trial 6 (–7/+ 5)	2 (6.9%)	4 (13.8%)	2 (8%)	2 (8%)	2 (8.7%)	2 (8.7%)	2 (6.4%)	4 (12.9%)
RAVLT trial 7 (–7/+ 6)	3(1.3%)	1 (3.4%)	3 (12%)	1 (4%)	4 (17.4%)	1 (4.3%)	2 (6.5%)	1 (3.2%)
ROCFT 30 Min delay (–7/+ 10)	4 (13.8%)	2 (6.9%)	3 (12.5%)	0 (0%)	5 (21.7%)	1 (4.3%)	2 (6.4%)	1 (3.2%)

MTS = mesial temporal sclerosis; Dominant = language dominant resection group; BNT = Boston Naming Test; RAVLT = Rey Auditory Verbal Learning Test; ROCFT = Rey–Osterrieth Complex Figure Test.
Note: Reliable Change Index points are raw points of the test.

patients did not experience a reliable decline in neuropsychological test scores known to be negatively affected by temporal lobectomy procedures.[18,19,26] Reliable decline in verbal memory was observed in 17% of patients having a language-dominant resection. While visual memory did not significantly change after surgery at a group level, reliable decline in visual memory was observed in 21.7% of patients having a language-dominant resection while 4.3% exhibited a reliable improvement. A greater proportion of patients exhibited a reliable increase in confrontation naming (n = 9) than patients exhibiting a reliable decline (n = 6).

DISCUSSION

This prospective study represents the first published series that evaluated neuropsychology outcomes in a relatively uniform group of patients that underwent an ITG approach for AH to treat medically refractory MTLE. These findings are generally consistent with current understanding of neuropsychology outcomes in language-dominant resections.[18,19,20-26] Patients having a language-dominant resection exhibited a significant decline in verbal memory at a group level when evaluated about 17 mo after surgery. At an individual level, 17% of patients exhibited a reliable decline in verbal memory and 22% of patients exhibited a decline in visual memory following a language-dominant AH. This compares favorably to a previous meta-analysis[19] in which 44% of subjects having a left (language-dominant) resection exhibited a reliable decline in verbal memory based on a weighted average across studies [Min = 22%, Max = 63%]. The observed decline in visual memory (22%) of this study mirrored the weighted pooled average across studies for dominant language resections (21%). Our observation that 17% of patients having a language-dominant resection exhibited a reliable decline in confrontation naming is consistent with existing literature in that selective temporal resections reduce the risk of confrontation naming deficits compared to standard temporal lobectomy approaches.[18,19,24,26,33,34] Our data also supported research that found that patients having a nonlanguage-dominant resection are at less risk for decline in confrontation naming as measured by the Boston Naming Test than are patients undergoing a language-dominant resection.[18,24,26,33,34] Similarly, these data generally support research finding that MTS reduces risk of postoperative neuropsychological change,[18,19,54,55] in which patients without MTS and a language-dominant resection exhibited a decline in verbal and visual memory measures.[56,57] However, the presence of MTS alone did not eliminate postoperative neuropsychological declines from occurring in our sample, which mirrors studies finding that other variables including neuropsychological preoperative function is critical in determining likely postoperative outcome.[18,19,22,23] This study demonstrates that the ITG approach to AH minimizes neuropsychological comorbidities that meet or exceed the neuropsychological outcomes reported for other selective AH surgical approaches more than 1 yr after surgery.[19,20-26] The lower rate of neuropsychological comorbidity following AH reported here may reflect less disruption of extra-hippocampal temporal structures allowed by the ITG approach.

The hypothesis of improved neuropsychological outcomes with tissue-sparing approaches for selective temporal lobe resections coincides with many anatomic publications that demonstrate the functionality of the lateral neocortex of the temporal lobe in language/semantic memory networks.[19,22,23,53] Approaches that preserve the temporal lobe neocortex have led to less consistent postoperative declines in neuropsychological functions.[19,20,26,34,58] Comparison of neuropsychology outcomes among selective MTL approach surgeries is limited,[20-26,57] but has favored transcortical/subtemporal approaches over the transsylvian approach when differences in neuropsychological outcomes are observed,[20,21,58] but not consistently.[22] Interestingly, the transcortical approach demonstrated less phonemic fluency[24] and more verbal recognition memory[22] deficits than patients who underwent a transsylvian approach. Alternatively, another study found that the subtemporal approach negatively affected visual memory[56] and semantic verbal fluency more than a transsylvian approach.[22] Unlike Rhein et al,[22] we did not find a decline in semantic verbal fluency regardless if a patient underwent a dominant or nondominant resection, which likely highlights the value of the ITG approach in minimizing disruption of semantic networks in the anterior and lateral neocortex. The failure to find replicable visual memory deficits is expected since the majority of neuropsychological outcome research has failed to document consistent visual memory deficits following temporal lobe resection regardless of surgical procedure or visual memory tests employed.[19,40] The increase in perceptual reasoning intellectual index we observed postoperatively after a language-dominant resection was not unexpected, given some studies reporting improvements following language-dominant resections.[18]

Seizure freedom rates for the ITG approach[31,59,60] are similar to outcomes reported for other selective-AH and en bloc ATL procedures that have class I evidence in the treatment of pharmacoresistant MTLE.[14,15] The selection of surgical procedure and approach to treat MTLE is guided by epilepsy disease factors, including EEG abnormalities, age of seizure onset, presence of MTS, etc., as well as increasing emphasis to minimize neuropsychological postsurgical deficits.[18,19,20-26] The conflicting findings regarding postoperative neuropsychological outcomes across selective AH reports require additional consideration.[20-26,58] Confounding factors for the observed variability in neuropsychological outcomes reflect a combination of factors, including a wide variety of approaches and techniques to gain access to the MTL structures, variations in the extent of mesial/lateral temporal cortex resected, different neuropsychological tests, and differences in reporting meaningful change in neuropsychological function with repeated assessment.[50-53] The extent of tissue manipulation and resection is not homogenous across techniques or even among a single series. While one might consider that the differential neuropsychological outcomes between techniques may be due to less damage to the anterior temporal neocortex, the reported improvement in visual/figural memory may also be due to differences in neuropsychological measures used and variations in how change in scores was determined.

When considering the technical nuances of surgical approaches, our technique is most comparable to the subtemporal approach, but with several exceptions. The subtemporal approach utilizes a narrow corridor to gain access to the mesial temporal structures. The use of brain retraction, hyperosmolar substances, or cerebrospinal fluid drainage may be necessary in order to complete the surgery safely. In the ITG approach, resection of the inferior-most segment of the ITG provides a compromise between negating the need for aggressive retraction and sparing the lateral neocortical tissue. Another advantage compared to other techniques is preservation of the temporal stem; disruption of these fibers can negatively impact cognition and language.[22-25,58]

Limitations

Several notable limitations to this study warrant discussion, including that it is a single-center study and has a limited sample size. However, all patients underwent a similar work-up and represent a fairly homogenous population. Importantly, this study utilized the neuropsychological measures of the NINDS common data elements[40] and supplements other neuropsychological outcome reports for selective temporal lobe resection procedures. A previously unrecognized psychometric limitation in the analyses of reliable change in neuropsychological function is a floor effect. A number of patients' preoperative neuropsychological test scores were so impaired that it was not possible for these patients to obtain a score that would exceed the 90% CI for the RCI of the test. For example, 17 patients with MTS (9 Dominant; 8 nondominant) had a preoperative verbal memory delayed (RAVLT trial 7) score that was 6 or below, prohibiting these patients from obtaining a score that would exceed the 90% CI for a reliable decline in memory. This floor effect did not adversely affect results of comparison of reliable change in the dominant and nondominant language resection groups, since there was an equal number in each group (n = 11). Unfortunately, the floor psychometric effect is rarely documented in the temporal lobectomy outcome literature,[19] but reflects a limitation in this methodology to document change in cognitive status over time. To account for this limitation, data reporting included both group level analyses as well as intraindividual reliable change metrics. Study strengths include using the NINDS-recommended common data elements for neuropsychological measures as well as a homogenous sample with detailed follow-up data. Our results show neuropsychology outcomes similar to previously reported selective procedures that use a subtemporal approach[22,23,58] with comparable seizure-free outcomes.[31,59-60] Using NINDS common data elements and reporting group/individual neuropsychological outcomes allows these data to compare outcomes of novel surgical techniques to treat pharmacoresistant epilepsy.

CONCLUSION

Cognitive outcome and seizure freedom are the most important criteria of the success of epilepsy surgery. The ITG approach for AH achieves surgical freedom rates comparable to en bloc resections and the current data confirm neuropsychological outcomes that meet or exceed those reported for other selective AH approaches. This approach provides a surgical option to treat refractive MTLE while limiting collateral damage of functional tissue in the temporal lobe.

Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article.

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COMMENTS

The rationale purported for selective resections in the treatment of mesial temporal lobe epilepsy is better neuropsychological outcomes compared to a standard temporal lobe resection, involving removal of more tissue while maintaining equivalent outcomes in terms of seizure freedom. However, there still remains some controversy regarding the validity or degree of validity to this assertion. This manuscript contributes additional documentation regarding the neuropsychological outcomes in a fairly large surgical series using an inferior temporal gyrus approach to the resection of the amygdala and hippocampus for patients with mesial temporal lobe epilepsy. The main findings were consistent declines in verbal and visual memory in patients with language-dominant resections without mesial temporal sclerosis (MTS), and no significant declines in those patients undergoing non-dominant resections or those with MTS and language-dominant resections. These findings are not new, but the findings make a significant contribution to the documentation of neuropsychological outcomes following this particular and commonly used approach to a selective resection.

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This is a very well done and reported investigation examining the neuropsychological outcome of inferior temporal gyrus approach to amygdalohippocampectomy for patients with mesial temporal lobe epilepsy (MTLE). Fifty-four patients were operated including 28 left and 26 right MTLE (23 dominant and 31 non-dominant surgeries). The cognitive battery was comprehensive and well selected. Pre- to postoperative (approximately 18 months) outcomes were assessed using reliable change procedures corrected for practice. Surgical specimens were graded according to Blumcke criteria (25 patients were MTS negative and 29 were MTS positive). Cognitive outcomes were related to side of surgery, dominance, and hippocampal pathology. Nondominant resections were unassociated with cognitive change while dominant resections were associated with verbal memory but not language decline and improvement in nonverbal reasoning. Dominant resections that were MTS negative showed declines in both verbal and visual memory but no decline in language. Analyses of individual patient outcomes were also presented. The paper concludes with a discussion of limitations which is appreciated. Overall, this is a well conducted, thoughtful, and clinically important report.

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