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Effects of dual pathology on cognitive outcome following left anterior temporal lobectomy for treatment of epilepsy

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ABSTRACT

The objective of this retrospective study was to determine if dual pathology [DUAL — focal cortical dysplasia (FCD) and mesial temporal sclerosis (MTS)] in patients with left temporal lobe epilepsy is associated with greater risk for cognitive decline following temporal lobectomy than single pathology (MTS only). Sixty-three adults (M_{age} = 36.5 years, female: 52.4%) who underwent left anterior temporal lobectomy for treatment of epilepsy (MTS = 28; DUAL = 35) completed preoperative and postoperative neuropsychological evaluations. The base rate of dual pathology was 55.5%. Repeated measures ANOVAs yielded significant 2-way interactions (group × time) on most measures of language and memory with generally moderate effect sizes. Specifically, patients with MTS only demonstrated postoperative declines, while those with dual pathology remained unchanged or improved. Results suggest that dual pathology may be associated with better cognitive outcome following epilepsy surgery than MTS alone, possibly reflecting limited functionality of the resected tissue or intrahemispheric reorganization of function in the context of a developmental lesion.

1. Introduction

Anterior temporal lobectomy (ATL) is an effective treatment option to eliminate seizures but confers risk for memory and language declines following dominant-sided resections [1,2]. Factors associated with cognitive risk following ATL include preoperative cognitive ability, neuroimaging findings, age at onset, and duration of epilepsy [3–7]. Pathology of the resected tissue is also important. Mesial temporal sclerosis (MTS) is associated with low risk for postoperative cognitive morbidity. Patients with high hippocampal neuronal densities in the resected tissue demonstrate greater verbal memory declines after dominant ATL than those with clear neuronal loss [8–13]. However, it is unclear whether the presence of dual pathology confers additional cognitive risk following ATL. Focal cortical dysplasia (FCD), a developmental lesion caused by problems in neuronal formation and migration, is also commonly observed in patients with epilepsy and is known to cooccur with MTS in some patients [14–16]. However, only one known study has compared cognitive outcome between patients with MTS and those with MTS + FCD (hereinafter referred to as "dual pathology"). Martin et al. [17] found no difference in postoperative cognitive outcome between these two groups; however, findings were considered preliminary, given their small sample size (i.e., 10 with dual pathology) and reliance on preoperative MRI to define groups.

The current study investigated the role of dual pathology in cognitive outcome following left ATL in patients with intractable temporal lobe epilepsy using histopathological diagnosis. The primary goal of this exploratory investigation was to determine whether dual pathology is associated with greater risk for cognitive decline following ATL than MTS alone.

2. Methods

2.1. Participants

This study involved an Institutional Review Board-approved, retrospective review of previously collected and archived data from patients with medically intractable left temporal lobe epilepsy (TLE) who were evaluated through the Neuropsychology Section at Cleveland Clinic as part of preoperative investigations for potential surgery. Patients were included in the study if they met the following criteria: 1) had a standard anterior left temporal lobe resection that included mesial structures, 2) had MTS identified in the initial surgical pathology report and confirmed by a neuropathologist (RP) via re-review of hippocampal histological sections, 3) completed preoperative and postoperative neuropsychological tests that were judged to be a valid representation of the patient's ability, 4) had no history of prior neurosurgery, 5) had a Full Scale IQ score ≥ 70 as measured by the Wechsler Adult Intelligence

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Scale — Third Edition [WAIS-III [18]], 6) were right-handed or left-hemisphere dominant for language as determined with Wada testing or functional MRI, and 7) did not have MRI evidence of bilateral mesial temporal sclerosis or atypical hippocampal volumetric asymmetry in which the hippocampus ipsilateral to side of surgery was larger than the contralateral hippocampus.

Of 355 adult patients with left temporal lobe epilepsy evaluated through the Neuropsychology Service between February 1997 and October 2011, a total of 63 patients (female: 52.4%; Caucasian: 95.2%, Black: 3.2%, Hispanic: 1.6%) were identified who met all study criteria. Patients ranged in age from 18 to 63 years ($M = 36.5$, $SD = 12.3$) and in education from 10 to 18 years ($M = 13.1$, $SD = 1.8$). The mean age at seizure onset for the group was 14.7 years ($SD = 11.1$), and the mean duration of epilepsy was 21.6 years ($SD = 13.4$). Race was self-designated by patients on a history form with a free response race/ethnicity prompt.

2.2. Standard protocol approvals, registrations, and patient consents

This retrospective study was approved by the Cleveland Clinic Institutional Review Board.

2.3. Surgery

"Standard" temporal lobectomy implies a consistent, reproducible operative procedure from patient to patient. At our institution, dominant temporal lobectomy involves removal of 4.5 cm of anterior neocortical tissue (superior, middle, inferior, and fusiform gyrus), near complete resection of the amygdala (sparing superior nucleus), and 3-cm resection of the hippocampus and parahippocampus. All the patients receive intravenous antibiotics and dexamethasone prior to the start of the procedure. Antiepileptic medications are administered as necessary to maintain therapeutic blood levels. The patients are monitored in intensive care postoperatively for one night and then transitioned to the regular nursing floor. Standard anterior temporal lobectomy was performed in a uniform fashion over the period of time encompassed by this study by the same neurosurgeon (W.B.).

2.4. Pathology

All available histological sections for the 63 study patients were retrieved from surgical pathology files and reviewed. A diagnosis of MTS was confirmed in all cases, marked by neuronal loss and gliosis involving the dentate gyrus and hippocampal subfields CA1–CA4 [19] (see Fig. 1A). In each case, tissues excised from the ipsilateral lateral temporal lobe were also examined for evidence of FCD. Focal cortical dysplasia types were classified according to the Palmini et al. [19] classification (see Figs. 1B and 1C). In 25 cases, all of the tissue excised was reviewed microscopically, and in 38 patients, only representative tissue sections from excised tissues were reviewed (mean = 6.5 slides, range = 4–14 microscopic slides).

2.5. Measures

As part of standard presurgical and postsurgical evaluations, all the patients completed a comprehensive neuropsychological battery that included the following measures: Controlled Oral Word Association Test [COWAT/FAS [20]], semantic verbal fluency [Animals [21]], Boston Naming Test [BNT [22]], and Wechsler Memory Scale — Third Edition [WMS-III [23]]. The following subtests of the WMS-III were examined: Logical Memory (LM) I and II, Verbal Paired Associates (VPA) I and II, and World List (WL) I and II. These commonly used language and verbal memory measures were selected to assess cognitive functions most likely to change following a dominant temporal resection. All measures were administered and scored according to their respective test manuals. Standard scores were used for all measures

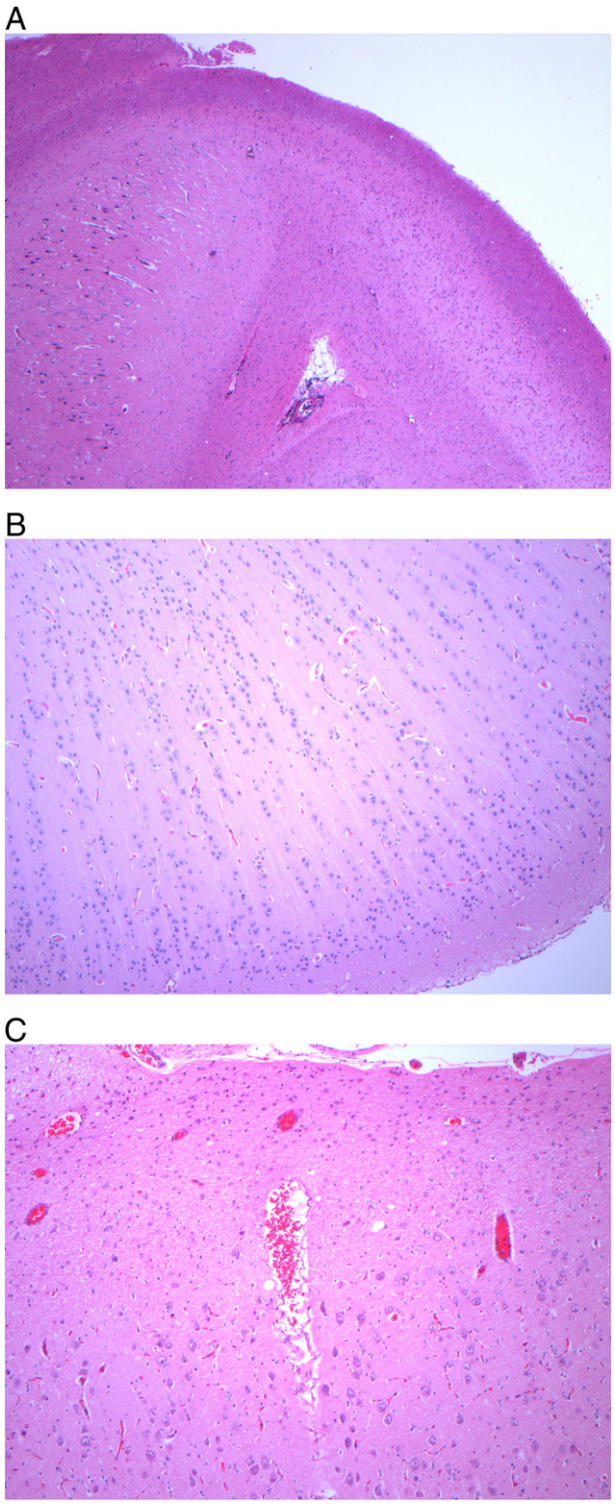

Fig. 1. A. Hippocampal sclerosis marked by discernible loss of neurons in the Sommer sector (CA1) region (right). There is a relative sparing of neurons in the subiculum region (left) (hematoxylin and eosin, original magnification 50×); B. Section from the lateral temporal lobe showing a focal absence of cortical layer two and a prominent vertical linear orientation of neurons, corresponding to a Palmini et al. Type IA focal cortical dysplasia or ILAE Type Ic focal cortical dysplasia (hematoxylin and eosin, original magnification 100×); C. Section from the lateral temporal lobe marked by molecular layer gliosis, an absence of cortical layer two and neuronal cytomegaly in cortical layer 3, corresponding to a Palmini et al. Type IB focal cortical dysplasia or ILAE Type Ib focal cortical dysplasia (hematoxylin and eosin, original magnification 100×).