Epilepsy Research 142 (2018) 29–35

Contents lists available at ScienceDirect

Epilepsy Research

journal homepage: www.elsevier.com/locate/epilepsyres

Corpus callosum atrophy and post-surgical seizures in temporal lobe epilepsy associated with hippocampal sclerosis

Reinaldo Uribe-San-Martín[a,b,*], Ethel Ciampi[a,b], Roberta Di Giacomo[c], Macarena Vásquez[a], Claudia Cárcamo[a], Jaime Godoy[a], Giorgio Lo Russo[d], Laura Tassi[d]

[a] Neurology Department, Pontifical Catholic University of Chile, Santiago, Chile
[b] Neurology Service, "Dr. Sótero del Río" Hospital, Santiago, Chile
[c] Department of Neuroscience, Imaging and Clinical Sciences, "G. ĎAnnunzio" University, Chieti, Italy
[d] "Claudio Munari" Epilepsy Surgery Centre, Niguarda Hospital, Milano, Italy

ARTICLE INFO

Keywords:
Corpus callosum
Epilepsy surgery
Hippocampal sclerosis
Multiple sclerosis

ABSTRACT

Objective: Our aim in this retrospective study was to explore whether corpus callosum atrophy could predict the post-surgical seizure control in patients with temporal lobe epilepsy associated with Hippocampal Sclerosis (HS).
Methods: We used the Corpus Callosum Index (CCI) obtained from best mid-sagittal T2/FLAIR or T1-weighted MRI at two time-points, more than one year apart. CCI has been mainly used in Multiple Sclerosis (MS), but not in epilepsy, so we tested the validity of our results performing a proof of concept cohort, incorporating MS patients with and without epilepsy. Then, we explored this measurement in a well-characterized and long-term cohort of patients with temporal lobe epilepsy associated with HS.
Results: In the proof of concept cohort (MS without epilepsy n:40, and MS with epilepsy, n:15), we found a larger CCI atrophy rate in MS patients with poor epilepsy control vs. MS without epilepsy (p:0.01). Then, in HS patients (n:74), annualized CCI atrophy rate was correlated with the long-term Engel scale (Rho:0.31, p:0.007). In patients with post-surgical seizure recurrence, a larger CCI atrophy rate was found one year before any seizure relapse. Univariate analysis showed an increased risk of seizure recurrence in males, higher pre-surgical seizure frequency, necessity of invasive EEG monitoring, and higher CCI atrophy rate. Two of these variables were independent predictors in the multivariate analysis, male gender (HR:4.87, p:0.002) and CCI atrophy rate (HR:1.21, p:0.001).
Conclusion: We demonstrated that atrophy of the corpus callosum, using the CCI, is related with poor seizure control in two different neurological disorders presenting with epilepsy, which might suggest that corpus callosum atrophy obtained in early post-surgical follow-up, could be a biomarker for predicting recurrences and guiding treatment plans.

1. Introduction

In patients with focal drug-resistant epilepsy, the main therapeutic strategy to achieve seizure control is resective surgery, being the antero-mesial temporal lobectomy one of the most common and associated with the best results in patients with temporal lobe epilepsy (TLE) (Wiebe et al., 2001). Unfortunately, up to half of patients undergoing epilepsy surgery may suffer of a seizure relapse (de Tisi et al., 2011) and currently, few tools are available to early identify patients at risk of seizure recurrence after epilepsy surgery.

Presumed Wallerian degeneration can lead to corpus callosum atrophy in focal and generalized epilepsies (Liu et al., 2011; Weber et al., 2007). In particular, corpus callosum atrophy is associated with refractory epilepsy in TLE patients (Kim et al., 2008; Caligiuri et al., 2016), independently of the presence of hippocampal sclerosis (HS) (Concha et al., 2009). Corpus callosum involvement has also been described in other focal epilepsies, such as frontal lobe epilepsy (O'Dwyer et al., 2010), or with different etiologies (Unterberger et al., 2016), such as cortical developmental malformations (Andrade et al., 2014) or periventricular nodular heterotopias (Pardoe et al., 2015). Although these reports show associations between abnormalities or atrophy of the corpus callosum and worse epilepsy control, it has not been precisely explored how the corpus callosum morphologically changes after performing resective surgery, nor if it is related to post-surgical seizure control.

Many corpus callosum measurements have been studied to establish

* Corresponding author at: Neurology Department, Pontifical Catholic University of Chile, Marcoleta 350, 2° Floor, Neurology Laboratory, Santiago, Chile.
E-mail address: ruribe@med.puc.cl (R. Uribe-San-Martín).

https://doi.org/10.1016/j.eplepsyres.2018.03.001
Received 18 November 2017; Received in revised form 28 February 2018; Accepted 1 March 2018
Available online 03 March 2018
0920-1211/

its changes, including functional and structural evaluations, such as diffusion tensor, fractional anisotropy, mean diffusivity, volume, area and index. The measurement of the corpus callosum index (CCI) stands out because of its simplicity, quickness and feasibility, which has been compared with other more elaborated and time-consuming structural methods and software, with a good intra/inter raters' agreements (Granberg et al., 2015). However, CCI has been mainly studied in Multiple Sclerosis (MS) with no studies in epilepsy patients. This measurement has shown good correlation with clinical outcomes such as cognition performance (processing speed and working memory) and disability scales, suggesting its relevance as a biomarker in MS (Van Schependom et al., 2017).

Our objectives in this article are two: 1) to explore for the first time the measurement of the CCI in patients with epilepsy and 2) to know how the atrophy of the corpus callosum is related to post-surgery seizure control in drug-resistant epilepsy patients. We hypothesized that the atrophy of corpus callosum could predict the seizure control in epilepsy patients. For this, first we tested our expertise in this measure in a proof of concept cohort of MS patients with and without epilepsy, including the longitudinal follow-up of a previous observational study (Uribe-San-Martín et al., 2014). Then, we explored if corpus callosum atrophy has a relationship with the development of seizures recurrence in a well-characterized and long-term cohort of patients with TLE and HS undergoing resective surgery.

2. Material and methods

2.1. MRI imaging and CCI measurements

CCI was applied on best mid-sagittal slices obtained in a 1.5T magnet Scanner. All MRI scans were analyzed by the same examiner (R.U-S-M) and for reliability analysis, all CCI were measured independently by another additional investigator (E.C). Both raters were blind to patient clinical data at assessment and the concordance rate between investigators was 0.91 (Cronbach alpha). For the measurements, the images were oriented by the interhemispheric fissure, the vein of Galen, and the cerebral aqueduct from T2/FLAIR or T1-weighted sequences (in each patient the same sequence was used), performed at two time-points separated by at least one year. CCI was calculated on standard radiological PACS Workstations of OsiriX 5.7.1, summing the anteroposterior length of the genu and the splenium and the cranio-caudal height of the body of corpus callosum, divided by the length of the corpus callosum (Yaldizli et al., 2010; Figueira et al., 2007). The formula for calculating cross-sectional global, regional, and longitudinal annualized CCI atrophy is illustrated in Fig. 1. A positive annualized CCI atrophy rate means atrophy, while a negative value means corpus callosum growth.

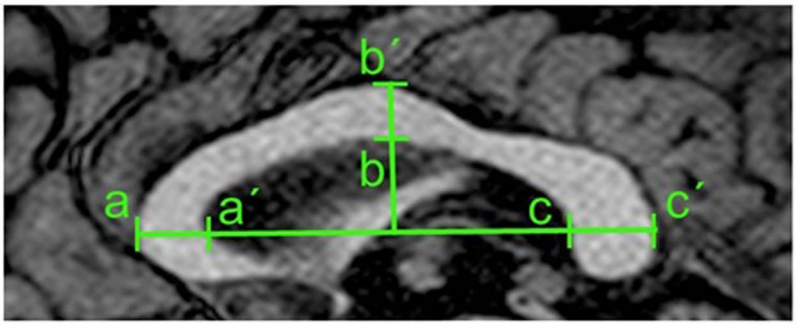
2.2. Proof of concept MS cohort

The CCI is mainly described in patients with MS, and because there are no reports of this measurement in patients with epilepsy, a retrospective sample of MS patients with and without epilepsy obtained from a prospective registry of the Multiple Sclerosis Program of the Pontifical Catholic University of Chile over a 9-year time-period (2008–2017), was selected under strict inclusion criteria to be used as a proof of concept cohort. Database collection for investigational purposes was approved by the local Ethics Committee and informed consent was signed by all patients.

Inclusion criteria considered: patients with Relapsing-Remitting MS diagnosis according to McDonald 2010 criteria (Polman et al., 2011) with or without epilepsy; age between 25 and 55 years-old (in order to exclude periods of corpus callosum growth or atrophy, observed in healthy growing or normal aging); patients under strict clinical care, every three to six months evaluating relapses, Expanded Disability Status Scale (EDSS) (Kurtzke, 1983), treatment compliance and MRI; interval between first and second MRI of at least one year; Neuropsychological assessment was performed using measurements of processing speed with the Symbol Digit Modality Test (SDMT) and working memory with the Paced Auditory Serial Addition Test (PASAT), within three months of the first MRI; and for recognizing the effect of seizures in patients with MS, we retrospectively collected specific data from patients presenting epilepsy from electronic medical notes, including revision of EEG and MRI scans performed during epileptic episodes. Patients with missing data were telephoned for data accrual.

We performed a correlation between CCI and a) Z score in processing speed test with SDMT (Symbol Digit Modality Test); b) Z score in working memory test with PASAT (Paced Auditory Serial Addition Test) and c) score in disability scale using EDSS (Expanded Disability Status Scale). These scales were selected to assess the validity of our results, compared with previous reports (Granberg et al., 2015; Van Schependom et al., 2017; Yaldizli et al., 2010; Figueira et al., 2007).

In addition, we explored the association between annualized atrophy rate of corpus callosum obtained by CCI and seizure control in MS patients with epilepsy. We considered patients with "good epilepsy



Regional CCI	Global CCI	Annualized Regional or Global CCI atrophy (%)
Anterior CCI aCCI: aa´/ac´	CCI: (aa´+ bb´+ cc´) / ac´	[(Regional or Global CCI MRI 1 – MRI 2) / Regional or Global CCI MRI 1] x 100 / Annualized
Middle CCI mCCI: bb´/ac´		
Posterior CCI pCCI: cc´/ac´		

Fig. 1. Corpus Callosum Index (CCI) measurements. CCI is calculated by summing the antero-posterior length of the genu and the splenium and the cranio-caudal height of the body of corpus callosum, divided by the length of the CC. Annualized CCI atrophy rate (%) is calculated:first MRI CCI minus second MRI CCI, and dividing by the first MRI CCI, multiplying for 100, and annualizing using the time between the two MRI.